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Original Article

Contributing Factors for Coagulopathy in Traumatic Brain Injury

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Abstract

Context: In traumatic brain injury patients, coagulation disorder causes secondary brain injury, thereby increasing mortality and morbidity. **Aims:** The aim of this study is to identify the factors responsible for coagulopathy in traumatic brain injury. **Settings and Design:** This prospective longitudinal study from June 2012 included 100 patients with moderate and severe head injury presenting to National Institute of Neurological and Allied Sciences, Kathmandu, over 1-year period. **Subjects and Methods:** Patients were evaluated for the development of coagulopathy, defined as collectively three abnormal hemostatic parameters, and associated risk factors for coagulopathy. They were then analyzed for correlation with coagulopathy. **Statistical Analysis Used:** SPSS version 16 was used for the analysis of data. For identification of contributing factors, a stepwise logistic regression analysis was performed, including the factors with $P < 0.05$ from the analysis. **Results:** Among the 100 patients, coagulopathy was present in 63% of cohort. Forty-three patients had severe head injury, and 76.7% ($n = 33$) of them had coagulopathy compared to 52.7% ($n = 30$) in 57 patients with moderate head injury ($P = 0.013$). Statistically significant correlation with coagulopathy was present with polytrauma, severity of head injury, blood transfusion, surgical intervention, and Marshall's classification of CT of the head; however, stepwise logistic regression analysis showed that blood transfusion, surgical intervention, polytrauma, and severity of head injury were significant independent variables responsible for the development of coagulopathy. **Conclusions:** Traumatic brain injury is complicated with coagulopathy in up to 63% of patients. Blood transfusion, surgical intervention, polytrauma, and severity of head injury are significant independent variables responsible for coagulopathy.

Keywords: *Coagulopathy, secondary brain injury, traumatic brain injury*

Introduction

Primary brain injury results from the mechanical injury that occurs at the time of the trauma, whereas secondary brain injury is not closely related to the mechanism of injury. It occurs after the initial trauma and is affected by various factors. Posttraumatic coagulopathy, in particular, appears to be linked to secondary cerebral injury.[1,2] Coagulopathy not only exacerbate secondary brain injury but it may also be a marker of the degree of the primary injury.[3-5] Coagulation abnormalities are evident soon after trauma.[6-8] This study is an attempt to identify the factors responsible for the occurrence of coagulopathy in traumatic brain injury.

Subjects and Methods

One hundred patients with moderate-to-severe traumatic brain injury presenting to National Institute of Neurological and Allied Sciences, Kathmandu, Nepal, from June 2012 were included in this prospective analytical study. Nonprobability, purposive sampling technique was adopted, and patients with known coagulation disorder or on anticoagulants were excluded from the study.

Demographical data, causes of injury, and Glasgow Coma Scale (GCS) with findings of computed tomography (CT) of the head were recorded at the time of admission. Evaluation of hemostatic parameters, namely, platelet count, bleeding time (BT), computed tomography (CT), prothrombin time (PT), international normalized ratio (INR), activated partial thromboplastin time (aPTT), and fibrin degradation product (FDP) was measured at the time of admission and every 12 hourly thereafter for the first 7 days of admission. Patients with features suggestive of rapidly progressing coagulopathy were evaluated in the line of disseminated intravascular coagulation by evaluating D-dimer every 24 h.

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Coagulopathy was defined as abnormality of at least any three of the above parameters collectively.

Development of coagulopathy was analyzed with individual risk factor and its association was evaluated. SPSS version 16 (Chicago, SPSS Inc) was used for the analysis of data. All analyses with $P < 0.05$ were regarded significant. Continuous variables were evaluated with Wilcoxon two-sample test and Chi-square test or two-sided Fisher's exact test wherever required. Values were reported as mean ± standard deviation for continuous variables and as percentages for categorical variables. For identification of risk factors for the development of coagulopathy, a stepwise logistic regression analysis was performed, including the risk factors with $P < 0.05$ from the analysis. From each logistic regression analysis, adjusted odds ratio and 95% confidence interval were derived for each risk factor. An adjusted $P < 0.05$ was considered statistically significant.

