Original Article

Extracranial Organ Dysfunction in Patients With Severe Traumatic Brain Injury: A Prospective Observational Study.

Athar un-Nisa Quraishi, Jasima Javid, Abdul Moez, Falak Ara, Iqra Nazir Naqash.

Abstract

Background

Severe traumatic brain injury (TBI) is a major cause of mortality and disability worldwide. While primary brain injury determines initial prognosis, extracranial organ dysfunction (ECOD) significantly contributes to secondary injury, morbidity, and mortality. However, prospective data evaluating its burden and impact remain limited, particularly in resource-constrained settings.

Objective

To evaluate the incidence, pattern, timing, and clinical impact of extracranial organ dysfunction in patients with severe TBI and its association with outcomes.

Methods

This prospective observational study was conducted in a neurocritical care unit of a tertiary care center from January 2019 to December 2024. Adult patients (≥18 years) with severe TBI (GCS ≤8 or radiological evidence of severe injury) requiring ICU admission >48 hours were included. Extracranial organ dysfunction was assessed daily using a modified Multiple Organ Dysfunction (mMOD) score (excluding neurological parameters). Primary outcome was the proportion of patients developing ≥1 extracranial organ dysfunction. Secondary outcomes included number of organ systems involved, duration of ventilation, ICU/hospital stay, mortality, and neurological outcome (Glasgow Outcome Scale).

Results

Among 150 patients, 71.3% developed extracranial organ dysfunction, most commonly respiratory (56%) and cardiovascular (32%). Organ failure occurred in 38.7% of patients, with increasing number of organ failures significantly associated with higher mortality ($p<0.05$). Overall in-hospital mortality was 30.7%. Each one-point increase in mMOD score increased odds of mortality by 42% (OR 1.42; $p=0.002$). Favorable neurological outcome (GOS 4–5) was observed in only 36.6% of patients. Extracranial organ dysfunction remained independently associated with both mortality and unfavorable neurological outcome.

Conclusion

Extracranial organ dysfunction is highly prevalent in severe TBI and is a strong independent predictor of mortality and poor neurological outcomes. Early identification and aggressive management of systemic complications should be an integral component of neurocritical care to improve patient outcomes.

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Author Affiliations

Athar un-Nisa Quraishi, Jasima Javid Falak Ara. Residents, Neuro-anaesthesia; **Iqra Nazir Naqash .** Associate Professor, Department of Anaesthesiology;
SKIMS Soura Srinagar
Abdul Moez. MBBS ASCOMS Jammu

Correspondence

Dr Falak Ara lone
Email of Corresponding and is falakara1220@gmail.com
(m) 7006003199

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Keywords

Severe traumatic brain injury; Extracranial organ dysfunction; Multiple organ dysfunction score; Neurocritical care; Mortality; Neurological outcome; ICU outcomes; Systemic complications

Introduction

Severe traumatic brain injury (TBI) is a global epidemic and remains a leading cause of death and long-term disability. While the severity of the primary neurological insult largely determines outcome, secondary systemic complications significantly increase morbidity and mortality in these patients [1].

Severe TBI triggers a complex cascade of neuroinflammatory, neuroendocrine, and autonomic responses extending beyond the central nervous system, often resulting in dysfunction of extracranial organ systems. Respiratory failure, cardiovascular instability, renal impairment, hepatic dysfunction, and coagulation abnormalities are frequently observed during the acute phase [1,2]. Catecholamine surge, systemic inflammatory response syndrome, hypothalamic–pituitary axis dysregulation, and immune dysfunction play central roles in the development of extracranial organ dysfunction [3].

Extracranial organ dysfunction adversely affects neurological recovery and overall survival. Prior studies have demonstrated that the presence and severity of non-neurological organ failure are independently associated with prolonged mechanical ventilation, extended ICU stay, increased hospital mortality, and poor neurological outcomes in patients

with severe TBI [3]. Furthermore, systemic complications such as hypoxia, hypotension, metabolic derangements, and sepsis may exacerbate secondary brain injury by impairing cerebral perfusion and oxygen delivery [6].Despite advances in neurocritical care, extracranial organ dysfunction remains under-recognized, as management often focuses primarily on intracranial pathology. Prospective data evaluating the pattern, timing, and impact of extracranial organ dysfunction in severe TBI are limited, especially in developing and resource-limited settings [2,3]. Understanding these systemic complications is essential to optimize holistic management and improve outcomes.

