JSSN 2014; 17 (1)

Original Article

Correlation of D-Dimer level with outcome in traumatic brain injury

Pradip Prasad Subedi [1] , Sushil Krishna Shilpakar [2]

Department of surgery, Tribhuvan University Teaching Hospital, Maharajgung, Kathmandu, Nepal

Email: subedipradip81@gmail.com

Abstract

Introduction: Traumatic brain injury (TBI) is a common neurosurgical emergency and a common public health problem with high mortality and long term morbidity. The cost incurred by TBI is immense. The major determinant of outcome following TBI is the severity of the primary injury. However, secondary injuries including coagulopathy are treatable prognostic factors. Many studies have revealed that coagulopathy of trauma depicted by increasing level of D-dimer is associated with poor prognosis in TBI. So, early dectection and correction of such abnormality is very important in management of TBI.

Methods: This is a prospective observational study conducted at Department of Surgery TUTH (Tribhuvan University Teaching Hospital), Kathmandu,Nepal over a period of one year. One hundred and forty eight patients of TBI were included in the study. Clinical profile of the patients and D-dimer level were monitored during the hospital course. D-dimer level was correlated with outcome variables including duration of hospital stay, duration of Intensive care unit (ICU) stay and Glasgow outcome scale (GOS).

Results: A total of 194 patients were admitted with the diagnosis of traumatic brain injury during the study period and out of them 148 patients were enrolled for the study. Out of 148 patients one hundred and twenty (81.1%) were males and twenty eight (18.9%) were females. The mean age was 29.71±18.07 and the age ranged from 1 to 78 years. Seventy (47.3%) patient were between 21 to 40 years of age. The mean duration of hospital stay was 9.83±13.58 days and the mean duration of ICU stay was 3.78±7.06 days. Contusion was the most common lesion in our patients. Of the patients studied 111 patients (75%) had good recovery with GOS of 5, 9 patients (6.1%) had GOS of 4, 6 patients (4.1%) had GOS of 3, 1 patients (0.7%) had GOS of 2 and 21 patients (14.1%) had GOS of 1. Normal D-dimer was seen in 102 patients (68.9%) and elevated D-dimer in 46 patients (31.1%). Man –Whitney test shows higher D-dimer levels positively correlated with duration of hospital stay, duration of ICU stay and Glasgow Outcome Scale. Pearson chi-square test revealed higher levels of D-dimer correlated with grade of injury but not with mode of injury.

Conclusion: D-dimer is elevated in significant proportion of patients with TBI and abnormal D-dimer level is associated with poor outcome in TBI.

Key words: GOS (Glasgow outcome scale), Traumatic Brain injury, D-dimer

Introduction

Traumatic brain injury (TBI) is the result of an external mechanical force applied to the cranium and the intracranial contents, leading to temporary or permanent impairments, functional disability, or psychosocial maladjustment.[1,2] The definition of TBI has not been consistent and vary according to specialities and circumstances. Often the term brain injury is used synonymously with head injury, which may not be associated with neurologic deficits. The definition also has been problematic with variations in inclusion criteria.[3]

In patients with multiple trauma, head is the most common organ to be involved.[4] Head injury is one of the common causes of morbidity and mortality in most countries including Nepal. TBI affects 1.7 million people in the United States each year. Approximately 52,000 patients succumb to TBI , 275,000 are hospitalized and another 1.365 million are treated and discharged from the emergency department. TBI contributes about 30.5% of all injury related deaths in the US.[5,6,7] European rates of hospitalization for head injury have ranged from 91 cases per 100,000 persons per year in Spain in 1988 to 313 cases per 100,000 persons per year in Scotland from 1974-1976.[8] In New Zealand, 782 cases per 100,000 of mild head injury were seen in hospitals or emergency rooms in 1986.[9] The incidence in China is 56 cases per 100,000 persons per year which is lower compared to that in Europe and USA.[10] Approximately 1.4 million people in the UK suffer a head injury every year resulting in nearly 150 000 hospital admissions per year. Of these, approximately 3500 patients require admission to ICU.[11]

