https://doi.org/10.36570/jduhs.2021.3.1187

JDUHS

ORIGINAL ARTICLE

Characteristics and Outcome of Patients with Traumatic Brain Injury in the Intensive Care Unit of a Public Sector Hospital in Karachi, Pakistan

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ABSTRACT

Objective: To determine the characteristics, management and outcome of patients with traumatic brain injury (TBI) and associated risk factors.

Methods: This cross-sectional study was conducted at Shaheed Mohtarma Benazir Bhutto Institute of Trauma from January 2018 to April 2019. TBI patients ≥16 years of age that were admitted to the intensive care unit (ICU) or high dependency unit (HDU) and managed conservatively or surgically, were included. Central nervous system (CNS) infection, mortality and associated risk factors were noted.

Results: The mean age was 30.9 ± 13.6 years with 116 (91.3%) males. CNS infection developed in 72 (56.7%) patients. Of 72, 29 (40%) had positive CSF culture and in 28 (38.8 %) multidrug resistant *Acinetobacter spp*. susceptibile to only colistin was reported. Antimicrobial therapy with intravenous colistin with meropenem was used in 63 (87.5%) patients. A significant association of CNS infection was found with age (p-value 0.047), cerebrospinal fluid (CSF) leak at presentation (p-value 0.045), type of surgery (p-value 0.001), and duration of ER stay (p-value 0.047). Mortality occurred in 83 (65.4%) patients. A significant association of mortality was found with low Glasgow coma scale (GCS) at presentation (p-value 0.031), CSF leak at presentation (p-value <0.001), intraventricular hemorrhage, TBI type (p-value <0.001), polytrauma (p-value 0.003), CNS infection (p-value <0.001), and duration of emergency room stay (p-value 0.009).

Conclusion High mortality was observed in patients with traumatic brain injury. Intracranial infection is strongly correlated with mortality underscoring the need for strict infection control and prevention measures.

Key words: Traumatic Brain Injury, Central Nervous System Infection, Intensive Care Units, Neurosurgical Procedures

INTRODUCTION

Head trauma accounts for approximately half of trauma related deaths in hospitals. Around 44% of head injury cases are due to road traffic accidents.[1,2] Other causes include falls (especially in young children and older adults) and assault. According to a study in the United States, over 1.7 million visits to the emergency are due to traumatic brain injury (TBI) of which 52,000 die annually.[3] Pakistan, with population of 220 million, ranks first in Asia and 48th in the world for accident-related deaths, of whom nearly one third are reported to sustained TBI.[4] As per the prediction of World Health Organization, road traffic accident could become the seventh leading cause of death by 2030.[5]

In developing countries, pre-hospital care to trauma patients is usually provided by untrained personnel and consequently, monitoring and stabilization for hypoxia and hypotension is often not available during transfer.[6] Surgical management of extradural and subdural hematomas is an acceptable practice but its role in severe TBI is controversial. The Brain Trauma Foundation has defined the guidelines for the management and monitoring of patients with severe TBI to improve outcome and Intracranial pressure (ICP) monitoring is one of them.[7,8] However, in Pakistan many hospitals do not have ICP monitoring available and clinical and radiological findings are mainly relied upon for the decision of surgery.

There is limited local data and the aim of our study is to assess the clinical characteristics and outcome of patients with TBI and associated factors for mortality at a public sector hospital in Karachi, which will provide guidance for management and improved outcomes.

METHODS

This cross-sectional study was conducted in Shaheed Mohtarma Benazir Bhutto Institute of Trauma (SMBBIT) from January 2018 to April 2019. It is a chart review so requirement for patient consent was waived by the institutional review board (IRB-1389/DUHS/Approval/2019). Patient confidentiality was maintained, and patient data were kept secured without identifiers such as name and residential address.

SMBBIT is a tertiary care hospital established in Karachi by the Government of the province of Sindh in 2016, which offers care free of cost to patients of rural and urban Sindh and also from neighboring provinces.

Patients with TBI who were 16 years of age and above that were admitted to the intensive care unit (ICU) or high dependency unit (HDU) and managed conservatively or surgically, were included. Patients who had undergone intracranial surgery at an outside healthcare facility before transfer to SMBBIT, or had intracranial infection prior to their injury, were excluded from the study. All patients meeting the inclusion criteria admitted during the study period were enrolled. Convenience sampling method was used to collect cases over the given time period. Data were extracted by a manual chart review and documented in a proforma which included demographics, mechanism and type of injury, management, complications, and outcome of patients with TBI in terms of mortality and central nervous system (CNS) infection. Imaging, laboratory, and microbiological data were abstracted from the electronic medical system and documented.

