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Original Article

Association between Outcome of Severe Traumatic Brain Injury and Demographic, Clinical, Injury-related Variables of Patients

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Abstract

Background: Traumatic brain injury (TBI) is a main health problem among communities. There exists a variety of effective factors on the outcome of patients with TBI. We describe the demographic, clinical, and injury related variables of the patients with severe TBI, and determine the predictors of outcome. **Materials and Methods:** We did this cross-sectional study on all 267 adult patients with severe TBI admitted to three trauma centers of Isfahan University of Medical Sciences (IUMS) from March 20, 2014 to March 19, 2015. Data were extracted from patients' profiles. We considered the patients' outcome as discharged and died. We analyzed the collected data using descriptive (frequency, mean, and standard deviation) and analytical (independent *t*-test, Mann–Whitney U-test, Kruskal–Wallis test and logistic regression) statistics in Statistical Package for the Social Sciences (SPSS) 16.0. We considered $p < 0.05$ as the significance level. **Results:** The mean (SD) age of patients was 43.86 (18.40) years. The majority of the population was men (87.27%). Road traffic accidents (RTAs) were the most common mechanism of trauma (79.40%). The mean (SD) of Glasgow coma scale (GCS) was 6.03 (3.11). In 50.19% of the patients, the pupillary reflex was absent. One hundred and twenty-four patients (46.44%) died before discharge. We found age, gender, GCS, pupillary reflex, hypernatremia, and increased intracranial pressure (IICP) as the predictors of death in severe TBI. **Conclusions:** In this study, the mortality rate of patients with severe TBI was high. In addition, some factors were determined as the significant predictors of outcome. The findings can assist in planning to enhance the quality of care and reduce the mortality rate in the patients with severe TBI.

Keywords: *Head trauma, Iran, patients, traumatic brain injury*

Introduction

Traumatic brain injury (TBI) is a common cause of mortality and disability among communities affecting people of all age groups.[1] The clinical severity of TBI can be categorized into mild injury with the score of 13–15, moderate injury with the score of 9–12, and severe injury with the score of 3–8 based on Glasgow coma scale (GCS) as the most extensive used classification of the severity of TBI.[2] In general, 5-15% of TBI are severe. Despite the fact that severe TBI involves little percentage of overall cases of TBI, it injury is one of the most important health problems worldwide due to the high global burden on societies.[3]

Most mortality and burden following severe TBI occur in non-developed/developing countries.[4] In United States, the annual mortality rate related to severe TBI per 100000 population is 18 persons, and in Europe is 15 persons. However, in Asia this rate per 100000 population is within the range of 20 persons in India to 38 persons in Taiwan.[5] In Iran, trauma is the second cause of death and the most important reason of hospitalization.[6] According to Iranian forensic Medicine Organization, Isfahan province is in the fourth place in mortality rate related to road traffic accidents (RTAs) in 2016 (24697 died and injured were reported in the year which is 7.41% of the whole). Head trauma is the cause of 51.7% of mortalities. In addition, in a study by Zand and Rafiei, TBI following accidents have been stated as the most common cause of death in intensive care units (ICUs) in Iran.[7]

A latest report of the World Health Organization (WHO) has emphasized on doing more research regarding the epidemiological pattern of accidents in order to detect the expansions of the problem

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and also to recognize at risk individuals in non-developed and developing countries.[8] Currently, many researchers are interested in predicting the outcome following severe TBI; since to determine the predictors of outcome assists health care providers to make better decisions regarding the clinical situation of the patients.[9] Previous studies have identified some effective factors on the outcome of patients with TBI, such as age, GCS, primary hypoxia and hypotension, pupillary reflex, the cause of injury, secondary injuries, biochemical parameters, and computed tomography (CT) scan findings.[1,10-13] However, the epidemiologic patterns of these injuries and their outcomes change in different communities as they are dependent on geographic specializations, local health-service features and the sociocultural differences.[9]

Due to lack of a comprehensive trauma registry system in Iran, sufficient data on the epidemiological patterns of trauma and the outcomes are not available.[13] The purpose of this study is to describe the demographic, clinical, and injury-related variables and to determine the predictors of outcome in adult patients with severe TBI in Isfahan, Iran. We compare our findings to the existing literature in the field, and specify the agreements and differences. We also discuss the importance of this health problem in our region, and assess the local parameters that intensify this issue.

