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Evaluation of demographic, clinical characteristics and risk factors in patients with persistent hiccups due to traumatic brain injury: A trauma-ICU based study

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ABSTRACT

Background: Persistent hiccups in neurocritical care patients can lead to negative outcomes, including exhaustion, sleep deprivation, malnutrition, depression, and even death. This study aims to evaluate demographic and clinical characteristics, risk factors, and management in trauma intensive care unit patients.
Materials and Methods: This study investigates persistent hiccups in traumatic brain injury (TBI) patients admitted to the Trauma ICU at Banaras Hindu University, Varanasi, from July 2020 to January 2024. The study involved monitoring and recording hiccups during patients' ICU stays. Exclusion criteria included not participating, having GERD, advanced cancer, spinal cord injury, other CNS pathologies, deranged liver and renal profile, or on drugs causing hiccups, on sedative and neuro-muscular blocking agents.
Results: The study involved 59.8% of patients aged <40 years, with a mean age of 41.75±17.16 years. Most patients were male, with a male-to-female ratio of 1.88:1. Road traffic accidents (RTAs) were present in 60.3% of patients, followed by falls from height (17.5%). 75.7% of patients had severe type TBI, while the remaining had moderate type TBI. Out of 189 patients, 86 (45.5%) died and 103 (54.5%) survived. Age was a significant factor in TBI-related persistent hiccups, with severe TBI significantly associated with female gender and ventilator-associated pneumonia and the need for mechanical ventilation. The type of TBI (moderate or severe) and length of ICU stay were also associated with TBI-related persistent hiccups. A strong relationship was observed between severe TBI patients who fall from height and were not responsive to drugs for hiccups compared to moderate TBI. The length of ICU stay was also associated with TBI-related persistent hiccups, with patients with a length of ICU stay of >14 days having a higher risk of hiccups.
Conclusion: Severe TBI is linked to female gender, ventilator-associated pneumonia, and mechanical ventilation. The type of TBI and length of ICU stay are also linked to persistent hiccups. Patients with severe TBI who fell from height are less responsive to hiccup drugs. Patients with over 14 days of ICU stay have a higher risk of developing persistent hiccups.

1. Introduction

Persistent hiccups are a common occurrence in neurocritical care patients, with an unknown incidence leading to

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unfavorable outcomes and morbidity.[1] Hiccups can have detrimental effects, causing exhaustion, sleep deprivation, malnutrition, dehydration, depression, wound dehiscence, and even death in extreme cases. They can lead to prolonged hospital stays and negatively impact rehabilitation.[1] In mechanically ventilated patients, hiccups can cause respiratory alkalosis, lung damage, and hemodynamic alterations.[1] Brain injury is a known cause of persistent or intractable hiccups.[2] Central nervous system tumors, particularly brain stem tumors, can elicit persistent hiccups which often resolve after surgical resection.[2] Lateral medullary syndrome, a type of stroke affecting the brain stem, can present with persistent hiccups as the main symptom.[3] Patients with neurological disorders require intubation and mechanical ventilation for acute respiratory insufficiency, or they may be unable to protect their airways due to bulbar dysfunction and impaired consciousness.[4] The prevalence of persistent or intractable hiccups in neuro-ICU patients is unknown, and there is a lack of literature on the disease's nature and management. The aim of this study was to evaluate the demographic and clinical characteristics, as well as the risk factors, in patients with persistent hiccups due to traumatic brain injury (TBI) in a trauma intensive care unit (ICU) setting.

2. Materials and Methods

This prospective observational study was designed to perform an epidemiological investigation on persistent hiccups in traumatic brain injury (TBI) patients admitted to the trauma ICU of Trauma Center, Institute of Medical Sciences, Banaras Hindu University, Varanasi from July 2020 to January 2024.This study involved monitoring and recording the occurrence of persistent hiccups in TBI patients throughout their ICU stay. The study was approved by the Ethical Committee of Institute of Medical Sciences, Banaras Hindu University (No. Dean/2020/EC/2031).