TBI was defined using the Centers for Disease Control and Prevention (CDC) definition which stated TBI as an injury to the head resulting from blunt or penetrating trauma or from acceleration-deceleration of force causing neurological or neuropsychological abnormalities, such as altered level of consciousness, intracranial lesion, memory loss, skull fracture, or death.[3]

We used the Glasgow Coma Scale (GCS) in the assessment of severity of head injury, with GCS 9 to 15 considered as mild to moderate head injury, and 8 and below as severe head injury. [12]

Intracranial infection was defined as any case of TBI in which the diagnosis was clinically suspected by the attending physician due to symptoms and signs that included fever, headache and decrease in GCS, with at least one of the following laboratory data as supportive evidence: microorganisms cultured from the cerebrospinal fluid (CSF) analysis with increased white cells, elevated protein, low glucose and/or CSF gram stain showing microorganisms. Outcome was measured in terms of CNS infection and mortality. Data entry and analysis were done using a Statistical Package for Social Sciences (SPSS) version 20.0. Mean ± SD were computed for normally distributed quantitative variables while median (IQR) were computed for those quantitative variables which were not normally distributed. Frequency and percentages were computed for categorical variables like, gender, co-morbidities, type of TBI, GCS and CSF leak at presentation, CNS infection, duration of emergency room (ER) stay (days), and mortality. Mean difference of ER and ICU stay was computed for CNSinfection and mortality using independent t-test. Moreover, Chi-square/Fisher exact test was applied to see the association of outcome variable (CNS infection and mortality) with baseline and clinical characteristics. The p-value of ≤ 0.05 was considered statistically significant.

RESULTS

Of 127 patients with TBI, the mean age was 30.9 ± 13.6 years. There were 116 (91.3%) males and 11 (8.7%) females. Motorcycle accidents were the most common cause of TBI 78 (61.4 %). Comorbidities were observed in 17 (13.4%) patients.

On CT imaging, the most common type of TBI was contusions 55 (43.3%) followed by extradural hemorrhage (EDH) 48 (37.7%), subdural hemorrhage (SDH) 46 (36.2%), skull fracture 33 (26.0%), subarachnoid hemorrhage (SAH) 30 (23.6%), intracranial (IC) bleed 14 (11.0%), intra-ventricular hemorrhage (IVH) 8 (6.3%), and diffuse axonal injury (DAI) 8 (6.3%). Based on GCS, 73 (57.3%) TBI patients had a severe head injury while, the rest 54 (42.5%) patients had mild to moderate TBI. Majority of patients did not have CSF leak at presentation, i.e., 106 (83.4%). The average duration of ICU stay was 16.9 ± 11.0 days whereas the average duration of ER stay was 1.7 ± 3.36 days.

CNS infection developed in 72 (56.7%) patients. Of these 72 patients, 29 (40.3%) patients had positive CSF culture (28 out of 29 had MDR *Acinetobacter species* spp with sensitivity to colistin only) while 43 (59.7%) patients had negative CSF culture. The most common concomitant incision site infection was *pseudomonas aeruginosa* 06 (30.0%) and *klebsiella* spp 07 (35.0%). Colistin intravenous (IV) with meropenem antimicrobial therapy was used in majority, i.e., 63 (87.5%) patients. Mortality in patients with CNS infection was found

Table 1: Intracranial infection in 72 patients with traumatic brain injury

Days to develop intracranial infection	**Median (IQR)**
Since Admission	7 (4-8)
Since Surgery	6 (3-7)
Intracranial Infection diagnosed by	**n (%)**
CSF analysis with bacterial picture and culture negative	43 (59.8)
CSF analysis with bacterial picture and culture positive	28 (38.8)
CSF analysis negative/CSF culture positive	1 (1.4)
CSF culture positive (n= 29)	
Acinetobacter spp	28 (96.5)
Staphylococcus aureus	1 (3.5)
Concomitant incision site infection	
Staphylococcus aureus	03 (15.0)
Acinetobacter spp.	04 (20.0)
Klebsiella spp	06 (30.0)
Pseudomonas aeruginosa	07 (35.0)
Antimicrobial Therapy	
Colistin IV with Meropenem	63 (87.5)
With intrathecal colistin	07 (9.7)
Meropenem and Vancomycin	01 (1.3)
Other	08 (11.1)
Outcome	
Died	39 (54.2)
Discharged from hospital	33 (45.8)