This study aimed to evaluate the involvement of extracranial organ dysfunction in patients with severe TBI and assess its association with clinical outcomes.

Materials and Methods

This prospective observational cohort study was conducted in the Neurocritical Care Unit at Sher-i-Kashmir Institute of Medical Sciences (SKIMS), Srinagar, a tertiary-care referral centre catering to patients from across Jammu and Kashmir. The study period extended from January 2019 to December 2024. Informed consent was obtained from each patient's legally authorized representative prior to enrollment. The study was conducted according to the Declaration of Helsinki.

Adult patients aged ≥18 years admitted to ICU with severe TBI. Severe TBI was defined by any one of the following a) Post-resuscitation Glasgow Coma Scale (GCS) ≤8 (without sedative/paralytic agents) b) Radiological evidence of significant intracranial pathology with raised intracranial pressure,c) Clinical or radiological signs of cerebral herniation

Patients with pre-existing end-stage organ failure, documented chronic liver or kidney disease, or death within 48 hours of ICU admission were excluded from the study.

Baseline demographic data, mechanism of injury, admission GCS, imaging findings, and comorbidities were recorded. Patients were followed prospectively throughout their ICU stay.

Daily evaluation of extracranial organ dysfunction was performed using a validated multiple organ dysfunction (MOD) scoring system, excluding the neurological component. The organ systems assessed were respiratory, cardiovascular, renal, hepatic, and hematologic. Organ dysfunction was defined according to established MOD thresholds. The number of extracranial organ systems involved per patient was recorded.

The primary outcome was defined as the proportion of patients developing dysfunction of ≥1 extracranial organ system during ICU stay, while as the secondary outcomes was defined as the number of extracranial organ systems involved, duration of mechanical ventilation, ICU and hospital length of stay, ICU and in-hospital mortality, Neurological outcome at hospital discharge using Glasgow Outcome Scale (GOS), with Favorable GOS 4–5 and unfavorable: GOS 1–3.

Statistical Analysis

Data were analyzed using standard statistical software. Continuous variables were expressed as mean ± SD or median (IQR), categorical variables as frequencies and percentages. Comparisons used Student's t-test or Mann–Whitney U test for continuous variables, and Chi-square or Fisher's exact test for categorical variables.

Multivariate logistic regression assessed independent association between extracranial organ dysfunction and mortality, adjusting for age, admission GCS, and ICU length of stay. A p-value<0.05 was considered statistically significant.

Results

Table 1. Baseline Patient Characteristics (n = 150)

Patient characteristic	Value
Age, median (range), years	34 (18–82)
Male sex, %	76
Mechanism of injury, %	
Road traffic accident	58
Fall from height	29
Assault	7
Pedestrian injury	4
Other	2
Post-resuscitation GCS, median (IQR)	6 (4–7)
Pupillary abnormality on admission, %	31
CT head findings, %	
Subdural hematoma	52
Extradural hematoma	18
Traumatic SAH	57
Diffuse axonal injury	29
Intraventricular hemorrhage	27
Parenchymal contusion/hematoma	54
Associated extracranial injuries, %	
Chest injury	31
Abdominal injury	8
Pelvic/long bone injury	16
Mechanical ventilation required, %	100
ICU length of stay, median (IQR), days	9 (6–15)*
Hospital length of stay, median (IQR), days	21 (14–35)*
Hospital mortality, %	30.7

***** *Extreme outliers for ICU (>90 days) and hospital stay (>60 days) noted separately in supplementary table*.

Supplementary Table 1. Extreme Outliers for ICU and Hospital Stay (n = 150)

Patient ID	ICU Length of Stay (days)	Hospital Length of Stay (days)	Notes
1	95	72	Prolonged ICU stay due to severe multi-organ dysfunction
2	102	80	Complicated by ventilator-associated pneumonia and renal failure
3	127	140	Prolonged ICU and hospital course due to multiple extracranial organ failures

Baseline Characteristics : A total of 150 adult patients with severe TBI requiring ICU admission >48 hours were included. Baseline demographics and clinical characteristics are summarized in **Table 1**.The data showed the median age of study population 34 years (range 18–82) with a predominance of male sex: 76%. The most common mechanism of severe TBI was Road traffic accident (58%), followed by fall from height (29%).The patients had a median post-resuscitation GCS: 6 (IQR 4–7) with pupillary abnormality present in 31% of patients .