All moderate and severe TBI patients with persistent hiccups aged 18-65 years admitted to the ICU were included in the study. The exclusion criteria were: not willing to participate, patients with GERD, advanced cancer, spinal cord injury, other CNS pathologies, deranged liver and renal profile, patients on drugs causing hiccups and patient on sedative and neuro-muscular blocking agents. The sample size for this prospective observational study was calculated based on the estimated prevalence of persistent hiccups in traumatic brain injury (TBI) patients and the desired confidence level and margin of error. Considering the expected incidence of persistent hiccups in TBI patients, a preliminary estimate suggested that at least 100 patients would be needed to achieve adequate statistical power for the analysis.

Patients aged 18-65 years with moderate to severe TBI who met the inclusion criteria were enrolled during their ICU stay. Given the exclusion criteria, it was anticipated that a sufficient number of eligible patients would be admitted to the trauma ICU at the Institute of Medical Sciences, Banaras Hindu University, Varanasi, over the study period from July 2020 to January 2024. The final sample size was determined based on the number of patients who consented to participate in the study and met the inclusion criteria, allowing for robust analysis of the epidemiological factors associated with persistent hiccups in this patient population.

Data extraction includes patient demographic and physical characteristics, mode and type of injury, severity score, operative intervention, seizure prophylaxis (administered or not), Marshall CT score, hiccup characteristics i.e. time of onset of hiccups, need of mechanical ventilator, ventilator-associated pneumonia (VAP), length of ICU stay and response to drug treatment for hiccups.

Once the general condition of the patient is stabilized and the clinical evaluation is completed, biochemical and radiological investigations are carried out depending on the need of the patient.

Statistical analysis was performed using statistical package for the social sciences (SPSS), Version 23.0. IBM Corp., NY). We compiled a cross-tabulation table based on the age (<40 vs >40 years), gender (male vs female), ventilator associated pneumonia (present vs absent), type of injury based on GCS score (moderate vs severe), length of ICU stays (<14 vs >14 days) and response to drug treatment for hiccups (yes vs no) and compared their proportions using the Chi-square and Fisher exact test. A p-value of less than 0.05 was considered was statistically significant at 95% confidence interval.

3. Results

Total 250 patients of traumatic brain injury (TBI) who were experiencing hiccups were enrolled in the period of July 2020 to January 2024, out of which 189 patients experienced persistent hiccups. The majority (59.8%) of patients in our study were <40 years of age, with an overall mean age of 41.75±17.16 years, ranging from 18 to 81 years, and most of them were male (75.7%), with a male-to-female ratio of 1.88:1. Road traffic accidents (RTAs) were present in 60.3% of patients, followed by falls from height (17.5%). On the basis of the GCS score, 75.7% of patients had severe type TBI (GCS 3–8), and the remaining had moderate type TBI (GCS 9–13). We performed operative treatment on 65 (34.4%) patients and non-operative treatment on 124 (65.6%) patients. Out of 189 patients, 86 (45.5%) had died and 103 (54.5%) had survived. The detailed patient characteristics are shown in Table 1.

The age group under 40 years old had a significant association with the male gender (p = 0.025). The age group over 40 years old was significantly associated with a higher BMI (25.0–29.0 kg/m^2), a higher APACHE II score (>15), and greater mortality (p = 0.026, p = 0.030, and p