Materials and Methods

We conducted this cross-sectional, retrospective study during one year from March 20, 2014 to March 19, 2015 in three trauma centers of Isfahan University of Medical Sciences (IUMS), Isfahan, Iran. Data were obtained from the patients' profiles (secondary source of data). There were 1,204 profiles of adult patients with TBI, admitted to trauma centers of IUMS during the above-mentioned period. All 267 profiles of patients aged 18 years or older with a GCS of 8 or less (severe TBI) during the first 24 hours after admission[2] were included in our study. Exclusion criteria were lack of access to patient's information and incomplete information recorded in the medical profiles. We collected the data after getting permission from the IUMS and the hospitals' managers. From the patients' profiles, we acquired the data on some demographic and injury related characteristics named as age, gender, cause of injury, date and time of incident, and time of arrival to Emergency Department (ED). Moreover, for the clinical variables, we collected the data on the level of consciousness on admission measured by the GCS, pupillary reflex, hospitalization duration, the duration of ventilator dependent, secondary injuries, the presence of concomitant injuries, and the outcome (discharged and died). The brain CT scan results were extracted in terms of cerebral edema, epidural/subdural/intracerebral hematoma, and intraventricular/subarachnoid hemorrhage. In addition, we assessed the laboratory parameters measured at the time of admission and during the hospitalization. The measured parameters were hemoglobin concentration, platelet count, international normalized ratio (INR), sodium level, and blood sugar level. Data were recorded in a data collection form with a special code for each patient. The instrument is a researcher-made form, which includes demographics, clinical, and injury related characteristics. Some neurosurgery specialists and faculty members of nursing confirmed the face and content validity of the form.

We analyzed the collected data using the Statistical Package for the Social Sciences (SPSS) (version 16, SPSS Inc, Chicago, IL, USA). We demonstrated the continuous variables in terms of mean and standard deviation, and the categorical variables in terms of frequency and percentage. Also, we used independent *t*-test and, Mann–Whitney U or Kruskal–Wallis tests to compare the continuous and categorical variables, respectively, in dead and discharged patients. Logistic regression analysis was used to determine the predictor variables associated with the outcome. We tested the following variables in logistic regression analysis: age (as a continuous variable), gender, GCS on admission (as a continuous variable), presence of cerebral hematoma, presence of cerebral edema, mechanism of injury, time from accident to ED (as a continuous variable), pupillary reflex on admission, presence of concomitant injuries, mechanical ventilation, and presence of secondary injuries (Increased Intracranial Pressure (IICP), hypoxia, hypernatremia, hyperglycemia, hypotension, seizure, coagulopathy). We also calculated odds ratio and 95% confidence intervals (95% CI). We considered a $p < 0.05$ (two-tailed) as statistically significant.

Ethical considerations

Ethics committee of IUMS approved this study. It should be noted that all the information gathered from the patients' profiles was considered confidential.

Results

In this study, 267 patients (out of 1,204) with severe TBI were assessed (87.27% were male with the mean (SD) age 43.86 (18.40) years). The most common cause of injury was RTAs (79.40%). The majority of injured patients (52.06%) were between 18–40 years old. Table 1 shows the demographic, clinical, and injury-related variables of patients.

The mean time from accident to ED was 45.01 (33.15) minutes (median = 36). The mean GCS of the patients at the time of admission to ED was 6.03 (3.11). The pupillary reflex at the time of admission was absent in 134 cases (50.19%). The mean duration of the hospitalization was 18.18 (28.70) days. A number of 243 patients (91.01%) were under mechanical ventilation during hospitalization (12.02 (19.90) days). The most common findings of the initial brain CT scans were

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Table 1: Demographic, clinical, and injury-related characteristics of samples