CSF: cerebrospinal fluid, IV : intravenous, spp: species, IQR: interquartile range

to be 39 (54.2%). (Table 1)

In comparison of CNS infection with baseline and clinical characteristics it was observed that a significant association of CNS infection was found with age (p-value 0.047), CSF leak at presentation (p-value 0.045), type of surgery (p-value 0.001), and duration of ER stay (p-value 0.047). (Table 2)

Mortality rate of TBI patients was 83 (65.4%). A significant association of mortality was found with GCS at presentation (p-value 0.031), CSF leak at presentation (p-value <0.001), IVH type of TBI (p-value <0.001), polytrauma (p-value 0.003), CNS Infection (p-value <0.001), and duration of ER stay (p-value 0.009). (Table 3)

DISCUSSION

This study has provided a better understanding of the demographic, hospital course and outcome of patients with TBI. We found that patient were predominantly young males, mostly motorcycle riders, with median age of thirty years, as reported in numerous other studies of TBI.[1, 3] The fact that young males are more likely to suffer from TBI is because they are more likely to travel for work, while females are under represented in the workforce and do not generally ride motorcycles. Pakistan has a poor safety record regarding compliance with traffic rules and use of helmets and safety belts.

Most of our patients with severe head injury and admission GCS below 8 were found to have subdural hematoma whereas in China patients of severe head injury more commonly had intracerebral hematoma.[9]

In our study, CNS infection developed in more than half of the patients. While a study from China among patients with TBI reported that seven percent patients developed intracranial infection.[9] Another study from India reported CNS infection in twenty eight percent of patients with TBI.[10] In several published studies risk factors for bacterial meningitis was CSF leak, concomitant incision site infection, prolonged duration of surgery, prolonged external ventricular drainage, and repeated surgeries.[9-11]

We observed mortality in one-third of our patients which is comparable with studies from other developing countries.[13-17] Delay from time of injury till arrival at the hospital and inadequate pre-hospital management is undoubtedly a contributing factor to

Table 2: Comparison of CNS infection with baseline and clinical characteristics of patients with traumatic brain injury (n = 127)

	Total	CNS Infection		p- value
		With CNS Infection (n = 72)	Without CNS Infection (n = 55)	
Age, year				
≤ 25	61	29 (47.5)	32 (52.5)	0.045^*
> 25	66	43 (65.2)	23 (34.8)	
Gender				
Male	116	66 (56.9)	50 (43.1)	0.999˜
Female	11	6 (54.5)	5 (45.5)	
GCS at presentation				
Severe	73	44 (60.3)	29 (39.7)	0.344^
Mild to moderate	54	28 (51.9)	26 (48.1)	
CSF leak at presentation				
Yes	21	19 (90.5)	2 (9.5)	0.001^*
No	106	53 (50.0)	53 (50.0)	
Management				
Conservative	34	16 (47.1)	18 (52.9)	0.185^
Surgical	93	56 (60.2)	37 (39.8)	
Type of surgery (n = 93) $				
Craniotomy	22	8 (36.4)	14 (63.6)	0.015^*
Craniectomy	71	48 (67.6)	23 (32.4)	
GCS at discharge				
Severe	29	17 (58.6)	12 (41.4)	0.066^
Mild to moderate	63	24 (38.1)	39 (61.9)	
Duration of ICU stay (days)	16.9 ± 11.0	18.6 ± 11.8	14.7 ± 9.8	0.047€
Duration of ER stay (days)				
≤ 1 day	89	56 (62.9)	33 (37.1)	0.024^*
> 1 day	38	16 (42.1)	22 (57.9)	