Head injury data are difficult to compare internationally for multiple reasons, including inconsistencies and complexities of diagnostic coding and inclusion criteria, case definitions, ascertainment criteria (for example, hospital admissions versus door-to-door surveys), transfers to multiple care facilities (for example, patient admissions may be counted more than once), and regional medical practices.[12]

The true data of the incidence of head injury in Nepal and its public health impact is not available. A retrospective review from the Western Regional Hospital reported that head injury constituted 17% of all surgical admissions, out of which 84% were mild, 9% moderate, and 7% severe.[13] Due to limited resources and lack of neurosurgical centres outside the capital, most cases are either referred to Kathmandu or treated by General Surgeons. The time, a patient spends in an ambulance during transport averages more than 6 hours from any centre outside the capital.[14]

The cost incurred by head injury to the society is incredible, from both an economic and psychological perspective. The cost incurred upon by the TBI is estimated to be $60 million in the US in the year 2000.[5,6,7]

Almost 100% of patients with severe head injury and as many as two thirds of those with moderate head injury will be permanently disabled and will not return to their pre-morbid level of function.[15] This cost of head injury is a huge burden for an underdeveloped country like Nepal. Besides, head injury involves the younger productive age of the population, increasing the economic burden to the community.

Road traffic accident is the leading cause of head injury in adults and fall injury in children.[16] Alcohol consumption is the major contributing factor for all trauma including head injury.

The prognosis of head injury depends on various factors. The uncertainty about the likely outcome after TBI is encapsulated in the Hippocratic aphorism: “No head injury is so serious that it should be despaired of nor so trivial that it can be ignored.”[17] It still remains impossible to say with certainty what will be the future course of events in an individual after TBI. The major determinant of outcome from TBI is the severity of the primary insult, which is irreversible. However secondary insults, mainly cerebral ischemia, intracranial hypertension, systemic hypotension, hypoxia, hyperpyrexia, and hypoglycaemia have been shown to independently worsen survival after TBI.[11] However an estimate of the patient’s prognosis should never be the main factor influencing clinical decisions in management of the brain-injured patients.[17]

TBI patients are susceptible to coagulopathy of trauma due to high thromboplastin content of the brain and this coagulopathy has major impact on the outcome of the patients.[18] This study is done to see the correlation of coagulopathy, as depicted by rising D-dimer level, with outcome in the brain injured patients.

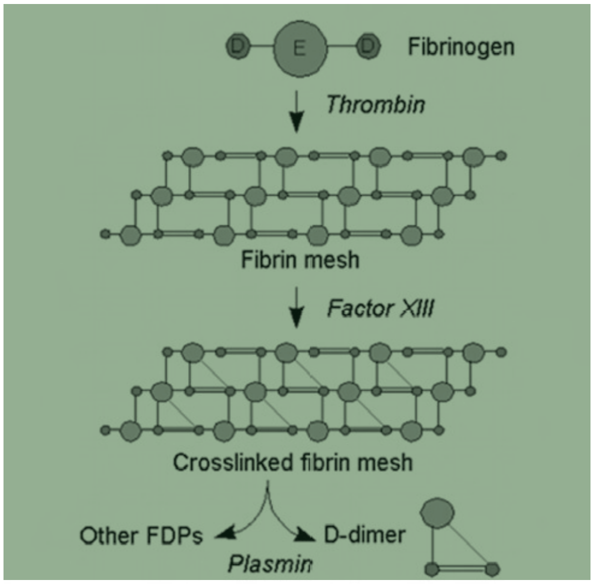

Figure 1: Formation of D-dimer [45]

Objectives

Primary objective

- To correlate the D-dimer level with the outcome in TBI.

Secondary objectives

- To determine the incidence of D-dimer increment in TBI.
- To determine the duration of ICU stay and the hospital stay in relation to D-dimer level.

Hypothesis

Null hypothesis (H0): In TBI, patients with increased D-dimer level do not have higher morbidity and mortality.

Alternate hypothesis (H1): In TBI, patients with increased D-dimer level have higher morbidity and mortality.

Materials and methods

This is a prospective observational study conducted at the department of Surgery Tribhuvan University Teaching Hospital (TUTH), Kathmandu, Nepal over a period of one year (between October 2010 and September 2011). Informed consent was taken from the patient or their relatives. Approval for the study was taken from Instutional review board of Institute Of Medicine. One hundred and ninety four patients were admitted with the diagnosis of head injury during that period and patients (N=148) who met the inclusion criteria were included in the study.