Table 1: Patient characteristics

Characteristics	Number	Percentage
Age group (years)		
<40	113	59.8
>40	76	40.2
Sex		
Male	143	75.7
Female	76	24.3
BMI (kg/m2)		
<18.5	4	2.1
18.5-24.9	128	67.7
25.0-29.0	57	30.2
Mode of Injury		
Road traffic injury	114	60.3
Fall from height	33	17.5
Assault	17	9.0
Others	25	13.2
Type of TBI		
Moderate (GCS 9-13)	46	24.3
Severe (GCS 3-8)	143	75.7
APACHE		
5-9	10	5.3
10-14	82	43.4
15-19	55	29.1
20-24	23	12.2
25-29	13	6.9
30-34	6	3.2
Marshall CT classification		
II	34	18.0
III	22	11.6
IV	37	19.6
V	60	31.7
VI	36	19.0
Seizure prophylaxis		
Levetiracetam	136	72.0
Phenytoin	53	28.0
Treatment		
Non-operative	124	65.6
Operative	65*	34.4
ICU Stay		
<14	23	12.2
>14	166	87.8
Ventilator associated pneumonia		
Yes	71	37.6
No	118	62.4
Mechanical ventilation		
Yes	175	92.6
No	14	7.4
Responsive to drugs for hiccups		
Yes	123	65.1
No	66	34.9
Mortality		
Non-survived	86	45.5
Survived	103	54.5

* Five individuals had EVD (External Ventricular Drain) procedures

= 0.001), respectively. Rest other risk variables were not significantly associated with age. The association between age and several risk variables for TBI-related persistent hiccups are depicted in Table 2.

Table 3 presents the association between gender and several risk variables for TBI-related persistent hiccups. Severe TBI was significantly associated with female gender (69.9% vs. 93.5%; p = 0.001), and ventilator-associated pneumonia and the need for mechanical ventilation were significantly associated with male gender (p = 0.001 and p = 0.024). The other risk variables were not significantly associated with gender. The significant relationship were observed between incidence of VAP and Marshall CT classification and non-survived patients (p<0.001 and p<0.001) and rest other risk variables had no significant relation. The association between incidence of ventilator associated pneumonia and several risk variables for TBI-related persistent hiccups is present in Table 4.

Table 5 shows the association between type of TBI (moderate or severe) and several risk variables for TBI-related persistent hiccups. A strong relationship was observed in severe TBI patients who had fallen from height and were not responsive to drugs for hiccups (p = 0.019 and p = 0.004) as compared to moderate TBI.

Table 6 shows the association between length of ICU stay and several risk variables for TBI-related persistent hiccups. A strong relationship was observed between patients who had fallen from height with a length of ICU stay of >14 days (p = 0.027) and non-survived patients with a length of ICU stay of<14 days (p = 0043). The other risk variables had no significant relationship.

4. Discussion

This study evaluates the demographic, clinical characteristics, as well as the risk factors of persistent hiccup patients due to traumatic brain injury in a trauma intensive care unit (ICU). The prevalence of persistent hiccups in neurotrauma-ICU patients is unknown, and there is a lack of literature on the disease's nature, pattern and associated risk factor in TBI patients.

The study found that 59.8% of patients were under 40 years old, with a mean age of 41.75±17.16 years. Most were male (75.7%), with a male-to-female ratio of 1.88:1. Majority of patients (67.7%) had BMI range 18.5-24.9 kg/m^2 followed by BMI 25.0-29.0 kg/m^2 (30.2%). This aligns with a 2019 study by Kirankumar et al.,[5] which found that the majority of TBIs were in the age group of 21-40 years (47.4%), followed by 41-60 years (35.6%). Another study by Agrawal et al.[6] identified 93 cases (61.5%) of TBI among adults aged 18-73 years old. This suggests that the 18-40 age group is the most common for TBI due to risk factors such as risky behaviors, high motor vehicle crashes, and increased participation in sports. Most work-related TBI fatalities occur in men due to their higher participation in

Table 2: Association between age group and several risk variables of persistent hiccups due to TBI