GCS: Glasgow coma scale, CSF: cerebrospinal fluid, ER: emergency room, CNS: Central nervous system infection, ICU: intensive care unit, $ Surgery was not performed in 34 patients
€Independent t-test and ^Chi-Square/˜Fisher Exact test applied, *p-value ≤ 0.05

high mortality. Low GCS on admission, CSF leak and CNS infection are known risk factors for mortality as reported in numerous studies, including this study.[4,9,10,18] The multicenter trial (STITCH) surgical trial in traumatic intracerebral hemorrhage which was conducted in UK showed better outcomes in early surgery within 12 hours. This is contrary to our study which demonstrated a poor outcome in patients who had surgery performed earlier than 24 hours possibly suggesting a need for better evaluation for viable candidates for surgery.[8] Brain trauma foundation recommends decompressive craniectomy, prophylactic hypothermia, hyperosmolar therapy, CSF drainage along with other supportive therapies. Additionally, ICP, cerebral perfusion pressure and advanced cerebral monitoring, for example, jugular venous oxygen saturation are recommended to reduce mortality and improve outcome.[7] However, non-availability of ICP monitoring, which is recommended by Brain Trauma Foundation to guide decisions regarding surgical intervention, may be a factor in poor surgical outcome at our institution.[7]

In a study by Kourbeti et al, median time from surgery to infection was seven days similar to our study where surgery to infection time was six days.[19] Retention in the emergency room of patients with TBI could also predispose to poor outcome. In a study by Mowery et al, mean length of stay in ER was three hours and increase of stay to 4 to 5 hours increased mortality by eight percent with every hour proving it to be an independent risk factor for mortality in trauma

Table 3: Comparison Of Mortality with Baseline and Clinical Characteristics of Patients with Traumatic Brain Injury (n = 127)

	Total	Mortality Yes (n = 83)	Mortality No (n = 44)	p- value
Age, year				
≤ 25	61	18 (29.5)	43 (70.5)	0.242^
> 25	66	26 (39.4)	40 (60.6)	
Gender				
Male	116	43 (37.1)	73 (62.9)	0.062~
Female	11	1 (9.1)	10 (90.9)	
Co-morbidities				
Yes	17	9 (52.9)	8 (47.1)	0.088^
No	110	35 (31.8)	75 (68.2)	
GCS at presentation[€]				
Severe	73	31 (42.5)	42 (57.5)	0.031^*
Mild to moderate	54	13 (24.1)	41 (75.9)	
CSF leak at presentation				
Yes	21	14 (66.7)	7 (33.3)	<0.001^*
No	106	30 (28.3)	76 (71.7)	
Type of TBI as per CT Imaging at Presentation				
IVH	8	7 (87.5)	1 (12.5)	<0.001~*
EDH	48	14 (29.2)	34 (70.8)	0.312^
SDH	46	16 (34.8)	30 (65.2)	0.981^
SAH	30	13 (43.3)	17 (56.7)	0.253^
IC bleed	14	8 (57.1)	6 (42.9)	0.061^
Contusions	55	20 (36.4)	35 (63.6)	0.722^
Skull fracture	33	13 (39.5)	20 (60.5)	0.505^
DAI	8	2 (25.0)	6 (75.0)	0.554~
Polytrauma				
Yes	37	20 (54.1)	17 (45.9)	0.003^*
No	90	24 (26.7)	66 (73.3)	
Management				
Conservative	34	15 (44.1)	19(55.9)	0.175^
Surgical	93	29 (31.2)	64 (68.8)	
Type of surgery (n = 93)[$]				
Craniotomy	22	6 (27.2)	16 (72.7)	0.650^
Craniectomy	71	23 (32.4)	48 (67.6)	
CNS Infection				
Yes	72	39 (54.2)	33 (45.8)	<0.001^*
No	55	5 (9.1)	50 (90.9)	
Duration of ICU stay (days)	16.9 ± 11.0	15.45 ± 11.9	17.64 ± 10.6	0.292€
Duration of ER stay (days)				
≤ 1 day	89	37 (41.6)	52 (58.4)	0.014^*
> 1 day	38	7 (18.4)	31 (81.6)	

[$]Surgery was not performed in 34 patients
GCS: Glasgow coma score, CSF: cerebrospinal fluid, ER: emergency room, CNS: Central nervous system, ICU: intensive care unit, IVH: intra-ventricular hemorrhage, EDH: extradural hemorrhage, SDH: subdural hemorrhage, IC: intracranial, SAH: subarachnoid hemorrhage, DAI: diffuse axonal injury
[€]Independent t-test and [^]Chi-Square/[~]Fisher Exact test applied, [*]p-value ≤ 0.05

patients. [20,] In our study, average ER retention time of patients with TBI was around 2 admission days, due to non-availability of ICU or HDU beds. However, we found that patients with longer ER stay had better outcome as compared to those who were shifted within a day. This is likely to be a reflection of severity of injury where patients with more severe head injuries and potentially poorer outcome were shifted earlier.

