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Red Flags in Pediatric Head Trauma: A Multicenter Analysis of Predictors of Intracranial Injury

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Background: Pediatric traumatic brain injury (TBI) is a leading cause of childhood mortality. Early identification of variables predicting adverse outcomes may refine clinical decisions. This study aimed to determine the variables associated with poor outcomes in pediatric TBI.
Methods: A retrospective multicenter study was conducted in pediatric patients with TBI admitted at a public and a private reference center in Minas Gerais, Brazil. Nineteen demographic and clinical variables were assessed as predictors of intracranial hemorrhage, skull fracture, and neurosurgical intervention using multivariable logistic regression; mortality was pre-specified but could not be modeled (sparse events) and is reported descriptively.
Results: A total of 3,049 patients were evaluated (58.9% male) from 2019 to 2020. The mean age was 5.6 years (SD 5.3; median 3.6). Falls were the most frequent mechanism of trauma (84%), and cranial tomography was performed in 37.4% of cases. Significant predictors ($p < 0.05$) of intracranial hemorrhage were severe TBI (OR 63.0), periorbital ecchymosis (OR 7.07), and traffic accident (OR 5.05). Skull fracture was associated with retromastoid ecchymosis (OR 22.8), severe TBI (OR 16.3), and post-traumatic seizure (OR 9.05). Severe TBI (OR 50.2), anisocoria (OR 6.44), and abusive head trauma (OR 4.32) were related to neurosurgical intervention. Borderline associations ($0.05 \le p < 0.10$) are hypothesis-generating only.
Conclusions: This large multicenter study reinforces the importance of TBI severity (Glasgow Coma Scale) and abusive head trauma as predictors of poor outcomes. The development of novel algorithms should be encouraged to improve care for pediatric trauma.

Keywords: Brain Injuries, Traumatic; Child; Risk Factors; Tomography, X-Ray Computed.

INTRODUCTION

Traumatic brain injury (TBI) comprises lesions of the skull, brain, and meninges resulting from external mechanical forces [1-4]. In children, it is a relevant public health concern, affecting approximately 3 million children annually worldwide, with a mortality rate of 7% [5-7]. In Brazil, the direct costs of pediatric TBI admissions are estimated at around 30,000 dollars annually [5-9].

Children, particularly during the first two years of life, present morphological and physiological particularities such as lower consistency of brain tissue, greater skull elasticity, and ongoing myelination, axogenesis, and neurogenesis, as well as language development that complicates the application of the Glasgow Coma Scale (GCS) [8,10-17]. These features increase both their susceptibility to brain injury and their vulnerability to radiation-induced malignancy from the ionizing radiation of cranial computed tomography (CT) [18-20]. This concern is particularly relevant for patients presenting with a GCS score of 14–15, that is, mild TBI [6,21].

Clinical decision guidelines such as the Pediatric Emergency Care Applied Research Network (PECARN), CATCH (Canadian Assessment of Tomography for Childhood Head Injury), and CHALICE (Children's Head Injury Algorithm for the Prediction of Important Clinical Events) are generally efficient in identifying children at high risk for TBI-related complications and in justifying the indication of CT in mild TBI [22-25]. Nevertheless, a "grey zone" has been reported for patients with an apparently significant trauma mechanism but no clear clinical signs, in whom the decision to perform CT remains uncertain [22,26-27].

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In this context, identifying the demographic and clinical variables most strongly associated with unfavorable outcomes is valuable both to stratify risk and to support neuroimaging decisions. The aim of this study was to identify, through multivariable logistic regression, the variables most strongly associated with intracranial hemorrhage, skull fracture, neurosurgical intervention, and mortality in a large data set of pediatric TBI.

MATERIALS AND METHODS

Study design and setting

This retrospective multicenter study was reported in accordance with the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines. It was conducted using a database compiled from a public (João XXIII Hospital) and a private (Vila da Serra Hospital/Oncoclínicas) trauma reference center in Minas Gerais, Brazil. The study was approved by the institutional Research Ethics Committee (protocol 4.757.440), which granted a waiver of informed consent given the retrospective analysis of de-identified registry data, in accordance with institutional and national regulations.