Results

Over a period of 1 year, 100 consecutive patients with moderate and severe head injuries were included in the study. Abnormality of at least one hemostatic parameter among BT, CT, PT/INR, aPTT, platelet, FDP, and D-dimer was seen in 73 patients; however, only 63 developed coagulopathy as evident by abnormality of any three of the above-mentioned parameters.

Age of patients ranged from 7 to 77 years with mean age being 32.7 ± 14.5 years. Among the 63 patients with coagulopathy, 34.9% ($n = 22$) were in 20–30 years' age group. However, no significant correlation was found ($P = 0.735$) when age groups of patients were analyzed for coagulopathy. Males comprised 84% of the population, and among them, 63.1% had coagulopathy compared to 62.5% of females ($P = 0.964$) as shown in Table 1.

The time lapse from onset of injury to presentation to hospital ranged from 1 h to 72 h with a median of 11 ± 9.61 h. Patients were then grouped into 4 hourly intervals for the first 12 h and then subsequently into 12 and 24 hourly groups. Fourteen patients presented within 4 h of incident. Most number of patients, 38%, presented within 8 to 12 h of injury to the hospital. Development of coagulopathy was irrespective of delay in hospital presentation ($P = 0.491$) as shown in Table 2.

Out of 100, 72 patients sustained injury due to road accidents. Fall injury was the second most common cause of injury, followed by physical assault. Coagulopathy was seen in all groups of patients irrespective of different causes of injuries. No significant correlation was seen between the causes of injuries and development of coagulopathy ($P = 0.506$) as shown in Table 3.

History of alcohol consumption at the time of injury was present in 13 patients. Six of them sustained injuries from road traffic accidents (RTAs), 3 sustained fall injuries, and 4 had physical assaults.

Table 4 shows that coagulopathy was not related to alcohol intake at the time of injury as 61.5% of patients with history of alcohol intake had coagulopathy compared to 63.2% of patients with no history of alcohol ($P = 0.907$).

Severity of head injury was graded according to the GCS of the patients at the time of presentation. GCS of 3–8 was grouped as severe head injury and GCS of 9–12 as moderate head injury. Among the patients included in the study, 43 had severe head injury and 57 had moderate head injury. Coagulopathy was present in 76.7% of severe head injury patients compared to 52.7% in moderate head injury ($P = 0.013$) in Table 5.

Patients sustaining other injuries in addition to head injuries, including blunt abdominal injury or fracture of bones other than skull bones, were grouped as having polytrauma. A total of 63 patients were found to have polytrauma along

Table 1: Coagulopathy in different genders

Gender	Coagulopathy		Total	*P*
	Absent (%)	Present (%)		
Female	6 (37.5)	10 (62.5)	16	0.964
Male	31 (36.9)	53 (63.1)	84	
Total	37	63	100	

Table 2: Coagulopathy in delayed presentation

Delay in presentation (h)	Coagulopathy		Total	*P*
	Absent (%)	Present (%)		
0-4	4 (28.6)	10 (71.4)	14	0.491
4-8	8 (47)	9 (53)	17	
8-12	14 (36.8)	24 (63.2)	38	
12-24	11 (42.3)	15 (57.7)	26	
24-48	0	3	3	
48-72	0	2	2	
Total	37	63	100	

Table 3: Coagulopathy in different modes of injury

Modes of injury	Coagulopathy		Total	*P*
	Absent (%)	Present (%)		
RTA	26 (36.2)	46 (63.8)	72	0.506
Fall	7 (33.3)	14 (66.7)	21	
Physical assault	4 (57.2)	3 (42.8)	7	
Total	37	63	100	

RTA – Road traffic accident

Table 4: Coagulopathy in alcohol users

History of alcohol intake	Coagulopathy		Total	*P*
	Absent (%)	Present (%)		
Absent	32 (36.8)	55 (63.2)	87	0.907
Present	5 (38.5)	8 (61.5)	13	
Total	37	63	100	

with head injuries. Among the patients with polytrauma, 83.7% had coagulopathy as compared to 50.8% of patients without polytrauma ($P = 0.001$) as in Table 6.

Out of 100 patients, 81 patients required some form of surgical intervention within the period of study. Major surgical intervention requiring general anesthesia was performed in 67 patients, whereas minor interventions under local or intravenous anesthesia were performed in 14 patients. Among 67 patients undergoing major cranial surgeries, 70.14% developed coagulopathy compared to 21.43% among 14 patients undergoing minor surgical interventions ($P = 0.001$) as shown in Table 7.