	Age group	**p-value**			
Risk variables	<40 years	< 40 years			
	No.	%	No.	%	
Gender					0.025
Male	92	81.4	51	67.1	
Female	21	18.6	25	32.9	
BMI					
<18.5	4	3.5	0	0.0	
18.5-24.9	82	72.6	46	60.5	0.026
25.0-29.0	27	23.9	30	39.5	
Mode of Injury					
Road traffic injury	66	58.4	48	63.2	
Fall from height	21	18.6	12	15.8	0.909
Assault	11	9.7	6	7.9	
Others	15	13.3	10	13.2	
Type of TBI					
Moderate (GCS 9-13)	31	27.4	15	19.7	0.227
Severe (GCS 3-8)	82	72.6	61	80.3	
APACHE II score					
5-9	3	2.7	7	9.2	
10-14	51	45.1	31	40.8	
15-19	37	32.7	18	23.7	0.030
20-24	16	14.2	7	9.2	
25-29	4	3.5	9	11.8	
30-34	2	1.8	4	5.3	
Marshall CT classification					
II	25	22.1	9	11.8	
III	11	9.7	11	14.5	
IV	18	15.9	19	25.0	0.117
V	40	35.4	20	26.3	
VI	19	16.8	17	22.4	
Seizure prophylaxis					
Levetiracetam	82	72.6	54	71.1	0.820
Phenytoin	31	27.4	22	28.9	
Treatment					
Non-operative	77	68.1	47	61.8	0.371
Operative	36	31.9	29	38.2	
ICU Stay					
<14	12	10.6	11	14.5	0.427
>14	101	89.4	65	85.5	
Ventilator associated pneumonia					
Yes	41	36.3	30	39.5	0.657
No	72	63.7	46	60.5	
Mechanical ventilation					
Yes	105	92.9	70	92.1	0.834
No	8	7.1	6	7.9	
Responsive to drugs for hiccups					
Yes	73	64.6	50	65.8	0.867
No	40	35.4	26	34.2	
Mortality					
Non-survived	40	35.4	46	60.5	0.001
Survived	73	64.6	30	39.5	

Table 3: Association between gender and several risk variables of persistent hiccups due to TBI

Risk Variables	Gender				p-value
	Male		Female		
	No.	%	No.	%	
BMI					
<18.5	3	2.1	1	2.2	0.357
18.5-24.9	93	65.0	35	76.1	
25.0-29.0	47	32.9	10	21.7	
Mode of Injury					
Road traffic injury	83	58.0	31	67.4	0.528
Fall from height	25	17.5	8	17.4	
Assault	15	10.5	2	4.3	
Others	20	14.0	5	10.9	
Type of TBI					
Moderate (GCS 9-13)	43	30.1	3	6.5	0.001
Severe (GCS 3-8)	100	69.9	43	93.5	
APACHE					
5-9	7	4.9	3	6.5	0.522
10-14	66	46.2	16	34.8	
15-19	37	25.9	18	39.1	
20-24	19	13.3	4	8.7	
25-29	10	7.0	3	6.5	
30-34	4	2.8	2	4.3	
Marshall CT classification					
II	26	18.2	8	17.4	0.225
III	13	9.1	9	19.6	
IV	32	22.4	5	10.9	
V	45	31.5	15	32.6	
VI	27	18.9	9	19.6	
Seizure prophylaxis					
Levetiracetam	104	72.7	32	69.6	0.678
Phenytoin	39	27.3	14	30.4	
Treatment					
Non-operative	95	66.4	29	63.0	0.674
Operative	48	33.6	17	37.0	
ICU Stay					
<14	16	11.2	7	15.2	0.467
>14	127	88.8	39	84.8	
Ventilator associated pneumonia					
Yes	63	44.1	8	17.4	0.001
No	80	55.9	38	82.6	
Mechanical ventilation					
Yes	129	90.2	46	100	0.024
No	14	9.8	0	0.0	
Responsive to drugs for hiccups					
Yes	96	67.1	27	58.7	0.296
No	47	32.9	19	41.3	
Mortality					
Non-survived	66	46.2	20	43.5	0.751
Survived	77	53.8	26	56	

Table 4: Association between the incidence of VAP and several risk variables for persistent hiccups

