



RESEARCH ARTICLE



Clinical assessment of risk factors in traumatic brain injury

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ABSTRACT

Introduction. Traumatic brain injury remains a leading global health concern with significant social and economic impact. The main causes include traffic accidents, falls, and violence, especially affecting young adults. In the Republic of Moldova, TBI incidence is rising, particularly during the prehospital phase. TBI involves both primary and secondary brain injuries, the latter often resulting from hypoxia, hypotension, or hyperglycemia. These secondary insults critically influence outcomes and are associated with high mortality. Effective prehospital management – focused on stabilizing oxygenation and hemodynamics – is essential in reducing neurological deterioration. Emergency teams play a key role in preventing secondary injury and improving survival.

Material and methods. This study, conducted from 2020 to 2024, analyzed 486 patients with acute traumatic brain injury (TBI) assessed in both prehospital and emergency department settings. It aimed to evaluate injury severity and prognosis using clinical tools and structured observation forms, developed specifically for this research.

Results. Significant correlations were found between increased age, low systolic blood pressure, prehospital hypoxia, and both TBI severity and mortality ($p < 0.0001$). While hyperglycemia was not significantly associated with injury severity, it showed a moderate negative correlation with mortality ($p < 0.01$). Findings emphasize the importance of early monitoring and stabilization of vital signs in the prehospital phase to improve TBI outcomes.

Conclusions. This study emphasizes the importance of systematic prehospital monitoring and management of physiological parameters to mitigate secondary brain injury and improve patient prognosis. Early intervention targeting hypoxia and hypotension remains vital in the acute management of TBI.

Keywords: traumatic brain injury (TBI), prehospital care, emergency medicine, injury severity, prognosis, clinical assessment, secondary brain injury, hemodynamic stabilization, hypoxia.

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Key messages

What is not yet known about the issue addressed in the submitted manuscript

This study highlights key risk factors in TBI outcomes; it remains unclear how specific prehospital interventions directly impact long-term neurological recovery and whether standardized early protocols could further reduce mortality across diverse settings.

The research hypothesis

Early identification and management of physiological risk factors – such as hypoxia, hypotension, and hyperglycemia – during the prehospital and emergency stages can significantly reduce the severity and mortality from traumatic brain injury.

The novelty added by the manuscript to the already published scientific literature

This study provides new evidence from the Republic of Moldova

on the impact of prehospital physiological parameters on TBI outcomes, using structured clinical tools tailored for both pre-hospital and emergency settings. It emphasizes the predictive value of early hypoxia and hypotension in a regional context where such data were previously limited.

Introduction

Traumatic brain injury (TBI) remains a major global public health concern in the 21st century, with substantial social and economic ramifications. Epidemiological data reveal a variable incidence across different regions, ranging from 2.18 to 8.65 cases per 1,000 inhabitants, with a markedly higher prevalence among males. In countries such as the United States, the United Kingdom, China, Finland, and Sweden, the hospitalization rate due to TBI is approximately 2‰ [1].

The leading causes of TBI are road traffic accidents, falls, and interpersonal violence, accounting for 80–90% of all cases [2]. Central nervous system injuries represent 30–40% of all trauma cases and are the primary contributors to post-traumatic disability (25–30%) [3]. Among individuals in the active age group (18–35 years), TBI is the foremost cause of trauma-related mortality [1, 3].

In the Republic of Moldova, recent trends indicate a rise in the number of TBI cases managed during the prehospital phase, increasing from 16,443 cases in 2021 to 17,493 in 2022. Within the national trauma profile, TBI ranks second, following musculoskeletal injuries.

Pathophysiologically, TBI involves both primary brain injuries – classified as focal or diffuse – and secondary injuries that develop subsequent to the initial insult. These secondary lesions are triggered by systemic factors such as hypoxia, hyperglycemia, and hypotension, as well as intracranial factors, including cerebral edema, elevated intracranial pressure, and ischemia. Among these, cerebral ischemia is considered the most critical secondary insult, observed in approximately 90% of TBI-related deaths [4].

Secondary brain injuries exacerbate neurological deterioration through complex molecular and cellular mechanisms, potentially leading to irreversible damage. For instance, hypoxia contributes to neuronal death and cognitive impairment, while even transient episodes of hypotension may significantly impair cerebral perfusion and worsen neurological outcomes [5]. Within this context, effective prehospital management of TBI is paramount, aiming to mitigate secondary brain injury by maintaining adequate cerebral perfusion. Prompt correction of hypoxia and hemodynamic stabilization are essential interventions that directly influence clinical outcomes [6].