High mortality in TBI has been associated with the type of brain injury. In our study, IVH was found to be associated with a higher mortality rate of eighty seven percent, also demonstrated in another study where seventy percent cases of IVH with blunt head injuries had poor outcome. [21]

Our study has reported a very high occurrence of CNS infection in over half the patients with TBI. We did not find local data of infection in TBI but when comparing with international data, it is much higher than in China reporting seven percent, and India reporting twenty eight percent.[9,10] The majority of infections in our study were in patients who had undergone emergency post-neurosurgical intervention and CSF cultures that were reported as positive demonstrated growth of hospital acquired pathogens, predominantly *Acinetobacter spp.*, known for its ability to survive in the hospital environment. The rate of post-neurosurgical infections due to *Acinetobacter spp.* has been increasing worldwide especially in TBI. Previously carbapenems were considered the treatment of choice for severe infections but now carbapenem-resistant *Acinetobacter* are increasingly being reported making management more challenging.[22,23] The causes of post-surgical hospital acquired infections have been correlated with poor infection control practices. Infection in operation theatre has been related to poor patient preparation, failure to give timely perioperative antibiotics and performance of surgery in emergency settings. We found a correlation between surgical site infection and development of CNS infection. A study by Anderson et al underscores the importance of prevention of incision site infection.[24] Moreover, aseptic technique needs to be strictly followed not only in operation theatre but also during surgical site dressing post-operatively, especially if there is a CSF leak.

Limitations of our study are that it is a retrospective study design. Therefore certain important predictor variables were missed. There have been studies that demonstrate gender has an impact on TBI outcomes but that could not be demonstrated in our study since our patients were mostly males. Moreover, since it is a non-randomized study, it may produce bias regarding data collection and analysis. Though CNS infection was strongly correlated with mortality in TBI patients, we did not document other infections such as ventilator associated pneumonia or central line associated blood stream infection which could have contributed to mortality. A prospective study design may have allowed us to incorporate environmental cultures and monitoring of central sterile services department quality, sterile technique in operation theatre and during surgical site dressing. Another limitation is that we could not follow the patients after discharge from the hospital and therefore cannot comment on their functional status, meaningful rehabilitation or length of survival post-discharge. Nevertheless, our data is useful as it has alerted us to a very high infection rate and mortality in patients with TBI. It has provided data on the best empirical management in our institute of TBI patients who develop signs of intracranial infection. Most importantly, our data should be an impetus to develop systems and institute interventions that decrease infection rates and lead to better patient outcomes. This study may also direct government health and road traffic and safety departments as well as hospital administration to formulate and implement policies in prevention and management of TBI.

CONCLUSION

Patients with TBI are predominantly young males with often motorcycle related accidents. There is a significant rate of post-neurosurgical CNS infection associated with high mortality. Moreover, infection is occurring with multi-drug resistant *Acinetobacter* spp. which makes management of these patients even more challenging. We need to ensure implementation of good infection control practices. To combat antibiotic resistance, antimicrobial stewardship should be implemented. As a nation, we must focus on prevention of TBI by mandating use of helmets and focusing on road safety while simultaneously upgrading our ambulance services without which loss of lives of young persons in their prime will continue unabated.

ETHICAL APPROVAL: Ethical approval was obtained from the institute prior conducting of the study (IRB: 1389/2019).

AUTHORS' CONTRIBUTIONS: AN**:** Supervise, conceived and designed the study, did data collection and manuscript writing, editing of manuscript. Acquisition analysis and interpretation of data, drafted the article and final revision of article. GR: Acquisition analysis and interpretation of data, drafted the article and final revision of article, data management, analysis and accountable for accuracy and integrity of article. MSB: Revising article critically for intellectual contents, revision of article critically for intellectual contents. SB: Revising article critically for intellectual contents, revision of article critically for intellectual contents.

CONFLICT OF INTEREST: There is no conflict of interest.

FUNDING: None.

Received: June 17, 2021
Accepted: Dec 02, 2021

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