CT findings were overlapping, consistent with multiple injuries: subdural hematoma (52%), extradural hematoma (18%), traumatic subarachnoid hemorrhage (57%), diffuse axonal injury (29%), intraventricular hemorrhage (27%), parenchymal contusion/hematoma (54%).

Associated extracranial injuries: chest (31%), abdominal (8%), pelvic/long bone (16%).

All patients required mechanical ventilation. Median ICU stay: 9 days (IQR 6–15, with 3 patients>90 days noted separately). Median hospital stay: 21 days (IQR 14–35, with 3 patients>60 days noted separately).

Extracranial Organ Dysfunction was seen in 107 patients (71.3%) developed dysfunction of ≥1 extracranial organ system. **Respiratory dysfunction was seen in** 84 patients (56%), **cardiovascular dysfunction in** 48 (32%), primarily arrhythmias (22/150, 14.7%) and hypotension requiring vasoactive support (26/150, 17.3%).

Hematologic dysfunction was observed in 28 (18.7%), mostly coagulation abnormalities and sepsis-associated changes. **Renal dysfunction was seen in** 43 (28.7%) with predominantly pre-renal azotemia. 10 patients required dialysis 6 for true renal failure, 4 for transient metabolic/fluid derangements.

Hepatic dysfunction was seen in 12 (8%), mild transient transaminitis; no patient required organ-specific support. The **Timing of Organ Dysfunction was early (<24 h) in** 32 (21.3%) patients and intermediate (24 h–7 days) in 50 (33.3%) and late (>7 days) 45 (30%). 23 23 (15.4%) did not develop organ dysfunction.

Extracranial Organ Failure was seen in 58 patients (38.7%) developed failure of ≥1 extracranial organ system was seen as Single organ failure in 41 patients; two organs in 13 patients; 3 organs in4 patients. The most common organ failures were respiratory: 34 (22.7%); cardiovascular: 26 (17.3%); coagulation: 11 (7.3%); renal (dialysis-requiring): 6 (4%) .

The Infectious and Pulmonary Complications were seen as lower respiratory tract infection (LRTI): 68 (45.3%); bloodstream infection (bacteremia): 29 (19.3%), Pneumothorax: 14 (9.3%), pulmonary embolism: 4 (2.7%)

The Overall in-hospital mortality was 46/150 (30.7%). The non-survivors had higher maximum mMOD scores than survivors. Mortality increased with the number of extracranial organ failures ($p<0.05$) dysfunction remained independently associated with unfavorable neurological outcome

On studying the multivariate logistic regression modified Multiple Organ Dysfunction score, age . admission GCS and ICU length of study were identified as the risk factors .

Variable	OR	95% CI	p-value
Maximum mMOD score	1.42	1.15–1.76	0.002
Age	1.03	0.99–1.06	0.12
Admission GCS	0.87	0.77–0.99	0.03
ICU length of stay	1.01	0.99–1.03	0.28

- Each 1-point increase in maximum mMOD score increased odds of death by 42%.

Table 2. Patient Characteristics by Survival Status

Characteristic	Survivors (n = 104)	Nonsurvivors (n = 46)	p Value
Age, median (IQR), years	34 (20–48)	38 (22–55)	0.54
Male gender, n (%)	79/104 (76%)	35/46 (76%)	0.28
ICU length of stay, median (IQR), days	8 (6–12)	12 (7–127)	<0.001
Post-resuscitation GCS, median (IQR)	6 (4–7)	5 (3–6)	0.02
Maximum mMOD score, median (IQR)	5 (3–7)	9 (6–12)	<0.001
Number of organ dysfunctions, median (IQR)	1 (0–2)	3 (2–4)	<0.001