Inclusion criteria

- All patients admitted with TBI

Exclusion criteria

- Patients admitted after 72 hours of the ictus
- Diabetics and hypertensives
- Patients with deep vein thrombosis, pulmonary embolism, malignancy and hepatic and renal disease
- Patients on anticoagulants
- Patients with known coagulopathic disorders
- Patients requiring blood transfusion
- Polytrauma

Indication of admission

- GCS < 15
- GCS = 15 with
    - History of loss of consciousness, amnesia, vomiting and seizure
    - Focal neurological deficit
    - Signs of basal or calvarial fractures
    - Penetrating skull injury
    - Lesions in the CT scan

Patients presenting to the emergency department with the history of sustaining TBI were initially evaluated by the residents of department of surgery. Detailed history and examination findings were recorded. CT scan of the head, D-dimer and other routine investigations as needed were done before admission or sent later from the ward as needed. Patients were treated by the neurosurgery team in ICU, SICU or neurosurgery ward according to the severity of the injury. Patients were followed up and evaluated regularly and data regarding GCS, vital signs, D-dimer and record of mortality were collected in a preset proforma. D-dimer was sent within 24 to 72 hours of the injury. The normal value of D-dimer was taken as less than 200ng/mL and all values above 200ng/mL were taken as abnormal.

Out of 194 patients, 148 patients were included in the study. 46 patients were excluded from the study.

Outcome variables

Primary outcome:

- Glasgow outcome score

Secondary outcome:

- Duration of hospital stay
- Duration of ICU stay

Definition of variables

1. GCS: GCS score was determined using following guidelines:

Glasgow coma scale (recommended for age ≥4 yrs) [48]

Points	Best eye opening	Best verbal response	Best motor response
6	-	-	Obeys command
5	-	Oriented	Localises to pain
4	Spontaneous	Confused	Withdraws to pain
3	To speech	Inappropriate words	Flexion to pain (decorticate)
2	To pain	Incomprehensible sounds	Extension to pain (decerbrate)
1	None	None	None

Glasgow coma scale (recommended for age < 4 yrs) [48]

Points	Best eye opening	Best verbal response		Best motor response
6	-	-		Obeys
5	-	Smiles, oriented to sound, follows objects, interacts		Localizes pain
4	Spontaneous	Crying	Interaction	Withdraws to pain
		Consolable	Inappropriate	
3	To speech	Inconsistently consolable	Moaning	Flexion (decorticate)
2	To pain	Inconsolable	Restless	Extension (decerebrate)
1	None	None	None	None

2. Severity of head injury : Severity of head injury was graded based on GCS score.

Severity	GCS
Mild	13-15
Moderate	9-12
Severe	1-8

3. Glasgow outcome scale: The Glasgow outcome scale is a 5 level score:[49]

- Dead
- Vegetative state (meaning the patient is unresponsive, but alive)
- Severely disabled (conscious but the patient requires others for daily support due to disability)

- Moderately disabled (the patient is independent but disabled)
- Good recovery

4. Duration of illness: time period between trauma and the patient's first visit to emergency department. It is measured in hours in this study.

5. Duration of hospital stay: Number of days the patient is in hospital. Staying for a night is taken as one day.

6. Normal D-dimer level: < 200ng/mL

Statistical Analysis

The data were analyzed using the Statistical program for social sciences (SPSS) for windows (release 17.0). The relationship between duration of hospital stay, duration of ICU stay and GOS with D-dimer level were studied using Man-Whitney test. In addition Pearson Chi-square test was used to study the correlation of mode of injury and grade of injury with D-dimer level. P value of <0.05 was considered significant.

Results

One hundred and ninety four patients were admitted with the diagnosis of traumatic brain injury during the study period and out of them 148 patients were enrolled for the study after meeting the inclusion and exclusion criteria. Out of 148 patients one hundred and twenty (81.1%) were males and twenty eight (18.9%) were females. The mean age was 29.71±18.07 and the age ranged from one to seventy six years. Seventy (47.3%) patient were between twenty one to forty years of age. The mean duration of hospital stay was 9.83±13.58 days and the mean duration of ICU stay was 3.78±7.06 days.