Characteristic	Mean (SD) or Number (%)
Age (years) Mean (SD)	43.86 (18.40)
18-40 *N* (%)	139 (52.06)
41-60	74 (27.72)
>60	54 (20.22)
Gender *N* (%)	
Male	233 (87.27)
Female	34 (12.73)
Mechanism of injury, *N* (%)	
RTAs	212 (79.40)
Falls	35 (13.11)
Others	20 (7.49)
GCS on arrival to ED Mean (SD)	6.03 (3.11)
3-4 *N* (%)	107 (40.07)
5-6	62 (23.22)
7-8	43 (16.11)
>8	55 (20.60)
Pupillary reflex on arrival to ED *N* (%)	
Yes	98 (36.70)
No	134 (50.19)
Not recorded	35 (13.11)
CT scan findings *N* (%)	
Normal	25 (7.84)
Epidural hematoma	17 (5.33)
Subdural hematoma	88 (27.59)
Subarachnoid hemorrhage	78 (24.45)
Intracranial hematoma	47 (14.73)
Intraventricular hemorrhage	11 (3.45)
Cerebral edema	53 (16.61)
Concomitant injuries *N* (%)	
Face	38 (16.45)
Thorax	38 (16.45)
Abdomen	4 (1.73)
Upper Limb	59 (25.54)
Lower Limb	64 (27.71)
Spines	28 (12.12)
Hospitalization duration (days) Mean (SD)	18.18 (28.70)
Mechanical ventilation (days) Mean (SD)	12.02 (19.90)
Yes *N* (%)	243 (91.01)
No	24 (8.99)
Secondary injuries *N* (%)	
Yes	258 (96.63)
No	9 (3.37)
Time from accident to ED (minutes) Mean (SD)	45.01 (33.15)
Outcome *N* (%)	
Discharged	143 (53.56)
Died	124 (46.44)

RTAs: Road traffic accidents; GCS: Glasgow coma scale; ED: Emergency department

subdural hematoma (27.59%). Up to 201 patients (75.28%) had concomitant injuries. A total of 258 patients (96.63%) experienced at least one secondary injury [Table 2].

Table 2: Frequency of secondary injuries in patients with severe TBI

Secondary injury	Number (%)
IICP	191 (71.54)
Hyperglycemia (>200 mg/dL)	134 (50.19)
Hypernatremia (>145 mmol/L)	92 (34.46)
Hyponatremia (<130 mmol/L)	52 (19.48)
Anemia (<10 g/dl)	177 (66.29)
Coagulopathy (INR>2.0)	109 (40.82)
Hypoxia ($Sa0_2$<90%)	21 (7.87)
Hypotension (SBP <90 mmHg)	12 (4.49)
Seizure	16 (5.99)

IICP: Increased intracranial pressure; INR: International Normalized Ratio; SaO_2: O_2 Saturation; SBP: Systolic blood pressure

Finally, 124 patients (46.44%) died in the hospitals. Motorcycles were the cause of head injuries in 30.60% of deaths.

The mean age (47.82 (18.67) years vs. 40.64 (16.85) years), lack of pupillary reflex (31.46% vs. 18.73%), concomitant injuries (43.82% vs. 32.21%), intracranial hematoma (13.11% vs. 4.50%), intraventricular hemorrhage (3.75% vs. 0.37%), IICP (37.83% vs. 33.71%), hypernatremia (20.97% vs. 13.48%), hyperglycemia (27.34% vs. 22.85%), hypotension (4.49% vs. 0.00%), and coagulopathy (23.22% vs. 17.60%), all had higher rates in dead patients. Also, the mean of GCS on arrival to ED (5.18 (2.90) vs. 6.76 (3.12)) in dead patients were less than discharged patients [Table 3].

According to the logistic regression analysis, six variables (out of 17) were selected as significant independent predictors of death with regard to the significant level of 5%, and the values of B and Beta. Age (Wald = 17.16, p <0.001), GCS on arrival to ED (Wald = 17.04, p <0.001), and pupillary reflex on arrival to ED (Wald = 12.05, p = 0.0005) were the stronger predictors in the presence of other variables. Table 4 shows the predictors of death according to logistic regression analysis.

Discussion

We found that younger men have higher rates of severe TBI due to ARTs. This can be due to varieties in their lifestyle, work, and activities; e.g., their high-risk jobs and more usage of motor vehicles.[14] This result is in accordance with several previous studies.[2,10-12] However, in a variety of studies a shift toward a greater incidence of injury in older people has been observed, particularly in developed countries.[14] Also, in two systematic review studies on the epidemiologic pattern of TBI in Europe, an evident shift from RTAs to falls during the time is observed as the cause of TBI, whereas in the studies that were focusing solely on severe TBI, RTAs were still kept as the most common cause of TBI.[15,16] This fact is in accordance with our

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Table 3: Factors associated with outcome in samples (univariate analysis)