Risk Variables	Ventilator associated pneumonia (VAP)				p-value
	Yes		No		
	No.	%	No.	%	
BMI					
<18.5	1	1.4	3	2.5	0.438
18.5-24.9	52	73.2	76	64.4	
25.0-29.0	18	25.4	39	33.1	
Mode of Injury					
Road traffic injury	51	71.8	63	53.4	0.072
Fall from height	8	11.3	25	21.2	
Assault	6	8.5	11	9.3	
Others	6	8.5	19	16.1	
Type of TBI					
Moderate (GCS 9-13)	17	23.9	29	24.6	0.922
Severe (GCS 3-8)	54	76.1	89	75.4	
APACHE					
5-9	3	4.2	7	5.9	0.797
10-14	32	45.1	50	42.4	
15-19	23	32.4	32	27.1	
20-24	7	9.9	16	13.6	
25-29	5	7.0	8	6.8	
30-34	1	1.4	5	4.2	
Marshall CT classification					
II	6	8.5	28	23.7	<0.001
III	14	19.7	8	6.8	
IV	19	26.8	18	15.3	
V	13	18.3	47	39.8	
VI	19	26.8	17	14.4	
Seizure prophylaxis					
Levetiracetam	46	64.8	90	76.3	0.089
Phenytoin	25	35.2	28	23.7	
Treatment					
Non-operative	43	60.6	81	68.6	0.257
Operative	28	39.4	37	31.4	
ICU Stay					
<14	11	15.5	12	10.2	0.278
>14	60	84.5	106	89.8	
Mechanical ventilation					
Yes	66	93.0	109	92.4	0.882
No	5	7.0	9	7.6	
Responsive to drugs for hiccups					
Yes	43	60.6	80	67.8	0.312
No	28	39.4	38	32.2	
Mortality					
Non-survived	48	67.6	38	32.2	<0.001
Survived	23	32.4	80	67.8	

Table 5: Association between the type of TBI (moderate /severe) and several risk variables for persistent hiccups

Risk Variables	Type of TBI: Moderate No.	%	Severe No.	%	p-value
BMI					
<18.5	1	2.2	3	2.1	0.915
18.5-24.9	30	65.2	98	68.5	
25.0-29.0	15	32.6	42	29.4	
Mode of Injury					
Road traffic injury	34	73.9	80	55.9	0.019
Fall from height	3	6.5	30	21.0	
Assault	1	2.2	16	11.2	
Others	8	17.4	17	11.9	
APACHE					
5-9	1	2.2	9	6.3	0.466
10-14	18	39.1	64	44.8	
15-19	13	28.3	42	29.4	
20-24	9	19.6	14	9.8	
25-29	4	8.7	9	6.3	
30-34	1	2.2	5	3.5	
Marshall CT classification					
II	13	28.3	21	14.7	0.278
III	4	8.7	18	12.6	
IV	7	15.2	30	21.0	
V	15	32.6	45	31.5	
VI	7	15.2	29	20.3	
Seizure prophylaxis					
Levetiracetam	37	80.4	99	69.2	0.141
Phenytoin	9	19.6	44	30.8	
Treatment					
Non-operative	30	65.2	94	65.7	0.949
Operative	16	34.8	49	34.3	
ICU Stay					
<14	5	10.9	18	12.6	0.757
>14	41	89.1	125	87.4	
Mechanical ventilation					
Yes	43	93.5	132	92.3	0.792
No	3	6.5	11	7.7	
Responsive to drugs for hiccups					
Yes	38	82.6	85	59.4	0.004
No	8	17.4	58	40.6	
Mortality					
Non-survived	17	37.0	69	48.3	0.181
Survived	29	63.0	74	51.7	

high-risk activities, occupational hazards, and differences in biological susceptibility.[7] These findings highlight the need for increased awareness and prevention strategies for TBI. A systematic review and meta-analysis revealed that TBI patients typically have a normal or slightly overweight BMI, with 59.4% in the normal range (18.5-24.9 kg/m2). This may be due to demographic factors like younger age and higher physical activity levels, as well as risk factors like underweight or severely obese individuals.[8]

In the present study, road traffic accidents (RTAs) were present in 60.3% of patients, followed by falls from height (17.5%). On the basis of the GCS score, 75.7% of patients had severe type TBI (GCS 3–8), and the remaining had moderate type TBI (GCS 9–13). We performed operative treatment on 65 (34.4%) patients and non-operative treatment on 124 (65.6%) patients. The need for mechanical ventilation was present in 92.6% of patients, and 37.6% of patients had an incidence of ventilator-associated pneumonia. Out of 189 patients, 87.8% had a length of ICU stay >14 days, and 86 (45.5%) had died.

