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The impact of coagulation profile derangements and their effect on the outcome of head injury patients. A prospective study

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ABSTRACT

Background: In traumatic brain injury patients, coagulation disorder causes secondary brain injury, thereby increasing mortality and morbidity.

Aim: This study aims to know the impact of coagulation profile derangements and their effect on the outcome of head injury patients.

Materials and methods: A total of 100 patients admitted with traumatic brain injury were included in the study. Samples of complete haemogram (CBC), prothrombin time (PT), partial thromboplastin time (PTTK), D-Dimers and fibrinogen were obtained. Coagulopathy was defined as platelet counts < 100,000 cells/mm2 and PTI >15 seconds or a DIC (Disseminated intravascular coagulation) score of more than 4. The outcome in each group was measured according to the Glasgow outcome score. The data were analysed with the Chi-square test and independent t-test.

Results: In patients with severe and moderate traumatic brain injury, there was no significant difference in the Haemoglobin, Fibrinogen and D-Dimer between the patients with and without coagulopathy. But the platelet count was significantly lower in the patients with coagulopathy and the PT and PTTK were significantly higher in the patients with coagulopathy in comparison to the patients without coagulopathy ($p<0.05$). There was no significant difference in the Fibrinogen and D-Dimer between the expired and discharged patients. But the platelet count was significantly higher in the discharged patients and the DIC score, PT and PTTK were significantly lower in the discharged patients ($p<0.05$).

Conclusion: Coagulation profile derangements are seen in patients with traumatic brain injury. Early diagnosis and prompt management can make remarkable improvements in the mortality of these patients.

Keywords
coagulation, head injury

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INTRODUCTION

Traumatic brain injury (TBI) is one of the most important causes of death and long-term disability in young adults (Boto et al. 2006). TBI has also been found to be a significant factor behind the deaths occurred in the very first day after trauma (Shackford et al. 1993). The incidence of coagulopathy in different types of TBI ranges from 10 to

97.3% (Lustenberger et al. 2010, Harhangi et al. 2008) and in case of acute brain injury, coagulopathy leads to hemorrhagic lesions (Oertel et al. 2002, Allard et al. 2009, Tian et al. 2010) and increased chances of mortality (Talving et al. 2009, Wafaisade et al. 2009).

Although the pathophysiology of TBI induced coagulopathy has not been completely understood, the following factors have been proposed to be responsible for the same: release of tissue factors (Goodnight et al. 1974, Keimowitz et al. 1973, Scherer et al. 1998), disseminated intravascular coagulation (Stein et al. 2004, Stein et al. 2002, Hulka et al. 1996), thrombocytopenia or platelets dysfunction (Carrick et al. 2005, Schnu¨riger et al. 2010, Nekludov et al. 2007, Engstrom et al. 2005), activation of protein C pathways (Cohen et al. 2007, Frith et al. 2010).

Early recognition of coagulopathy is of value in predicting the occurrence of delayed brain injury and may contribute to prevention of bleeding disorders (Stein et al. 1992). Most studies, however, report a mixture of early and delayed coagulopathy in isolated TBI, and knowledge about the prognostic value of acute, early diagnosed coagulopathy is therefore limited. A recent evaluation of a large German trauma registry revealed that 23% of patients with isolated TBI are presented with acute coagulopathy upon arrival of the emergency department, which was associated with increased morbidity and mortality (Wafaisade et al. 2010). Although the prevalence of coagulopathy increases in the period after admission to the emergency department, there are only limited data available about the evolvement of hemostatic parameters and the relative number of patients that develop delayed coagulopathy in the first days post-trauma (Carrick et al. 2005, Zehtabchi et al. 2008).

Therefore, the aim of the present study was to know the impact of coagulation profile derangements and their effect on the outcome of head injury patients.

Materials and Methods

This prospective observational study was carried out on 100 patients of head injury admitted in the Neurosurgery department of SMS Medical College Attached Hospital, Jaipur, Rajasthan from June 2020 to September 2021. Ethical approval was obtained from the institutional ethical committee and informed consent was taken from the patient attendants.

The inclusion criteria for the patients was that they should be within the age range of 1 to 70 years. The exclusion criteria for the patients were: i) patients having other associated injuries such as chest injury, bony injury, abdominal solid and hollow viscus injury etc., ii) patients having known case of hypertension, diabetes or any other chronic disease, iii) patients having pre-existing coagulopathy, taking anticoagulants or drugs which interfere with the laboratory testing and iv) patient have history of chronic alcohol intake, ongoing liver disease; history of of hepatotoxic drug intake and history of long time anti-inflammatory drug intake.