Sixty-two patients received 2 or more units of blood transfusion during the study period. A single unit transfusion was avoided in all. Out of 67 patients requiring major cranial surgeries, 54 patients received transfusion whereas 2 patients with minor surgeries too required transfusion during the period because of blood loss before presentation to the hospital. Among 62 patients receiving blood transfusion, 75.8% had coagulopathy compared to 42.1% among 38 patients who had no transfusion ($P = 0.001$) as shown in Table 8.

Cranial CT scans of all patients were evaluated at the time of admission, and types of brain injuries were classified according to Marshall's classification.[9] No patient was categorized as "Evacuated Mass Lesions" according to Marshall's classification as the CT scans were evaluated at the time of admission itself before any intervention to the patient. Coagulopathy was frequent in patients having higher grade of diffuse injuries and mass lesion according to Marshall's classification compared to lower grades of injuries as shown in Table 9. Among 25 patients having Marshall's Grade I and II injuries, 44% developed coagulopathy, whereas among 75 patients having Marshall's Grade III and IV injuries and nonevacuated mass lesions, 69.33% developed coagulopathy ($P = 0.032$).

All independent parameters which had statistically significant correlation ($P < 0.05$) with coagulopathy were identified, and stepwise logistic regression analysis performed. Variables included were polytrauma, severity of head injury, blood transfusion, surgical intervention, and Marshall's classification. Table 10 shows that among the variables analyzed, blood transfusion ($P = 0.001$; odds ratio 4.30; 95% confidence interval 1.81 ± 10.25), surgical intervention ($P = 0.021$; odds ratio 0.388; 95% confidence interval 0.174 ± 0.867), polytrauma ($P = 0.028$; odds ratio 3.346; 95% confidence interval 1.138 ± 9.839), and severity of head injury ($P = 0.009$; odds ratio 0.249; 95% confidence interval 0.088 ± 0.706) were significant independent variables responsible for the development of coagulopathy.

Table 5: Coagulopathy in patients with moderate and severe head injuries

Severity of injury (GCS)	Coagulopathy		Total	*P*
	Absent (%)	Present (%)		
Severe (3-8)	10 (23.3)	33 (76.7)	43	0.013
Moderate (9-12)	27 (47.3)	30 (52.7)	57	
Total	37	63	100	

GCS – Glasgow Coma Scale

Table 6: Coagulopathy in polytrauma

Polytrauma	Coagulopathy		Total	*P*
	Absent (%)	Present (%)		
Absent	31 (49.2)	32 (50.8)	63	0.001
Present	6 (16.3)	31 (83.7)	37	
Total	37	63	100	

Table 7: Coagulopathy in operated patients

Surgical intervention	Coagulopathy		Total	*P*
	Absent (%)	Present (%)		
Major	20 (29.86)	47 (70.14)	67	0.001
Minor	11 (78.57)	3 (21.43)	14	
Total	31	50	81	

Table 8: Coagulopathy in transfused patients

Transfusion	Coagulopathy		Total	*P*
	Absent (%)	Present (%)		
None	22 (57.9)	16 (42.1)	38	0.001
Present	15 (24.2)	47 (75.8)	62	
Total	37	63	100	

Table 9: Coagulopathy in brain injuries according to Marshall's classification

Marshall's classification	Coagulopathy		Total	*P*
	Absent	Present		
Diffuse injury I	0	2	2	0.032
Diffuse injury II	14	9	23	
Diffuse injury III (swelling)	4	15	19	
Diffuse injury IV (shift)	5	16	21	
Nonevacuated mass lesion	14	21	35	
Total	37	63	100	

Table 10: Stepwise logistic regression for coagulopathy

Variables	*P*1	*P*2	*P*3	*P*4
Transfusion	0.001	0.001	0.023	0.064
Surgical intervention		0.021	0.026	0.027
Polytrauma			0.028	0.008
Severity of head injury				0.009

Variables examined: Polytrauma, severity of head injury, blood transfusion, surgical intervention, and Marshall's classification

Discussion

Traumatic brain injury patients are at risk of secondary brain injury due to various causes, coagulopathy being a major one. This study included 100 patients with moderate-to-severe traumatic brain injuries. Male comprised 84% of cohort and majority in all age groups, a

finding consistent with other studies.[7,10] Talving *et al.* had 78% males with overall mean age of 37 ± 20 years in his study of 436 patients with head injury, whereas a study by Affonseca *et al*. had 69.1% males.[11,12] The age distribution did not had significant correlation with the development of coagulopathy.