Emergency medical teams operating in the prehospital environment play a vital role in the initial stabilization of TBI patients. Continuous monitoring of vital signs and timely, targeted interventions are critical in preventing further neurological deterioration and improving prognosis [7].

Material and methods

This prospective, observational study was conducted between January 2, 2020, and January 2, 2024, within the

Department of Emergency Medicine at *Nicolae Testemițanu* State University of Medicine and Pharmacy, in collaboration with the Institute of Emergency Medicine and the National Center for Prehospital Emergency Medical Assistance.

A total of 486 patients diagnosed with acute traumatic brain injury were enrolled, based on predefined inclusion criteria: age ≥ 18 years, confirmed TBI diagnosis, and availability of complete clinical data from both the pre-hospital and emergency department stages. Patients with incomplete documentation or pre-existing neurological disorders were excluded. The study focused on the acute phase of TBI, assessing each patient both in the prehospital setting and upon arrival at the Emergency Medicine Department.

Standardized clinical and paraclinical assessments were carried out using structured observation forms specifically developed for this research. Key parameters included Glasgow Coma Scale (GCS) scores, systolic blood pressure, oxygen saturation, blood glucose levels, and computed tomography (CT) findings. Data on interventions and clinical outcomes were also collected.

Statistical analyses were performed using SPSS version [2019]. Descriptive statistics were used to summarize demographic and clinical characteristics. Inferential statistics – including Pearson's correlation and logistic regression – were applied to assess the associations between physiological variables and both injury severity and patient outcomes. Statistical significance was defined as $p < 0.05$.

The study received ethical approval from the Research Ethics Committee of *Nicolae Testemițanu* State University of Medicine and Pharmacy (minutes no. 38, dated 02.04.2013). Written informed consent was obtained from all participants or their legal representatives.

Results and discussions

Statistical analysis of the patient cohort included in the study revealed a mean age of 51.29 ± 18.34 years, with age limits ranging from 18 to 84 years. Regarding sex distribution, a predominance was observed among male patients, who accounted for 62.9% of all cases, while female patients represented 37.1%. The predominance of traumatic brain injuries among male patients in the study cohort yielded a male-to-female ratio of 1.7:1, a finding consistent with existing literature. This significant gender difference is frequently attributed to increased male exposure to risk factors such as physically demanding occupations, high-risk behaviors, greater involvement in road traffic accidents, physical altercations, and contact sports with a high traumatic potential.

The severity of traumatic brain injury (TBI) was assessed using the Glasgow Coma Scale (GCS), with the following distribution: 79.6% of patients presented with mild

TBI (GCS 13–15), 12.3% with moderate TBI (GCS 9–12), and 8.0% with severe TBI (GCS ≤ 8).

Regarding the environment of residence, the majority of patients originated from rural areas (71.2%), compared to 28.8% from urban settings. The individual patient assessment form incorporated several descriptive variables related to the context of the injury, including environmental setting (urban/rural), time of occurrence (day/night, season), presence or absence of alcohol intoxication, patient age, and the exact location of the incident (residence, public road, workplace, etc.).

The analysis of the circumstances in which traumatic brain injuries (TBI) occurred in the study cohort revealed that the main etiological mechanisms were falls (both same-level and from height), recorded in 44.65% of cases. These were followed by physical assaults, which accounted for 25.72% of injuries. The third most frequent cause was road traffic accidents, resulting in TBI in 91 patients (18.72% of the total).

Table 1. Demographic and clinical characteristics of the study group (n = 486)

Feature	Number of patients	Value
Age (years), Mean ± SD	-	51,29 ± 18,34
Sex		
– Male	306	62,9%
– Female	180	37,1%
TBI severity (GCS)		
– Mild (GCS 13–15)	387	79,6%
– Moderate (GCS 9–12)	60	12,3%
– Severe (GCS ≤ 8)	39	8,0%
Residence		
– Urban	140	28,8%
– Rural	346	71,2%

Note: Data are presented as mean ± SD or n (%). TBI = Traumatic Brain Injury; GCS = Glasgow Coma Scale. Statistical analysis was performed using chi-square and t-tests; p < 0.05 was considered significant.