In a study by Gururaj[9] reveals that road traffic injuries are the leading cause of head injuries (TBIs) in India,

Table 6: Association between the length of ICU stay and several risk variables for persistent hiccups

Risk variables	ICU Stay <14 days No.	%	ICU Stay >14 days No.	%	p-value
BMI					
<18.5	0	0.0	4	2.4	0.753
18.5-24.9	16	69.6	112	67.5	
25.0-29.0	7	30.4	50	30.1	
Mode of Injury					
Road traffic injury	20	87.0	94	56.6	0.027
Fall from height	0	0.0	33	19.9	
Assault	2	8.7	15	9.0	
Others	1	4.3	24	14.5	
APACHE					
5-9	2	8.7	8	4.8	0.761
10-14	10	43.5	72	43.4	
15-19	5	21.7	50	30.1	
20-24	4	17.4	19	11.4	
25-29	2	8.7	11	6.6	
30-34	0	0.0	6	3.6	
Marshall CT classification					
II	4	17.4	30	18.1	0.511
III	5	21.7	17	10.2	
IV	4	17.4	33	19.9	
V	5	21.7	55	33.1	
VI	5	21.7	31	18.7	
Seizure prophylaxis					
Levetiracetam	16	69.6	120	72.3	0.785
Phenytoin	7	30.4	46	27.7	
Treatment					
Non-operative	16	69.6	108	65.1	0.670
Operative	7	30.4	58	34.9	
Mechanical ventilation					
Yes	21	91.3	154	92.8	0.801
No	2	8.7	12	7.2	
Mortality					
Non-survived	15	65.2	71	42.8	0.043
Survived	8	34.8	95	57.2	

accounting for 60% of all TBIs. This is 25 times higher than in developed countries. The Indian Head Injury Foundation reports a fatality rate of 70 per 10,000 vehicles, with falls being a major cause, particularly in the young and elderly. A study of 1,012 TBI patients revealed that 58.7% had severe TBI, while 21.6% had moderate TBI and 19.7% had mild TBI[9]. These findings support the predominance of severe TBI cases among hospitalized TBI patients. Non-operative management is suitable for many TBI patients, especially those with mild injuries and no significant mass effect or CT scan shift. Operative intervention is recommended for patients with significant mass lesions, hematomas causing mass effect, or refractory intracranial hypertension. Operative treatment in isolated TBI patients over 80 years old is associated with lower mortality rates, but a higher rate of poor neurological outcomes.[10] A study by CENTER-TBI found that 84.7% of TBI patients required invasive mechanical ventilation during their ICU stay.[11] Another study by Asehnoune et al[12] reported 91% of moderate-to-severe TBI patients also required mechanical ventilation. Robba et al[13] estimated the pooled incidence of mechanical ventilation in TBI patients to be 82.3%. Mechanical ventilation is crucial for airway protection, gas exchange optimization, and preventing secondary brain injury from hypoxia or hypercarbia.

The incidence of VAP in TBI patients has varied across studies, with a meta-analysis revealing a pooled incidence of 37.6%.[14] Other studies have reported a range of 10% to 65%.[15]. A multicenter study found a VAP incidence of 34.1%.[13] Variations in reported incidence may be due to differences in patient populations, diagnostic criteria, and clinical practices. However, the current study found that 35.2% of TBI patients developed VAP, which is within the existing literature's range.