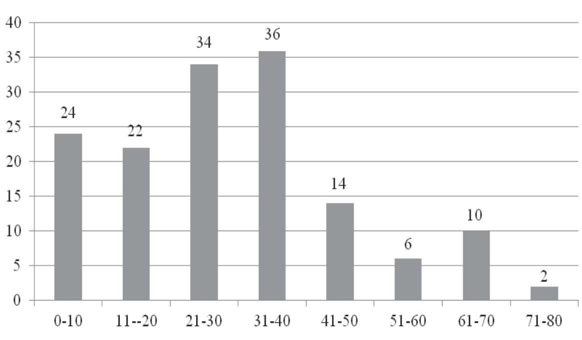

Figure 2 : Bar diagram showing distribution of patients according to age

Figure 3: Figure showing the frequency of patients in different sexes

The most common cause of TBI was fall injury which consisted of 72 (48.6%) patients.RTA was the second common cause with 58 (39.2%) patients, followed by physical assault in 11 (7.4%) patients and other modes in 7 (4.7%) patients. One hundred and fourty (94.6%) cases were accidental whereas 8 (5.4%) were homicidal.

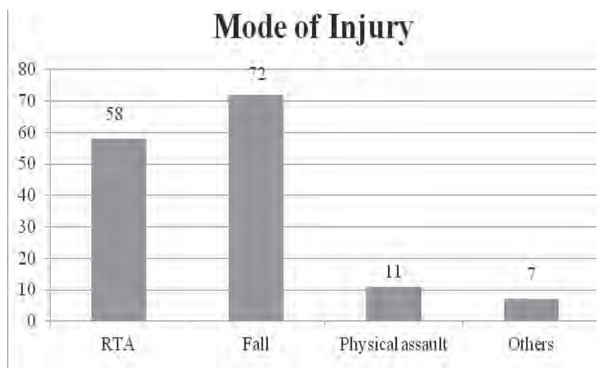

Figure 4: Figure showing frequency of patients with different modes of injury

Among the 148 patients ninety two (62.2%) patients sustained mild head injury, thirty (20.3%) patients sustained moderate head injury and twenty six patients (17.6%) sustained severe head injury. The most common symptom in these patients was headache followed by loss of consciousness and vomiting. Frontal lobe and the parietal lobe were the most common sites involved by trauma.

Different lesions seen in the CT scan are :

Table 1: Lesions in CT scan of the head

CT scan findings	Number	Percentage
Linear fracture	34	22.9
Depressed fracture	15	10.1
Epidural hematoma	42	28.3
Subdural hematoma	28	18.9
Contusion	48	32.4
Diffuse axonal injury	12	8.1
Pneumocephalus	12	8.1
Sub arachnoid hemorrhage	19	12.8
Global ischaemia	1	0.6
MCA territory infarct	1	0.6

Of the patients studied one hundred and eleven (75%) patients had good recovery with GOS of 5, nine patients (6.1%) had GOS of 4, six patients (4.1%) had GOS of 3, one patients (0.7%) had GOS of 2 and twenty one (14.2%) patients had GOS of 1.

Table 2: Number of patients with normal and elevated D-dimer level

D-dimer level	Frequency	Percentage (%)
<200	102	68.9
>200	46	31.1

Table 3: Man-Whitney test showing correlation between D-dimer and duration of hospital stay, duration of ICU stay and GOS

Man-whitney Test (Ranks)

	D-dimer	N	Mean Rank
Duration of hospital stay	<200	102	66.70
	>200	46	91.80
	Total	148	
GOS	<200	102	90.14
	>200	46	39.82
	Total	148	
ICU stay	<200	102	61.84
	>200	46	102.58
	Total	148	

Test statistics

	Duration of Hospital Stay	GOS	ICU Stay
Mann-Whitney U	1550.000	750.500	1054.500
Wilcoxon W	6803.000	1831.500	6307.500
Z	-3.312	-8.717	-5.759
Asymp. Sig. (2-tailed)	.001	.000	.000

Man-Whitney test shows higher D-dimer levels positively correlated with duration of hospital stay, duration of ICU stay and Glasgow Outcome Scale. Pearson chi-square test revealed higher levels of D-dimer correlated with grade of injury but negatively correlated with mode of injury.