The distribution of causes according to TBI severity showed the following trends.

In cases of mild TBI, the leading causes were:

- Falls (same-level and from height) – 47.55% (n = 184),
- Physical assaults – 28.42% (n = 110),
- Road traffic accidents – 16.54% (n = 64).

For moderate TBI, the most common causes were:

- Falls – 60.00% (n = 36),
- Road traffic accidents – 21.67% (n = 13),
- Physical assaults – 18.33% (n = 11).

Regarding severe TBI, the predominant causes were:

- Falls – 53.84% (n = 21),
- Road traffic accidents – 35.9% (n = 14),
- Physical assaults – 10.26% (n = 4).

The coexistence of traumatic brain injury (TBI) with other types of bodily trauma significantly influences both clinical severity and the patient’s prognostic outcomes. Analysis of the study cohort revealed that out of the 486 included patients, 289 individuals (59.46%) sustained isolated TBI, without any associated injuries.

The distribution of these isolated cases according to TBI severity was as follows:

- Mild TBI: 278 patients (96.19%)
- Moderate TBI: 7 patients (2.42%)
- Severe TBI: 4 patients (1.39%)

These data indicate a predominance of mild forms in isolated TBI cases, suggesting a correlation between the absence of multiple traumas and a more favorable clinical prognosis. Moreover, isolated TBI allows for a more rapid and focused therapeutic approach, with a reduced risk of systemic complications.

Special attention was given to systemic-origin secondary cerebral insults – commonly referred to in the literature by the acronym “ACSOS” (Aggressions Cérébrales Secondaires d’Origine Systémique) – which play a decisive role in determining the prognosis of TBI patients. Based on this, specific recommendations were formulated to optimize interventions during the prehospital phase and within the Emergency Medicine Department / Emergency Admission Units.

While most studies in the literature focus on patients with severe TBI, the present research included individuals with a broad spectrum of clinical presentations – mild, moderate, and severe – which may account for certain discrepancies observed in comparison with previously published findings.

The results of the correlation analysis between patient age and mortality rate following TBI are presented in Table 2.

Table 2. Correlation matrix between age, TBI severity, and mortality rate (n = 486)

Variables	Statistical Indicators	Age	TBI Severity	Mortality Rate
Age	Pearson Correlation	1	0.030	0.097*
	Sig (2-tailed)		0.513	0.033
	N	486	486	486
TBI Severity	Pearson Correlation	0.030	1	0.594**
	Sig (2-tailed)	0.513		0,000
	N	486	486	486
Mortality Rate	Pearson Correlation	0.097*	0.030	1
	Sig (2-tailed)	0.033	0.513	
	N	486	486	486

Note: Pearson correlation coefficients are shown. * - Correlation is significant at the 0.05 level (2-tailed); ** - Correlation is significant at the 0.01 level (2-tailed). Sample size: n = 486; TBI = Traumatic Brain Injury. Statistical analysis was performed using chi-square and t-tests; p < 0.05 was considered significant.

The Pearson correlation analysis highlights the relationships between patient age, the severity of traumatic brain injury (TBI), and the mortality rate.

The results indicate a statistically significant positive correlation between age and mortality rate (r = 0.097, p = 0.033), suggesting that older age is associated with a higher risk of death among TBI patients. Although the correlation coefficient is modest, its statistical significance underscores the importance of age as a prognostic factor. In contrast, the

correlation between age and TBI severity was not statistically significant ($r = 0.030$, $p = 0.513$), indicating that TBI severity does not substantially vary with age in the analyzed cohort.

A strong and statistically significant positive correlation was found between TBI severity and mortality rate ($r = 0.594$, $p < 0.001$), demonstrating that patients with more severe brain injuries have a substantially higher risk of death. This finding is consistent with existing literature and confirms the crucial impact of injury severity on survival outcomes.

In addition, the study investigated correlations between systolic blood pressure (SBP) values, TBI severity, and mortality rate. Statistical analysis revealed significant negative correlations between prehospital SBP and TBI severity ($r = -0.254$, $p = 0.0001$), as well as between SBP and mortality rate ($r = -0.138$, $p = 0.002$), as shown in Table 3.