Eligibility criteria and variables

Individuals younger than 19 years (i.e., up to 18 years of age, consistent with the institutional definition of the pediatric population, and with the modeled variable "age > 10 years") with a diagnosis of TBI registered in the database were included from January 2019 to December 2020. Nineteen predictor variables were analyzed in dichotomous form: age < 2 years; age > 10 years; moderate TBI (GCS 9–13); severe TBI (GCS ≤ 8); traffic accident; assault; fall; loss of consciousness; abusive head trauma; headache; vomiting; seizure; periorbital ecchymosis ("raccoon eyes"); retromastoid ecchymosis (Battle sign); rhinorrhea (cerebrospinal leak); anisocoria; post-traumatic amnesia; hemiparesis; and strabismus. The 19 candidate predictors were selected a priori on the basis of clinical relevance and prior literature. Four outcomes with major clinical impact were assessed in pediatric patients who underwent head trauma: intracranial hemorrhage, skull fracture, neurosurgical intervention, and mortality. Any type of intracranial hemorrhage (epidural, subdural, subarachnoid, intraparenchymal, or intraventricular) was included in this dichotomous variable.

Outcomes were ascertained from the electronic medical records and imaging reports. Intracranial hemorrhage and skull fracture were defined by the official radiology report of the cranial CT; neurosurgical intervention was defined as any cranial operative procedure related to the trauma; and abusive head trauma was classified according to the multidisciplinary child-protection assessment recorded in the chart. Cranial CT was performed at the discretion of the attending team following institutional protocols and clinical decision rules; consequently, the imaging-defined outcomes (intracranial hemorrhage and skull fracture) could be ascertained only among the 37.4% of patients who underwent CT, and patients without CT were assumed not to present these outcomes. This indication/ascertainment bias is acknowledged as a limitation.

Statistical analysis

As all outcomes were dichotomous, multivariable logistic regression was used to estimate the probability of each outcome, expressed as odds ratios (OR) with 95% confidence intervals (CIs) and a significance threshold of 0.05. Two strategies were applied: the ENTER method, in which all predictors were entered simultaneously to assess their multivariable significance; and the STEPWISE method, which begins with all predictors and progressively removes those with $p > 0.10$. Variables with $p < 0.05$ were interpreted as statistically significant, whereas variables retained with $0.05 \leq p < 0.10$ were kept in the final model for transparency and are interpreted only as hypothesis-generating. Model goodness-of-fit was assessed with the Hosmer–Lemeshow test. The events-per-variable ratio was limited for the least frequent outcomes, particularly neurosurgical intervention (44 events), which should be considered when interpreting the corresponding estimates. Owing to the small number of deaths, no stable logistic model could be fitted for mortality, which is therefore reported descriptively only. Analyses were performed using SPSS v26 and Minitab 21.2.

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RESULTS

A total of 3,049 patients were analyzed, of whom 1,797 (58.9%) were male. The mean age was 5.6 years (SD 5.3; median 3.6), with 953 children (31.3%) younger than 2 years. Concerning the injury mechanism, falls were the most frequent (2,560; 84.0%), followed by traffic accidents (235; 7.7%) and abusive head trauma (60; 2.0%). Most patients had mild TBI (2,942; 96.5%), followed by moderate (55; 1.8%) and severe TBI (52; 1.7%). The most frequent symptoms were vomiting (682; 22.4%), loss of consciousness (480; 15.7%), and post-traumatic seizure (56; 1.9%). Twelve (0.4%) deaths were registered. As this outcome was infrequent relative to the sample size, the logistic regression model did not yield a stable prediction and mortality is reported descriptively only.

CT was performed in 1,141 patients (37.4%) and identified epidural hematoma in 69 (2.3%), acute subdural hematoma in 55 (1.8%), traumatic subarachnoid hemorrhage in 59 (1.9%), intraventricular hemorrhage in 10 (0.3%), and skull fracture in 284 (9.3%). Hospitalization was required in 386 patients (12.7%), with a mean length of stay of 6.8 days (SD 15.49; median 2 days), and 44 patients (1.4%) underwent neurosurgical intervention.