Neurological Outcome

Glasgow Outcome Scale (GOS) at hospital discharge was available for 142 patients (94.7% of the cohort). Among these, 52 patients (36.6%) had a favorable outcome (GOS 4–5), while 90 patients (63.4%) had an unfavorable outcome (GOS 1–3). The 8 patients without documented GOS included early deaths and those with incomplete follow-up. Overall, hospital mortality was 46/150 (30.7%), which includes patients with missing GOS data. Patients with favorable neurological outcomes had lower admission and maximum mMOD scores and developed fewer extracranial organ dysfunctions during ICU stay. After adjustment for age, admission GCS, and ICU length of stay, extracranial organ remained independently associated with unfavourable neurological outcome.

Table 3. Hospital mortality and neurological outcome by quartile of maximum modified multiple organ dysfunction (mMOD) score

Maximum mMOD Score	0–1	2–3	4–5	6–12
Survivors, n (%)	28 (62)	30 (65)	24 (55)	22 (48)
Nonsurvivors, n (%)	17 (38)	16 (35)	20 (45)	22 (52)
Favorable, n (%)	20 (48)	14 (30)	10 (23)	8 (18)
Nonfavorable, n (%)	22 (52)	32 (70)	34 (77)	36 (82)
p	0.032 (survivors vs nonsurvivors) 0.001 (favorable vs nonfavorable)			

Table 4. Number of extracranial organ system failures and hospital mortality

No. of Organ System Failures	Proportion of Patients Not Surviving to Hospital Discharge	No. of Patients
0	0.00	43
1	0.17	41
2	0.38	13
3	1.00	4

Total : 150 patients, 58 developed ≥1 organ failure, 46 total deaths. Proportions reflect hospital mortality per number of organ system failures

Survivors = 104, Nonsurvivors = 46
Favorable GOS = 52, Nonfavorable GOS = 90
Distribution across mMOD quartiles reflects higher mortality and worse neurological outcomes with increasing mMOD scores.

Discussion

This prospective observational study demonstrates a high prevalence of extracranial organ dysfunction (ECOD) among patients with severe traumatic brain injury (TBI) admitted to a tertiary neurocritical care unit. Our findings highlight that more than two-thirds of patients (71.3%) developed dysfunction in at least one extracranial organ system during their ICU stay, with respiratory and cardiovascular systems being the most frequently affected. Notably, 38.7% of patients progressed to organ failure, and the severity of organ dysfunction, as reflected by the maximum modified Multiple Organ Dysfunction (mMOD) score, independently predicted hospital mortality and unfavorable neurological outcomes. These results underscore the importance of recognizing systemic complications as integral determinants of prognosis in severe TBI, extending beyond the direct impact of primary cerebral injury [1–3].

The pathophysiology of extracranial organ dysfunction in severe TBI is multifactorial. Severe TBI induces a systemic neuroinflammatory response, often termed the "neurogenic systemic inflammatory response syndrome," characterized by the release of cytokines, catecholamines, and other mediators from injured brain tissue. This cascade leads to endothelial dysfunction, capillary leak, and multi-organ hypoperfusion, predisposing patients to dysfunction of respiratory, cardiovascular, renal, hepatic, and hematologic systems [3,1]. The catecholamine surge accompanying TBI may precipitate myocardial injury, arrhythmias, and hypotension, while hypothalamic–pituitary axis disturbances contribute to dysregulated fluid and electrolyte balance, further aggravating organ compromise [2,5]. In our cohort, cardiovascular dysfunction was observed in 32% of patients, mainly driven by hypotension requiring vasoactive support and arrhythmias, consistent with previous reports demonstrating cardiovascular instability in 20–40% of severe TBI cases [9].