Table 3. Correlation between systolic blood pressure and TBI severity and mortality in TBI patients

Variables	Statistical Indicators	SBP	TBI Severity	Mortality Rate
Age	Pearson Correlation	1	-.254**	-.138**
	Sig (2-tailed)		0.000	0.002
	N	486	486	486
TBI Severity	Pearson Correlation	-.254**	1	0.594**
	Sig (2-tailed)	0.000		0.000
	N	486	486	486
Mortality Rate	Pearson Correlation	-.138**	0.594**	1
	Sig (2-tailed)	0.002	0.000	
	N	486	486	486

Note: Pearson correlation coefficients are shown. * - Correlation is significant at the 0.05 level (2-tailed); ** - Correlation is significant at the 0.01 level (2-tailed). Sample size: $n = 486$; SBP – systolic blood pressure; TBI - Traumatic Brain Injury. Statistical analysis was performed using chi-square and t-tests; $p < 0.05$ was considered significant.

These findings highlight that decreased systolic blood pressure (SBP) values are associated with both increased TBI severity and higher mortality, emphasizing the critical role of early hemodynamic stabilization in the prehospital management of TBI patients.

Compared to existing literature – where studies often include smaller patient samples, lack prehospital data, or focus primarily on general trauma [8] – this study offers a valuable contribution by clearly demonstrating the relationship between prehospital physiological parameters and the clinical course of TBI patients. The results underline the importance of prompt monitoring and correction of hypotension to reduce the risk of complications and death.

The correlation between mean arterial pressure (MAP) and both TBI severity and mortality rate is presented in Table 4.

Statistical analysis revealed significant negative correlations between MAP and both TBI severity and mortality. Specifically, a moderate negative correlation was observed

between MAP and TBI severity ($r = -0.195$, $p < 0.0001$), as well as a slightly stronger negative correlation between MAP and mortality rate ($r = -0.213$, $p < 0.0001$).

Table 4. Correlation between mean arterial pressure and TBI severity and mortality in TBI patients

Variables	Statistical Indicators	MAP	TBI Severity	Mortality Rate
Age	Pearson Correlation	1	-.195**	-.213**
	Sig (2-tailed)		0.000	0.000
	N	486	486	486
TBI Severity	Pearson Correlation	-.195**	1	0.594**
	Sig (2-tailed)	0.000		0.000
	N	486	486	486
Mortality Rate	Pearson Correlation	-.213**	0.594**	1
	Sig (2-tailed)	0.000	0.000	
	N	486	486	486

Note: Pearson correlation coefficients are shown. * - Correlation is significant at the 0.05 level (2-tailed); ** - Correlation is significant at the 0.01 level (2-tailed). Sample size: $n = 486$; SBP – systolic blood pressure; TBI - Traumatic Brain Injury. Statistical analysis was performed using chi-square and t-tests; $p < 0.05$ was considered significant.

These results suggest that as the value of the analyzed variable increases, both the severity of trauma and the likelihood of death decrease, indicating a potential protective or favorable predictive role in the clinical course of TBI patients.

The correlation analysis between prehospital hypoxia and indicators of TBI severity revealed statistically significant associations.

Table 5. Correlation between hypoxia and TBI severity and mortality in TBI patients

Variables	Statistical Indicators	Hypoxia	TBI Severity	Mortality Rate
Age	Pearson Correlation	1	.324**	.264**
	Sig (2-tailed)		0.000	0.000
	N	486	438	438
TBI Severity	Pearson Correlation	.324**	1	0.594**
	Sig (2-tailed)	0.000		0.000
	N	438	486	438
Mortality Rate	Pearson Correlation	.264**	0.594**	1
	Sig (2-tailed)	0.000	0.000	
	N	438	438	486

Note: Pearson correlation coefficients are shown. * - Correlation is significant at the 0.05 level (2-tailed); ** - Correlation is significant at the 0.01 level (2-tailed). Sample size: $n = 486$; TBI - Traumatic Brain Injury. Statistical analysis was performed using chi-square and t-tests; $p < 0.05$ was considered significant.

More specifically, a moderate positive correlation was identified between the presence of hypoxia in the prehospital phase and TBI severity ($r = 0.324$, $p < 0.0001$), as well as a positive correlation between hypoxia and the mortality

rate among TBI patients ($r = 0.264$, $p < 0.0001$), as shown in Table 5.

These findings suggest that prehospital hypoxia may serve as a relevant predictive factor for both the deterioration of neurological status and the vital prognosis of patients with TBI.