The associations between predictors and outcomes in the final (STEPWISE) logistic models, expressed as odds ratios with their 95% CIs and p-values, are shown in Tables 1 to 3. The ENTER and STEPWISE methods produced concordant directions of association, and the Hosmer–Lemeshow test indicated adequate goodness-of-fit.

Table 1. Final multivariable logistic regression model (STEPWISE) for intracranial hemorrhage.

Predictor	OR	95% CI	p-value
Severe TBI	63.0	28.62–138.70	< 0.001
Moderate TBI	7.71	3.89–15.28	< 0.001
Periorbital ecchymosis	7.07	3.77–13.25	< 0.001
Traffic accident	5.05	2.17–11.78	< 0.001
Post-traumatic seizure	3.44	1.52–7.81	0.003
Fall	2.80	1.28–6.13	0.010
Headache	2.58	1.60–4.16	< 0.001
Vomiting	2.13	1.42–3.18	< 0.001
Loss of consciousness	1.85	1.23–2.79	0.003
Age < 2 years	0.58	0.39–0.85	0.005

OR, odds ratio; CI, confidence interval. Age < 2 years showed an inverse (protective) association. ENTER-method estimates were concordant in direction and significance. 95% CI values

Table 2. Final multivariable logistic regression model (STEPWISE) for skull fracture.

Predictor	OR	95% CI	p-value
Retromastoid ecchymosis	22.8	2.16–240.90	0.009
Severe TBI	16.3	7.05–37.81	< 0.001
Post-traumatic seizure	9.05	3.44–23.79	< 0.001
Periorbital ecchymosis	6.84	3.18–14.72	< 0.001
Moderate TBI	6.30	2.25–17.63	< 0.001

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Post-traumatic amnesia	3.76	1.22–11.57	0.021
Abusive head trauma	2.95	0.92–9.43	0.069
Traffic accident	1.96	0.95–4.03	0.067
Age < 2 years	1.82	0.98–3.37	0.056
Vomiting	0.34	0.12–0.95	0.039

OR, odds ratio; CI, confidence interval. Vomiting showed an inverse (protective) association. Variables with 0.05 ≤ p < 0.10 (abusive head trauma, traffic accident, age < 2 years) were retained by the STEPWISE algorithm and are reported for completeness as hypothesis-generating.

Table 3. Final multivariable logistic regression model (STEPWISE) for neurosurgical intervention.

Predictor	OR	95% CI	p-value
Severe TBI	50.2	20.41–123.70	< 0.001
Moderate TBI	14.5	5.20–40.61	< 0.001
Anisocoria	6.44	1.06–39.01	0.043
Abusive head trauma	4.32	1.12–16.71	0.034
Traffic accident	3.89	1.74–8.67	0.001
Rhinorrhea (CSF leak)	26.8	0.67–1071.00	0.080
Post-traumatic amnesia	3.38	0.92–12.40	0.067
Periorbital ecchymosis	2.64	0.99–7.04	0.052
Vomiting	2.10	0.88–5.04	0.096

OR, odds ratio; CI, confidence interval. Variables with 0.05 ≤ p < 0.10 were retained by the STEPWISE algorithm and are reported for completeness as hypothesis-generating. The very wide OR for rhinorrhea (26.8; non-significant) reflects the small number of events and indicates model instability (see Discussion)

DISCUSSION

In this multicenter study, most patients were classified as having mild TBI (96%), a proportion considerably higher than the average of approximately 85% reported in the literature [1,23,28]. This discrepancy may reflect local characteristics of the studied Brazilian population. Moreover, it further underscores the importance of judicious CT indication to avoid unnecessary exposure to radiation.

For moderate and severe TBI, a progressively higher risk of skull fracture, intracranial hemorrhage, and neurosurgical intervention was observed, reinforcing that the application of the GCS is paramount in the assessment of pediatric TBI. All cases of moderate and severe TBI must be evaluated by CT, in contrast to mild TBI, which is less likely to be associated with brain damage, so that fewer patients need to be exposed to an imaging exam [25,29].