Out of 100 patients, 63 patients developed coagulopathy as evident by abnormality of collectively 3 or more hemostatic parameters evaluated. Coagulopathy was common in patients irrespective of gender as 63.1% of all males and 62.5% of all females developed coagulopathy. Coagulopathy was most common in age group of 20–30 as 22 patients in that age group developed coagulopathy.

Within 8–12 h of incident, 64% of patients presented to the hospital. However, analysis showed that the development of coagulopathy was not significantly related to delay in presentation to hospital. RTAs were most common cause of injury as 72% of cohort presented with RTA, followed by 21% with fall from height. Only 7 patients presented with history of physical assault. At the time of presentation, 6 out of 72 patients with RTA were under influence of alcohol, whereas 4 out of 7 with physical assault were under influence of alcohol at the time of presentation. Coagulopathy was equally common in all three groups of patients with different modes of injury. Role of alcohol intake at the time of presentation was found to be statistically insignificant in the development of coagulopathy, consistent to the findings by Lozance *et al*. in his study.[7]

Patients were divided as having moderate and severe head injury according to GCS at the time of arrival, mild head injury being excluded from the study. Out of 43 patients with severe head injury, 76.7% had coagulopathy compared to 52.5% of 57 patients with moderate head injury. Statistically significant association of coagulopathy with GCS was also reported by Talving *et al.* and Affonseca *et al*.[11,12] In the present study, 63 patients had polytrauma associated with head injury. Coagulopathy was frequent in patients with polytrauma as 83.7% of patients with polytrauma developed coagulopathy compared to 50.8% of patients with isolated head injuries. Affonseca *et al*.[12] had shown in his study that 65% of his patients had polytrauma, similar to our findings, and had concluded that the presence of coagulopathy is significantly higher in patients with associated chest and abdominal injuries.

About 2/3rd of patients required major surgical intervention out of which 80.6% required blood transfusion during the hospital stay. Major surgical interventions were performed in all the patients with diffuse injury IV and nonevacuated mass lesion group of Marshall's classification.[9] Coagulopathy was more common in patients with higher grades of Marshall's classification as they required major cranial interventions. Coagulopathy was seen in 70.14% of patients who had undergone major cranial surgeries compared to 21.43% of patients with minor interventions. Similarly, 75.8% of patients receiving blood transfusion developed coagulopathy as compared to 42.1% of patients among nontransfused patients. Pasternak has identified the use of blood transfusion as significant risk factors for the development of coagulopathy in his study which corresponds to our findings.[13] Kuo *et al.* had shown in his study that midline shift in CT scan correlated positively with development of coagulopathy, and degree of midline shift had inverse relationship with the Glasgow outcome scale of the patient.[1] The CT finding of midline shift in his study corresponds to Marshall's classification of Grade II and higher which has been followed in the present study.

The stepwise logistic regression performed including all parameters which were statistically significant in the development of coagulopathy confirmed that transfusion of blood, major surgical intervention, presence of polytrauma, and severity of injury as shown by GCS category of the patients were the most significant measurements in determining development of coagulopathy. Affonseca *et al*. reviewed 301 patients with traumatic brain injuries and found the following risk factors to be associated with the development of coagulopathy: GCS category, brain edema on CT, and polytrauma.[12] Talving *et al.* identified GCS score of <8, cerebral edema, and midline shift in CT scan as the independent risk factors for coagulopathy in patients with head injuries.[11] Marshall's classification of head injury in the present study was, however, found to be insignificant in the development of coagulopathy in the logistic regression analysis though it was found significant when analyzed individually.

Conclusion

Traumatic brain injury is often complicated by the presence of coagulopathy. In moderate-to-severe head injury patients, coagulopathy is present in about 2/3rd of the patients. Coagulopathy was equally common in both the genders and was not affected by the mode of injury. Blood transfusion, surgical intervention, presence of polytrauma, and severity of head injury according to GCS grading were significant independent variables responsible for the development of coagulopathy.

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Conflicts of interest

There are no conflicts of interest.

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