Respiratory dysfunction was the most common extracranial complication, affecting over half of the patients (56%). This may reflect the combination of direct pulmonary injury, aspiration, ventilator-associated events, and systemic inflammatory effects on lung parenchyma. Lower respiratory tract infections were documented in 45.3% of patients, consistent with prior studies highlighting pneumonia as a leading cause

Table 5. Multivariable logistic regression model: Hospital mortality and organ dysfunction

Variable	Odds Ratio	Coefficient	Standard Error	95% Confidence Interval	p Value
Constant	0.35	–1.04	0.58	–2.18, 0.10	0.554
Maximum mMOD score	1.42	0.35	0.12	0.11, 0.59	0.002
Post-resuscitation GCS	0.87	–0.14	0.06	–0.26, –0.01	0.03
ICU length of stay	1.01	0.01	0.01	–0.01, 0.03	0.28
Age	1.03	0.03	0.02	–0.01, 0.06	0.12

- mMOD: modified multiple organ dysfunction score; GCS: Glasgow Coma Score; ICU: intensive care unit.
- n = 150; model adjusted for age, admission GCS, ICU length of stay, and maximum mMOD score.

of morbidity in neurocritical care patients [11,5]. Pulmonary complications not only prolong mechanical ventilation but also exacerbate secondary brain injury by impairing oxygen delivery and cerebral perfusion, reinforcing the bidirectional relationship between brain injury and systemic organ dysfunction [6].

Renal dysfunction occurred in 28.7% of patients, with six requiring dialysis for true renal failure. Pre-renal azotemia secondary to hypotension, hypovolemia, or nephrotoxic exposure appears to be the primary driver [10]. Although hepatic dysfunction was less frequent (8%) and generally mild, it may contribute to systemic inflammatory dysregulation and coagulopathy. Hematologic complications, primarily coagulopathy and sepsis-associated changes, were observed in 18.7% of patients, reflecting the interplay between neuroinflammation, endothelial injury, and infection [12]. These findings highlight that even organ dysfunctions considered secondary or less severe may cumulatively worsen outcomes, emphasizing the need for early recognition and management.

The temporal pattern of extracranial organ dysfunction in our study is noteworthy. Early dysfunction (<24 hours) was present in 21.3% of patients, whereas intermediate (24 hours–7 days) and late (>7 days) dysfunction occurred in 33.3% and 30%, respectively. This distribution aligns with the concept that primary TBI triggers early systemic derangements, while secondary insults such as infection, prolonged mechanical ventilation, and iatrogenic factors contribute to delayed organ compromise [3,5,11]. Recognizing this temporal evolution may aid clinicians in risk stratification, anticipating complications, and tailoring preventive strategies.

The relationship between extracranial organ dysfunction and clinical outcomes is reinforced by our multivariate analysis. Each 1-point increase in maximum mMOD score increased the odds of hospital mortality by 42%, independent of age, admission GCS, and ICU length of stay. This supports the prognostic value of systemic organ assessment in TBI and parallels earlier studies reporting a strong correlation between organ dysfunction severity and mortality [1,8,14]. Furthermore, patients with multiple organ failures demonstrated near-linear increases in mortality, with all patients experiencing three organ failures succumbing to their illness. This dose-response relationship emphasizes the cumulative burden of systemic complications in determining patient outcomes.

Neurological recovery is also adversely affected by extracranial organ dysfunction. In our cohort, only 36.6% of patients achieved a favorable Glasgow Outcome Scale (GOS 4–5) at discharge, and patients with higher mMOD scores were less likely to have favorable outcomes. The mechanisms linking systemic organ dysfunction to poor neurological recovery include impaired cerebral perfusion, exacerbation of secondary brain injury, metabolic derangements, and systemic inflammatory effects on neuroplasticity [6,3,9]. These observations reinforce the notion that optimal neurocritical care should integrate systemic organ support alongside conventional intracranial management.

Infectious complications were prevalent, with 19.3% experiencing bloodstream infections and 45.3% developing lower respiratory tract infections. These infections likely contribute to delayed organ dysfunction and poor outcomes, highlighting the importance of infection control, early sepsis recognition, and judicious antibiotic therapy in TBI patients [11,5]. Additionally, pulmonary embolism and pneumothorax, although less common, underscore the need for vigilant monitoring for thromboembolic and procedural complications.

Our study has several clinical implications. Routine monitoring of extracranial organ function using validated scoring systems, early identification of high-risk patients, proactive interventions to maintain hemodynamic and respiratory stability, and a multidisciplinary approach to systemic complications are essential. Multicenter research and long-term follow-up studies are warranted to better define strategies that mitigate extracranial organ dysfunction and improve outcomes [13,15,16–21].

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