Table 4: Chi-square test showing correlation of D-dimer with grade of injury

		Grade of Injury			Total
		Mild	Moderate	Severe	
D- dimer	<200	82	16	4	102
	>200	10	14	22	46
Total		92	30	26	148

Chi-Square tests

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	55.733[a]	2	.000
Likelihood Ratio	56.410	2	.000

Table 5: Chi-square test showing correlation of D-dimer with mode of injury

		Mode of Injury				Total
		Fall	Others	Physical Assault	RTA	
D-dimer	<200	53	5	6	38	102
	>200	19	2	5	20	46
Total		72	7	11	58	148

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	2.135[a]	3	.545
Likelihood Ratio	2.086	3	.555

Discussion

Traumatic brain injury is a common neurosurgical emergency with long term morbidity and mortality. Early institution of resuscitative measures with simultaneous investigations to define the type of the lesion is critical to the early management to improve outcome in head injury. The severity of the primary injury generally dictates the outcome; nevertheless secondary injuries have a profound effect in TBI and if detected early are treatable. One of the secondary phenomenons after a TBI is the hemostatic abnormalities. Hemostatic abnormalities vary between 10 to 97.5% with a mean of 32.7% in different studies. It is estimated the coagulpathy occurs in more than 60% of patients of severe traumatic brain injury and it is less than 1% in mild head injuries. [43]

Our study was done in patients of traumatic brain injury. This study shows male preponderance (81.08%) similar to that of the International mission on prognosis and analysis of clinical trials (IMPACT). [50] This study included 8720 patients of which 77% were male. The reason for male preponderance is obvious because males are more socially active and more aggressive than female. In this study 70 (47.3%) patient were between 21 to 40 years of age; the age of maximum economic productivity. Thirty six patients (24.3%) were below 16 years of age similar to the finding as reported by Alissa et al and Thiruppathy et al where the reported 32.2% and 22% , respectively.[51,52]

Fall from height was responsible for traumatic brain injury in 45.2% of patient in a study conducted by Iskhakov et al [53] . In our study the most common cause of head injury was fall responsible in 72 (46.6%) patients followed by RTA responsible in 58 (39.2%) patients. Majority of our patients sustained mild head injuries similar to other injuries as reported by Centre for disease control .

Nearly 32% of our patients presented within 12 hours of the ictus and the rest 68.2% presented only after 12 hours of the ictus. This probably is due to lack of nearby health services, difficult transport and concentration of neurosurgical facilities within the capital only.

The most common intracranial lesion in our study was contusion in 48 (32.4%) patients followed by EDH in 28.3% of patients. This is similar to a study conducted by Naseri et al [54] which showed contusion in 32.9% of patients followed by EDH in 27.1% of the patients.

Our study shows abnormal D-dimer in 40 patients (31.1%) which is consistent to studies conducted by Avikainen et al, Carrick et al, Stein et al, Tan et al and Hulka et al.[43] Out of 26 patients of severe head injury twenty patients (84.6%) patients had abnormal D-dimer level. Out of 92 patients of mild head injury 10 cases (10.86%) had abnormal D-dimer level, a finding not consistent to as reported by Gomez PA et al .[55] Out of 21 patients who died ,20 (95.2%) patients had higher D-dimer level. One patient who had GOS of 2 also had a higher D-dimer level.

In our study elevated D-dimer correlated with duration of hospital stay, duration of ICU stay and Glasgow outcome scale (GOS). In similar studies by J.-R Kuo et al , Saggar V et al, Bayir A et al , high D-dimer level correlated with Glasgow outcome scale in TBI. [18,41,42]

Limitations of the study

- Outcome observed in both operated and non-operated cases

- Quantitative assay of D-dimer not available at our institute

Conclusion

Elevation of D-dimer occur in significant proportion of patients of TBI. High level of D-dimer is associated with poor outcome in TBI. Detection of post traumatic coagulation abnormalities is important as early diagnosis and early treatment may help in recovery.

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