In the current study, non-accidental mechanisms of TBI, such as abusive head trauma, were associated with an increased risk of skull fracture and neurosurgical intervention. This highlights the need to recognize this challenging type of pediatric TBI and to involve additional specialties, such as psychology, ophthalmology, and even forensic medicine [8,10-17]. Although the triad of encephalopathy, subdural hemorrhage, and bilateral retinal hemorrhage has a sensitivity of 85% for detecting this type of trauma, algorithms such as the Pittsburgh score, which incorporate head circumference and hemoglobin level,

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may further enhance diagnostic accuracy [30]. Conversely, accidental mechanisms of trauma, especially traffic accidents, were strongly correlated with intracranial hemorrhage and neurosurgical intervention in the current study as well as other series [28,31-32].

Notably, among focal clinical signs, periorbital and retromastoid ecchymosis showed a high predictive risk of adverse outcomes. Retromastoid ecchymosis was the strongest predictor of skull fracture (OR 22.8), whereas periorbital ecchymosis was independently associated with both intracranial hemorrhage and skull fracture. These findings reinforce that the physical examination provides valuable information about the severity of the trauma mechanism and should be considered when indicating CT, even in mild TBI. Of note, these signs are not formally included in the main clinical decision rules such as PECARN, CATCH, and CHALICE. Post-traumatic seizure was also strongly associated with skull fracture and hemorrhage and should be considered in patient care, given both the potential of seizures to cause brain injury and the need for pediatric neurology follow-up. In addition, anisocoria was strongly correlated with the need for neurosurgical intervention, as it is a classic sign of mass effect from intracranial injury and transtentorial brain herniation [1].

Interestingly, age younger than 2 years showed an inverse association with intracranial hemorrhage, and vomiting an inverse association with skull fracture. These counterintuitive findings may reflect the dichotomization of variables, indication bias regarding who underwent CT, and the predominance of mild TBI in the cohort, rather than a true protective effect. The borderline variables retained by the STEPWISE algorithm ($0.05 \leq p < 0.10$) should be regarded as hypothesis-generating only. In particular, the very wide and clinically implausible OR for rhinorrhea in the neurosurgical-intervention model (26.8; $p = 0.080$) most likely reflects the small number of events for this predictor and consequent model instability, and should be interpreted with caution.

The proper analysis of the variables related to pediatric head trauma in a Brazilian population allows us to estimate the independent contribution of each variable, and its results are complementary to clinical decision rules such as PECARN, CATCH, and CHALICE [22]. Furthermore, alternative approaches using artificial intelligence techniques, such as deep learning, hold promise for creating more accurate and adaptable algorithms [26,33-38]. In addition, incorporating biomarkers into these data to create a multimodal algorithm could help address the decision “grey zone” of mild TBI [4,39-40].

This study has limitations. Its retrospective design and reliance on registered data expose it to information and indication bias; in particular, because cranial CT was performed in only 37.4% of patients at the discretion of the attending team, the imaging-defined outcomes are conditional on having undergone CT, which may underestimate their true frequency. The events-per-variable ratio was limited for the least frequent outcomes, especially neurosurgical intervention, reducing the precision of some estimates. In addition, the mortality model could not be estimated reliably owing to the small number of deaths, which would require a substantially larger data set.

CONCLUSION

In this large multicenter cohort of children with TBI, the variables most strongly associated with adverse outcomes were TBI severity (as classified by the GCS), abusive head trauma, traffic accidents, post-traumatic seizure, and periorbital and retromastoid ecchymosis. Expanding this data set and developing multimodal algorithms could help overcome the limitations of essentially clinical decision guidelines.

DISCLOSURES

Ethical approval

This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the local Ethics Committee xxxx, number: xxxxx

Consent to participate

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The patients gave consent to use their information and images for research purposes. *Consent for publication*

The patient gave consent to use his information and images for publication.

Conflict of interest

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper

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Artificial intelligence

The authors affirm that no artificial intelligence tools were used in the writing, editing, or content generation of this manuscript.

CONTRIBUTIONS

Leopoldo Mandic Ferreira Furtado: Conceptualization, Investigation, Methodology, Formal analysis, Writing – original draft.
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