All the selected patients were divided based upon their GCS into two groups based on their GCS. There were two subgroups of patient moderate head injury (GCS 9-13) and severe head injury (GCS < 9). Initial resuscitation and subsequent management was done as per Advanced Trauma Life Support (ATLS). Samples for complete haemogram (CBC), prothrombin time (PTI), partial thromboplastin time (PTK), D-Dimers and fibrinogen were drawn. The blood was collected by venepuncture in EDTA vacutainers as well as PT tubes containing anticoagulant sodium citrate and processed immediately. Based on results of these blood investigations, DIC score was calculated and severity of the DIC was graded. DIC score was calculated (Table 1). After calculating the DIC score severity of the DIC was graded (Table 2).

Table 1. DIC score

	Platelet count (in lac)	PT Time (in secs)	APTT (in secs)	D-Dimer (µg/dl)	Fibrinogen (g/l)	Score awarded
Normal	>1.5	13.5	26-34	<1000	>1	0
Mild derangement	1-1.5	13.5-15.0	>34	1000-2000	<1	1
Moderate derangement	0.60-1.0	15-18	>39	2000-4000	<1	2
Severe derangement	<0.60	>18	>54	>4000	<1	3

Table 2. Severity of DIC

DIC Score	Inference
0-3	Normal
3-6	Mild derangement
7-10	Moderate derangement
>10	Severe derangement

Outcome was defined by the GOS (Glassgow outcome Score) and the comparison of presenting GCS was done with the GOS and DIC score was done. Coagulopathy- Coagulopathy was defined as platelet counts < 100,000 cells/mm2 and PTI >15 seconds or a DIC score more than 4. The outcome in each group was measured as discharged (GOS- 5) or vegetative state (GOS-2) or dead (GOS-1). During follow up of the patients GCS, cranial nerve palsy, haematoma formation (surgically operated), local surgical site infection and fever were noted.

Statistical Analysis

The data was tabulated in Microsoft excel software and analysed with SPSS v.24 software Statistical analysis was done by using chi square method and independent t-test. The p-value of <0.05 was considered as statistically significant.

Results

A total of 100 patients of isolated head injury were included in the study and were further categorized into moderate and severe head injury on the basis of GCS. The patients with GCS 3-8 were categorized as Severe Head injury (n=54) and patients with GCS 9-13 were categorized as moderate head injury (n =46). Among severe head injury (GCS 3-8) group, 31 (57.4%) patients out of 54 developed coagulopathy and in moderate head injury group 18 (39.1%) patients out of 46 developed coagulopathy. The demographic parameters, hospital stay and in-house mortality of the patients with severe and moderate TBI are shown in tables 3 & 4. In both the tables, there was no significant difference in the age and gender between the groups. But, total stay, ICU stay and outcome (death) were found to be significantly higher in the patients with coagulopathy ($p<0.05$).

The laboratory parameters of the patients with severe TBI was shown in table 5. There was no significant difference in the Haemoglobin, Fibrinogen and D-Dimer between the patients with and without coagulopathy. But, the platelet count was significantly lower in the patients with coagulopathy and the PT and PTTK were significantly higher in the patients with coagulopathy in comparison to the patients without coagulopathy ($p<0.05$).

The laboratory parameters of the patients with moderate TBI was shown in table 6. There was no significant difference in the Haemoglobin, Fibrinogen and D-Dimer between the patients with and without coagulopathy. But, the platelet count was significantly lower in the patients with coagulopathy and the PT and PTTK were significantly higher in the patients with coagulopathy in comparison to the patients without coagulopathy ($p<0.05$).

Table 7 shows the comparison of total DIC scores and the laboratory parameters of expired and discharged patients with severe TBI. Out of the 54 patients, 34 expired and 20 were discharged. There was no significant difference in the Fibrinogen and D-Dimer between the expired and discharged patients. But, the platelet count was significantly higher in the discharged patients and the DIC score, PT and PTTK were significantly lower in the discharged patients ($p<0.05$).

Table 8 shows the comparison of total DIC scores and the laboratory parameters of expired and discharged patients with moderate TBI. Out of the 46 patients, 5 expired and 41 were discharged. There was no significant difference in the Fibrinogen and D-Dimer between the expired and discharged patients. But, the platelet count was significantly higher in the discharged patients and the DIC score, PT and PTTK were significantly lower in the discharged patients ($p<0.05$).