A multicenter study found that the median ICU stay for patients with TBI is 11 days, with 64% having a prolonged stay exceeding 72 hours.[16] Another study found that 76.4% of TBI patients stayed in the ICU for 1-7 days, followed by 8-14 days for 12.2%.[17] Severe TBI patients had a median stay of 8.3 days, with longer stays associated with poorer outcomes.[18]

In our study, the age under 40 years had a significant association with the male gender (p = 0.025) and the age over 40 years was significantly associated with a higher BMI (25.0–29.0 kg/m^2), a higher APACHE II score (>15), and greater mortality (p = 0.026, p = 0.030, and p = 0.001), respectively. The significant association between younger age (under 40 years) and the male gender could indicate that younger male patients may be more susceptible to developing hiccups following a traumatic brain injury. This information could be useful in identifying high-risk individuals and tailoring management strategies accordingly. The findings for patients over 40 years old suggest that this age group may experience more severe complications and poorer outcomes related to TBI-induced hiccups. The associations with higher BMI, higher APACHE II scores, and greater mortality indicate that older patients may require more intensive monitoring and targeted interventions to address the underlying factors contributing to these adverse outcomes.

A study found that the incidence of persistent or intractable hiccups is significantly higher in males than in females.[19] The review article on Hiccups in Neurocritical Care also noted that gender is the most common risk factor for hiccups.[1] A study indicated that higher BMI significantly increases the risk of postoperative hiccups in patients undergoing deep brain stimulation for Parkinson's disease. This implies that higher BMI is a risk factor for developing hiccups in various neurological conditions, including TBI.[19] The APACHE II score is a widely used measure of disease severity in TBI patients. Higher scores indicate more severe injuries, which are associated with poorer outcomes, including increased mortality.[20] Older age itself is a risk factor for worse outcomes after TBI, including increased mortality. This is due to decreased physiological reserve and higher rates of comorbidities.

In the present study, we found that severe TBI was significantly associated with female gender (69.9% vs. 93.5%; p = 0.001). This is an interesting finding, as previous research has often shown a higher incidence of TBI in males compared to females.[21,22] This finding is due to differences in injury mechanisms, such as the type of trauma or the location of the injury. Alternatively, it could be related to differences in physiological responses to injury, such as the body's ability to respond to and recover from severe trauma.

The study also found that ventilator-associated pneumonia (VAP) was significantly associated with male gender (p=0.001). This is an important finding, as VAP is a common complication in critically ill patients, including those with TBI. The higher incidence of VAP in males may be due to differences in immune response and respiratory physiology, such as the presence of more severe lung injury or a higher risk of developing pneumonia. It could also be related to differences in the management of mechanical ventilation, such as the use of different ventilator settings or the presence of underlying respiratory conditions.The meta-analysis results showed that compared to female patients, male patients with traumatic brain injury (TBI) had a significantly higher risk (about 46%) of developing VAP (RR=1.46, 95% CI: 1.13-1.79, p<0.05).[23] Variations in ventilator management or other clinical practices between male and female TBI patients may also contribute to the disparities in VAP incidence.

The study also found that the need for mechanical ventilation was significantly associated with male gender (p=0.024). The greater prevalence of severe TBI in male patients would therefore translate to a higher need for mechanical ventilation in this group. The physiological factors that predispose males to more severe TBI, such as differences in brain anatomy, cerebrovascular regulation, and hormonal influences, may also contribute to the increased requirement for mechanical ventilation. A survey by Robba et al.[13] found that 66% of respondents managing severe TBI patients were male, suggesting a higher proportion of men requiring mechanical ventilation in this setting.

In the present study, we found a significant relationship were observed between incidence of VAP with Marshall CT classification and non-survived patients with persistent hiccups due to TBI (p<0.001 and p<0.001). The Marshall CT classification is a system used to categorize the severity of traumatic brain injury based on radiographic findings. Several studies have found associations between higher Marshall scores (indicating more severe injury) and increased risk of complications like VAP in TBI patients. Bronchardetal.[24] reported that a Marshall CT score >2 was significantly associated with VAP in TBI patients admitted to the ICU. These findings suggest that more severe structural brain injuries, as evidenced by higher Marshall scores, may predispose TBI patients to respiratory complications like VAP, potentially due to impaired cough reflex, aspiration risk, and immunosuppression.