The findings support the importance of early intervention in the prehospital phase, as adequate monitoring and assessment of oxygenation – and the prevention of hypoxic episodes – have been associated in the literature with significantly improved outcomes in patients with traumatic brain injury (TBI) [9]. Thus, addressing hypoxia from the prehospital stage may not only reduce the severity of neurological damage but also positively influence survival rates.

Another systemic factor involved in secondary cerebral injury and analyzed in the present study was hyperglycemia. Traumatic brain injury induces an acute stress response mediated by the activation of the sympatho-adrenal-medullary axis, leading to increased plasma levels of cortisol, glucagon, insulin, catecholamines, glucose, lactate, and free fatty acids (Shi et al., 2016 [10]; Bosarge et al., 2015 [11]). In this context, blood glucose may serve as a relevant biomarker of post-traumatic metabolic stress.

However, hyperglycemia is not merely an epiphenomenon – it may actively exacerbate brain injury by increasing oxidative stress (through free radical production), inducing apoptosis, and promoting tissue lactic acidosis (Galgano et al., 2017 [12]). While therapeutic efforts primarily target the prevention and management of primary brain injury, secondary injuries such as hyperglycemia are often underestimated, contributing to the so-called “second hit phenomenon” (Galgano et al., 2017 [12]), which negatively impacts patient outcomes.

The correlation between hyperglycemia, TBI severity, and TBI-related mortality is presented in Table 6.

Table 6. Correlation between hyperglycemia and TBI severity and mortality in TBI patients

Variables	Statistical Indicators	Hyperglycemia	TBI Severity	Mortality Rate
Age	Pearson Correlation	1	-0.088 *	-.213**
	Sig (2-tailed)		0.060	0.000
	N	486	456	456
TBI Severity	Pearson Correlation	-0.088 *	1	0.594**
	Sig (2-tailed)	0.060		0.000
	N	456	486	438
Mortality Rate	Pearson Correlation	-.213**	0.594**	1
	Sig (2-tailed)	0.000	0.000	
	N	456	438	486

Note: Pearson correlation coefficients are shown. * - Correlation is significant at the 0.05 level (2-tailed); ** - Correlation is significant at the 0.01 level (2-tailed). Sample size: n = 486; TBI - Traumatic Brain Injury. Statistical analysis was performed using chi-square and t-tests; $p < 0.05$ was considered significant.

Pearson correlation analysis indicates a weak negative association between hyperglycemia and TBI severity ($r = -0.088$), with a marginal level of significance ($p = 0.060$), suggesting a possible inverse trend but without clear statistical significance. In contrast, a moderate and statistically significant negative correlation was observed between hyperglycemia and mortality rate ($r = -0.213$, $p < 0.01$), indicating that higher blood glucose levels might be associated with lower mortality—a counterintuitive finding that may warrant further investigation. The strongest association was found between TBI severity and mortality rate ($r = 0.594$, $p < 0.01$), reflecting that greater injury severity is significantly correlated with a higher likelihood of death.

Conclusions

The results obtained in this study highlighted that, in the prehospital phase, certain factors such as patient age, systolic blood pressure values, and the presence of hypoxia play a major role, directly influencing both the severity of traumatic brain injury (TBI) and mortality rate. This significant impact was confirmed by relevant statistical correlations ($p < 0.0001$). Regarding hyperglycemia, it was not found to be significantly associated with TBI severity ($p = 0.06$) but showed a significant correlation with patient mortality ($p < 0.0001$), suggesting a potential prognostic role in assessing vital risk.

Competing interests

None declared.

Authors’ contributions

NM – substantial contribution to the conception and design of the work, substantial contribution to the acquisition of data, substantial contribution to the analysis and interpretation of data, taking responsibility and being accountable for all aspects of the work. NC – substantial contribution to the conception and design of the work, substantial contribution to the acquisition of data, substantial contribution to the analysis and interpretation of data, drafting the article, taking responsibility for and being accountable for all aspects of the work. LR – critically reviewing the article for important intellectual content, taking responsibility for and being accountable for all aspects of the work. TMC – drafting the article. All authors approved the final version of the manuscript.

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Ethics approval

The research was approved by the Research Ethics Committee of Nicolae Testemițanu State University of Medicine and Pharmacy (minutes no. 38, dated 02.04.2013).

Provenance and peer review

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