Factor	Category	Died (*N*=124)	Discharged (*N*=143)	Statistical results (df)	*p*
Age (years) Mean (SD)	-	47.82 (18.67)	40.64 (16.85)	3.30 (256)	0.001
Gender *N* (%)	Male	104 (38.95)	129 (48.32)	−1.55	0.12
	Female	20 (7.49)	14 (5.24)		
Time from accident to ED Mean (SD)	-	44.66 (34.60)	45.37 (31.78)	−0.15 (200)	0.88
GCS on arrival to ED Mean (SD)	-	5.18 (2.90)	6.76 (3.12)	−4.28 (265)	<0.0001
Pupillary reflex on arrival to ED *N* (%)	Yes	26 (9.74)	72 (26.97)	30.31 (2)	<0.0001
	No	84 (31.46)	50 (18.73)		
	Not recorded	14 (5.24)	21 (7.86)		
Mechanical ventilation *N* (%)	Yes	113 (42.32)	130 (48.69)	−0.06	0.95
	No	11 (4.12)	13 (4.87)		
Mechanism of injury *N* (%)	RTAs	96 (35.95)	116 (43.45)	0.76 (2)	0.38
	Falls	17 (6.37)	18 (6.74)		
	Others	11 (4.12)	9 (3.37)		
Concomitant injuries *N* (%)	Yes	117 (43.82)	86 (32.21)	−2.09	0.037
	No	7 (2.62)	57 (21.35)		
Subarachnoid hemorrhage *N* (%)	Yes	40 (14.98)	38 (14.23)	−1.02	0.31
	No	84 (31.46)	105 (39.33)		
Intracranial hematoma *N* (%)	Yes	35 (13.11)	12 (4.50)	−3.59	0.001
	No	89 (33.33)	131 (49.06)		
Intraventricular hemorrhage *N* (%)	Yes	10 (3.75)	1 (0.37)	−3.01	0.003
	No	114 (42.70)	142 (53.18)		
Cerebral edema *N* (%)	Yes	30 (11.24)	23 (8.61)	−1.65	0.09
	No	94 (35.21)	120 (44.94)		
Seizure *N* (%)	Yes	6 (2.25)	10 (3.75)	−0.74	0.46
	No	118 (44.19)	133 (49.81)		
IICP *N* (%)	Yes	101 (37.83)	90 (33.71)	−3.34	0.001
	No	23 (8.61)	53 (19.85)		
Hypernatremia *N* (%)	Yes	56 (20.97)	36 (13.48)	−3.42	0.001
	No	68 (25.47)	107 (40.08)		
Hypoxia *N* (%)	Yes	14 (5.24)	7 (2.62)	−1.90	0.053
	No	110 (41.20)	136 (50.94)		
Hyperglycemia *N* (%)	Yes	73 (27.34)	61 (22.85)	−2.64	0.008
	No	51 (19.10)	82 (30.71)		
Hypotension *N* (%)	Yes	12 (4.49)	0 (0.00)	−3.80	0.001
	No	112 (41.95)	143 (53.56)		
Coagulopathy *N* (%)	Yes	62 (23.22)	47 (17.60)	−2.83	0.005
	No	62 (23.22)	96 (35.96)		

ED: Emergency department; GCS: Glasgow coma scale; IICP: Increased intracranial pressure

results. In Iran as a developing country, the average age is less compared to the developed countries. In effect, it can lead into a difference in the mean age of patients with TBI. Also, the higher frequency of severe TBI related to RTAs especially motorcycles in Isfahan (79.40%) than some other studies in New Zealand (71%),[17] India (48.91%),[11] Brazil (60.3%),[18] and Tanzania (70.8%)[19] can be due to the fact that in Isfahan (1) there is much traffic in the external highways as it is connecting many cities, (2) the majority of motor vehicles are not safe,[20] and (3) many people are not following traffic rules as well as in Iran. Despite the fact that wearing helmets is mandatory, the executers are not harsh to this matter, so that in a study by Modaghegh *et al*. only 7.4% of the motorcyclists had used helmets.[21] Therefore, the absence of adequate protection and a quick reversal of the motorcycles at the time of accident put the riders at a high risk of head trauma. It is worth mentioning that compared to some other studies conducted in Iran in the last 10-12 years, this study shows no significant change in the frequency of TBI caused by

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Table 4: Predictor factors of outcome in samples

Factor	Beta	Wald	EXP (B)	95% confidence interval	*p*
Age	−0.79	17.16	0.92	0.89-0.96	0.001
Gender	−2.15	7.75	0.12	0.03-0.53	0.0054
GCS on arrival to ED	0.45	17.04	1.57	1.27-1.95	0.001
Pupillary reflex on arrival to ED	1.83	12.05	6.26	2.22-17.63	0.0005
Hypernatremia	−1.30	5.55	0.27	0.09-0.80	0.0185
IICP	−1.42	4.03	0.24	0.06-0.97	0.0447

ED: Emergency department; GCS: Glasgow coma scale; IICP: Increased intracranial pressure

RTAs.[22,23] This fact is calling for more attention in this subject.