Table 9 shows the comparison of total DIC scores and the laboratory parameters of expired and discharged patients with coagulopathy. Out of the 49 patients who developed coagulopathy, 35 expired and 14 were discharged. There was no significant difference in the platelet count, PT, PTTK, Fibrinogen and D-Dimer between the expired and discharged patients. But, the DIC score was significantly higher in the expired patients ($p<0.05$).

Table 10 shows the comparison of total DIC scores and the laboratory parameters of expired and discharged patients without coagulopathy. Out of the 51 patients who did not develop coagulopathy, 4 expired and 47 were discharged. There was no significant difference in the DIC score, PT, PTTK, Fibrinogen and D-Dimer between the expired and discharged patients. But, the platelet count was significantly lower in the expired patients ($p<0.05$).

Bivariate analysis was carried out to identify the risk factors associated with the development of coagulopathy (table 11). On bivariate analysis, severity of TBI, effaced basal cisterns on CT scan and low haemoglobin level were found to predict the development of coagulopathy ($p<0.05$).

Table 3. Association of demographic parameters, hospital stay and in-house mortality of severe TBI in presence or absence of coagulopathy

Parameters	Patients with coagulopathy (n=31)	Patients without coagulopathy (n=23)	P value
Age (years)	30.5±7.1	31.8±8.4	>0.05
Male:/Female	27:4	18:5	>0.05
Total stay (days)	13.4±2.7	6.8±1.5	<0.05*
ICU stay (days)	8.1±2.3	4.9±1.8	<0.05*
Outcome (Deaths)	20 (64.5%)	11 (47.8%)	<0.05*

Table 4. Association of demographic parameters, hospital stay and in-house mortality of moderate TBI in presence or absence of coagulopathy

Parameters	Patients with coagulopathy (n=18)	Patients without coagulopathy (n=28)	P value
Age (years)	33.5±8.6	29.2±6.4	>0.05
Male:Female	16:2	25:3	>0.05
Total stay (days)	12.7±3.5	7.1±2.9	<0.05*
ICU stay (days)	6.7±2.1	4.4±1.3	<0.05*
Outcome (Deaths)	8 (44.4%)	3 (10.7%)	<0.05*

Table 5. Association of laboratory parameters in severe TBI in presence and absence of coagulopathy

Parameters	Patients with coagulopathy (n=31)	Patients without coagulopathy (n=23)	P value
Hb	10.4±2.1	11.9±2.4	>0.05
Platelet	1.45±0.3	2.18±0.7	<0.05*
PT	20.2±4.4	14.6±4.1	<0.05*
PTTK	36.1±7.2	26.5±6.3	<0.05*
Fibrinogen	0.68±0.2	0.37±0.1	>0.05
D-Dimer	2761±884	2519±729	>0.05

Table 6. Association of laboratory parameters in moderate TBI in presence and absence of coagulopathy

Parameters	Patients with coagulopathy (n=18)	Patients without coagulopathy (n=28)	P value
Hb	11.2±2.7	12.9±3.1	>0.05
Platelet	1.52±0.4	2.37±0.8	<0.05*
PT	20.8±4.5	14.1±3.8	<0.05*
PTTK	35.7±7.3	25.9±6.9	<0.05*
Fibrinogen	0.73±0.2	0.42±0.1	>0.05
D-Dimer	2837±895	2489±706	>0.05

Table 7. Comparison of total DIC scores and the laboratory parameters of expired and discharged patients with severe TBI

Parameters	Expired (n=34)	Discharged (n=20)	P value
DIC Score	5.9±2.2	3.6±1.4	<0.05*
Platelet	1.72±0.4	2.61±1.3	<0.05*
PT	19.6±3.5	15.2±2.8	<0.05*
PTTK	34.3±7.1	24.1±6.4	<0.05*
Fibrinogen	0.75±0.2	0.47±0.1	>0.05
D-Dimer	2768±831	2504±634	>0.05

Table 8. Comparison of total DIC scores and the laboratory parameters of expired and discharged patients with moderate TBI

Parameters	Expired (n=5)	Discharged (n=41)	P value
DIC Score	7.6±3.1	3.4±1.1	<0.05*
Platelet	1.03±0.2	1.95±1.2	<0.05*
PT	18.7±3.2	14.2±2.4	<0.05*
PTTK	33.8±6.6	25.2±5.8	<0.05*
Fibrinogen	0.77±0.3	0.51±0.1	>0.05
D-Dimer	3015±912	2461±527	>0.05