While the literature on persistent hiccups in TBI is limited, a few studies have suggested an association between this complication and poorer outcomes. A case report by Wu et al.[25] described a TBI patient who developed intractable hiccups and had a prolonged hospital course. Another case report by Takemoto et al[26] reported on a patient with chronic subdural hematoma who presented with persistent hiccups and ultimately died. However, these are isolated case reports, and more research is needed to determine if persistent hiccups are truly an independent predictor of mortality in TBI patients.

Fall from height are the leading cause of traumatic brain injury (TBI) in children and older adults, and the second leading cause of TBI-related deaths overall.[27] Fall, especially from low heights (76% of all falls), were the most common trauma mechanism leading to moderate or severe TBI, followed by road traffic accidents.[28] Age, fall from height, and location of the fall were all significantly associated with mortality in severe TBI patients from falls. Among adults with severe TBI, the number of deceased persons due to fall from height was 437, representing 45% of the total TBI deaths.[29] In the present study, we found significant relationship was observed between patients who had fallen from height in severe TBI patients ($p = 0.019$).

In the present study, a significant relationship was observed between patients who had fall from height having an increased length of ICU stay (>14 days) ($p = 0.027$) and patients who had died due to TBI having a shorter length of ICU stay (<14 days) ($p = 0.043$). One study found a significant weak positive correlation between falling distance and the durations of ICU and hospital stay (ρ = 0.33, 0.32; $p < 0.05$).[30] This suggests that as the height of the fall increases, the length of ICU and hospital stay also tends to increase. Another study reported that falls from heights ≥25 feet were associated with significantly higher Injury Severity Scores (ISS) among admitted patients compared to falls from <25 feet (p=0.001).[31] Higher ISS is typically associated with longer ICU and hospital stays. There is no evidence provided to support the specific claim that a significant relationship was observed between fall height, ICU length of stay, and hiccups in severe TBI patients.

Patients who died in the ICU were significantly more likely to have shorter ICU stays. This indicates that shorter ICU LOS may be associated with higher mortality in severe TBI.[32]

To implement the new knowledge from the study, targeted prevention programs should be developed for younger male TBI patients at risk for persistent hiccups, and healthcare providers should be trained to recognize demographic risk factors, including gender differences in TBI complications. Enhanced monitoring protocols for older TBI patients with higher BMI and APACHE II scores should be introduced to address complications early and reduce mortality. The Marshall CT classification should be used more extensively to identify and manage respiratory complications in TBI patients. Comprehensive data collection through multicentre collaborations and extended follow-up periods is needed to enhance generalizability and capture long-term outcomes.

5. Limitations

The study has several limitations that may affect the generalizability and validity of its findings. Firstly, being a single-center study, the results may not be applicable to other populations or settings. Additionally, the limited follow-up period may not capture long-term outcomes and complications associated with persistent hiccups in TBI patients. The scarcity of research on this topic further limits the availability of relevant data. The study may not have adequately controlled for factors such as medication use that could influence the development of persistent hiccups.

Furthermore, the lack of a comparison group and standardized definition for persistent hiccups hinders the ability to isolate their specific impact on TBI. The observational nature of the study also prevents establishing causal relationships. Therefore, further research, including multicenter studies and randomized controlled trials, is necessary to validate and expand upon these findings.

6. Conclusion

This study concludes that younger male patients with severe traumatic brain injury are more likely to experience persistent hiccups, which can hinder their recovery. Older patients with higher Body Mass Index and APACHE II scores have increased mortality rates, highlighting the need for tailored management strategies for high-risk individuals. Further research is needed to better understand the association between hiccups and traumatic brain injury and develop effective management strategies.

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8. Conflict of Interest

None.

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