The in-hospital mortality rate of patients with severe TBI was 46.44%. In Iran, the mortality rate was reported 42.3% in Arak (in central Iran) for severe TBI, and 60.9% in Kashan (in central Iran) for TBI.[22,23] In the meta-analysis study of Georgoff *et al*. the mortality rate of severe TBI in developing countries was reported from 29.1% to 62.3%.[24] Difference in some factors such as habits, lifestyle, and health services in different societies are known as the reasons for the variety in mortality prevalence.[14] It should be noted that in this study, only patients with severe TBI were studied, while in some other studies such as study of Kasmaei *et al*. patients with any severity of TBI formed the samples, and it could result in lower mortality rates compared to our study.[13] Also, the findings of our study show a high rate of secondary injuries in the samples, which can affect the mortality rate. In Isfahan trauma centers, the healthcare team tried to avoid secondary brain injuries in patients with severe TBI. However, the lack of some facilities such as the IICP monitoring device can cause troubles in managing the injuries. Moreover, the existence of concomitant injuries in most cases can cause the secondary brain injuries. Nonetheless, identifying the causes of high rates of secondary injuries in this region needs further investigations.

The results of this study showed that age, gender, GCS on admission, hypernatremia, IICP, and papillary reflex on admission are the predictors of mortality. Researchers reported different associated factors with death in their studies. In several studies age, GCS, and papillary reflex were reported more frequently as the predictor factors in relation to mortality and morbidity of TBI[10,11,19,25,26] that are in accordance with the results of our study. Also, in a review study by Kulesza *et al*. age, GCS, and pupil response were recognized as the most important prognostic factors of outcome.[27] In the study by Perel, the level of consciousness had a linear relationship with mortality.[4] Saini *et al*. confirmed that the death of patients was associated with the ages more than 40, the level of consciousness, abnormal pupillary reaction, and hypoxia.[11] Kasmaei *et al*. described ages more than 60, trauma mechanism (motorcycle and falling), existence of intracranial and subdural hemorrhage, and GCS <9 as independent predictors of adverse outcome.[13] Also, Iba *et al*. demonstrated that age, papillary reflex, ICP, and subarachnoid haemorrhage were related to the unfavourable outcome.[26] While Fabbri *et al*. did not recognize any relation between age and outcome.[25] In the study by Leong *et al*. the mortality rate increased significantly in patients with serious extracranial injuries.[28] However, Baum *et al.* stated that serious extracranial injuries were not associated with the outcome.[12] These differences can be due to the sample sizes, study population, variables under study and the method. Hence, further investigations are needed in this topic. For instance, in this study only 16 patients had a seizure, and since this sample size is too small further information is needed to confirm the effect of seizure on the outcome.

In order to specify a limitation for this study, we point out that it is a retrospective study. A study based on the patients' profiles can lead to the loss of information due to non-registered information or inaccuracy in the registration. However, as in this study, most of the information recorded in patients' profiles were complete, and all patients with severe TBI were admitted only in the aforementioned centers in Isfahan, the acquired results should be reliable. In this study, we did not analyze the probable complications that can occur during hospitalization; if the death occurred due to the fatal complications and were not directly caused by TBI, this could have reduced the generalizability of the results with regard to the outcome of mortality in patients with severe TBI. Despite the limitations, this study provides some worthwhile information to establish effective safety principles according to the context.

Conclusion

Assessing the prognosis after TBI is important and difficult. Several different factors are associated with outcome of TBI that can assist the healthcare team.[9] The results of this study showed that severe TBI mostly happen in younger males and motorcycle riders. Also, the frequency of secondary injuries and in-hospital mortality rate are high in our region. Based on the findings, the outcome of severe TBI can be affected by various factors. Therefore, it is crucial to design and use local clinical guidelines for improving the trauma outcome. Moreover, having a comprehensive trauma registry system in Iran will make the researchers and authorities able to identify the effective factors on trauma. This would facilitate fast and appropriate proceedings to prevent injuries and disabilities/mortalities following them.

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Conflicts of interest

Nothing to declare.

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