Table 9. Comparison of total DIC scores and the laboratory parameters of expired and discharged patients with coagulopathy

Parameters	Expired (n=35)	Discharged (n=14)	P value
DIC Score	7.6±2.2	4.1±1.3	<0.05*
Platelet	1.26±0.2	1.57±0.5	>0.05
PT	35.1±7.2	31.7±4.3	>0.05
PTTK	36.7±8.4	34.2±7.1	>0.05
Fibrinogen	0.77±0.3	0.65±0.2	>0.05
D-Dimer	2806±793	2752±785	>0.05

Table 10. Comparison of total DIC scores and the laboratory parameters of expired and discharged patients without coagulopathy

Parameters	Expired (n=4)	Discharged (n=47)	P value
DIC Score	2.9±0.8	2.5±0.6	>0.05
Platelet	1.28±0.7	1.84±1.1	<0.05*
PT	16.5±3.1	14.7±2.2	>0.05
PTTK	28.4±6.1	25.7±5.9	>0.05
Fibrinogen	0.61±0.4	0.57±0.2	>0.05
D-Dimer	2513±844	2422±785	>0.05

Table 11. Risk factors for development of coagulopathy following isolated TBI

Parameters	Unadjusted odds ratio (95% CI)	P value	Adjusted odds ratio (95% CI)	P value
GCS ≤ 8	3.8 (1.6-5.9)	<0.05*	2.5 (1.4-4.8)	<0.05*
Effaced basal cisterns	2.1 (1.2-4.2)	<0.05*	2.5 (1.6-5.5)	<0.05*
Hb ≤10g/dl	2.4 (1.1-4.9)	<0.05*	2.9 (1.2-5.3)	<0.05*

*Statistically significant difference exists between the groups

Discussion

Traumatic brain injury is associated with activation of the coagulation cascade through fulminant cerebral tissue factor release, contributing to disseminated intravascular coagulation and cerebral microthrombi. This process is independent of bleeding. The subsequent disparity between clot formation and fibrinolysis in combination with coagulopathy may increase the risk for secondary bleeding and mortality. The present study showed a male predominance (86%) in the patients with TBI. This is in accordance with the studies done by Talving et al. in 2009 (78% males) and Affonseca et al. in 2007 (69.1% males).

In the present study, mortality was 39% which was at par with Affonseca et al. in 2007 and Greuters et al. in 2011. Coagulopathy was developed in 49% patients in our study which was in concordance with Affonseca et al. in 2007, but more than the mortalities reported in the studies by Greuters et al. in 2011 where it was 54% and by Harhangi et al. in 2008 where it was 33%.

The present study showed that the mean platelet count in the severe head injury group patients was lower than in patients of moderate head injury patients in our study. This finding is supported by the results of the study by Engstrom et al. in 2000, were they observed thrombocytopenia to be an independent risk factor for traumatic brain injury. In the present study, the mean PT in the severe head injury group was higher in the expired patients than the discharged patients. Saggar et al. in 2009 reported similar findings in their study.

In the present study, the mean D-dimers value was higher in the patients with severe than the patients with moderate head injury. Similar results were reported in the study by Scherer et al. in 1998 and Kuo et al. in 2007. They also reported that increased D-Dimer values was associated with poor prognosis in head injury patients. 35% of the patients in the present study had moderate DIC scores. Selladurai et al. in 1997, observed that 38% of their patients had moderate to severe DIC scores while Saggar et al. in 2009 observed 63% of their patients had moderate to severe DIC scores. Plasma fibrinogen concentration was found to be significantly higher among the patients who developed coagulopathy. Jovan et al. in 1998 in their study also reported similar results.

In the present study, severity of head injury (GCS ≤ 8), effaced basal cisterns on CT scan and haemoglobin level less than 10 g/dl strongly predicted the development of coagulopathy. Talving et al. in 2009 had also reported GCS ≤ 8 and presence of cerebral edema, SAH, SBP < 90 mm Hg, midline shift as the factors, which independently predicted development of coagulopathy. Similar findings were also reported by Affonseca et al. in 2007 in their study on pediatric patients where they found severity of head injury, presence of brain swelling, and injuries to chest and abdomen being associated with the development of coagulopathy

Conclusions

The present study concludes that, traumatic brain injury is complicated by the coagulopathy. The mortality of the patients with moderate or severe TBI can be predicted with the presence of coagulopathy and the severity of head injury. Early diagnosis and prompt management can make remarkable improvement in the survival rate of these patients.

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