

# Comparative Study of Derangement of Coagulation Profile between Adult and Pediatric Population in Moderate to Severe Traumatic Brain Injury: A Prospective Study in a Tertiary Care Trauma Center

## Abstract

**Object:** Coagulopathy is a common occurrence following traumatic brain injury (TBI). There are various studies showing incidence and risk factors of coagulopathy and their correlation with poor outcome in adult as well as paediatric age groups. Exact incidence, associated risk factors, treatment guideline for coagulopathy and its impact on outcome are still lacking. In our study we compared the adults and paediatric age groups TBI patients for incidence and risk factors of coagulopathy and its impact on outcome. **Methods:** Prospective study of 200 patients including 152 adult patients (age > 18 years) and 48 paediatric (Age < 18 years) patients of TBI admitted in intensive care unit of trauma centre of a tertiary care centre was performed from august 2015 to march 2016. Both population were further subdivided into moderate TBI and severe TBI as per Glasgow coma score (GCS). Patient with long bone injury, chest injury and abdominal injuries, coagulation disorder, liver disease, medical disease like diabetes mellitus and hypertension were excluded from study. Coagulation profile were compared in the both groups (Adult and paediatric) and correlated with the outcome. Chi-Square test, student t test and Odds ratios were used for statistical analysis. **Results:** Mean age among the adult and paediatric population were  $37.89 \pm 11.88$  years and  $11.41 \pm 5.90$ , respectively. Among the patient with moderate TBI, coagulopathy was seen in 30% patients of adult TBI whereas it was 12.5% among the paediatric TBI ( $P = 0.185$ ). Among the severe TBI group coagulopathy was observed in 68.03% and 37.5% of adult and paediatric age group respectively ( $P = 0.0016$ ). There was significant correlation found between midline shift and coagulopathy in the paediatric age group ( $P = 0.022$ ; OR - 4.58). E. There was significant association of coagulopathy and contusion on CT scan among the adult population ( $P = 0.007$ ; OR - 3.487) found whereas no such correlation were observed in paediatric population. **Conclusion:** Coagulopathy was significantly higher among the adult patient with severe TBI as compare to paediatric patient with severe TBI. There was no statistically significant difference in mortality among patients of both the age groups with coagulopathy.

**Keywords:** Adult, coagulopathy, Glasgow coma score, pediatric, traumatic brain injury

## Introduction

Traumatic brain injury (TBI) is the leading cause of mortality and disability among young adults and pediatric population. TBI, according to the World Health Organization, will surpass many diseases as the major cause of death and disability by the year 2020 with an estimated ten million people affected by TBI annually.<sup>[1]</sup> Coagulopathy is one of the important risk factors which leads to poor outcome in TBI patients similar to other risk factors including poor Glasgow coma score (GCS), absence of pupillary reaction, respiratory distress at the time of admission, and hypotension at the time of admission. The reported incidence of coagulopathy among

TBI patients varies from study to study and lies between 10% and 97%.<sup>[2-7]</sup>

Proposed mechanism of coagulopathy among TBI patients is the release of tissue thromboplastin from brain to circulation resulting in activation of clotting mechanism which leads to disseminated intravascular coagulation and consumption coagulopathy.<sup>[8]</sup> Coagulopathy has significant impact on the outcome of patient with TBI.<sup>[9]</sup> Mortality in severe TBI patients with coagulopathy is found to be nine times higher than severe TBI patients without coagulopathy.<sup>[10]</sup>

Immature brain reacts differently to insult due to TBI in comparison with mature brain as there is more neuroplasticity in the

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immature brain. Furthermore, there is significantly higher number of patients in the pediatric population with different mode of injury (fall from height [FFH]) than the adult patient with TBI. While reviewing literature thoroughly, not a single study was found which has compared the adult and pediatric population for variability of incidence and risk factors of coagulopathy and its impact on the outcome. Aims of the present study are to know the incidence of derangement of coagulation profile in moderate to severe TBI patients in adult as well as in pediatric population; to compare the differences in risk factors, magnitude of the problem, and their effect on prognosis and outcome among adult and pediatric population; and to know the prognostic significance of coagulopathy following TBI in moderate to severe TBI patients.

## Methods

Prospective study of 200 patients including 152 adult patients (age >18 years) and 48 pediatric patients (age <18 years) with moderate to severe TBI admitted to intensive care unit of trauma center of a tertiary care center was performed from August 2015 to March 2016. Patients with known coagulation disorder, liver disease, known medical diseases such as diabetes mellitus and hypertension (which is likely to influence the outcome) were excluded from the study. Patients with long bone injury, chest injury, and abdominal injuries were also excluded from the study.

After baseline evaluation of the patient, relevant blood investigations including coagulation profile such as platelet count, bleeding time (BT), clotting time (CT), prothrombin time (PT), international normalized ratio (INR), activated partial thromboplastin time (aPTT), fibrin degradation product (FDP) and D-dimer were sent. PostTBI coagulopathy was defined as platelet count <1 lakh, BT and CT more than the upper range of laboratory values, PT more than 1.5 times of the control, and aPTT more than 10 s of control, D-dimer >0.5 mg/l, and FDP >10 mg/l. Clinical status of all these patients was regularly followed to know the outcome (discharged or dead). Derangement of the laboratory values including coagulation profile was compared in both groups (adult and pediatric) and correlated with the outcome. The study was approved by ethical committee of the hospital.

Statistical analysis was performed with the MS Excel, PRIMER and SPSS, Trial version 20 for Windows statistical software package (SPSS Inc., Chicago, IL, USA). The categorical data were presented as numbers (percentage) and 95% confidence interval. To assess any significant association, Chi-square test and odds ratio (OR) were used. Groups were compared for quantitative data presented as mean and standard deviation by Student's *t*-test.  $P < 0.05$  was considered statistically significant.

## Results

A total of 200 patients including 152 adult patients (>18 years) and 48 pediatric patients (<18 years) were enrolled in this prospective study. We further subdivided both adult and pediatric groups into moderate (GCS; 9–12) and severe TBI (GCS;  $\leq 8$ ) groups. Male to female ratio among adult population was 5.3:1 (128 male and 24 female) whereas it was 3:1 (36 male and 12 female) among the pediatric population with TBI. Mean age among the adult and pediatric population was  $37.89 \pm 11.88$  years and  $11.41 \pm 5.90$ , respectively. Mean time lapsed from time of trauma to presentation at trauma center was  $224 \pm 36$  min among adult and  $108 \pm 26$  min among pediatric age group. Road traffic incidents (RTIs) were the most common mode of injury among both the age groups (90.73% vs. 59.18%) followed by the FFH (6.62 vs. 36.73).

Computed tomography scan (CT scan) finding among the adult population was commonly lobar contusions, acute subdural hematoma (SDH), subarachnoid hemorrhage (SAH), midline shift, scalp fracture, and extradural hematoma (EDH) in decreasing order of frequency, whereas among the pediatric population, lobar contusion, scalp bone fracture, EDH, acute SDH, and effaced cistern were common CT scan findings. Many of the patients had multiple CT finding among both the age groups.

Coagulopathy as defined in the methodology was present in 60.52% among the adult TBI group whereas it was 29.16% among the pediatric TBI group, irrespective of type of injury. Among the patients with moderate TBI, coagulopathy was seen in 30% of adult TBI group whereas it was 12.5% in the pediatric TBI group ( $P = -0.185$ ). Likewise in patients with severe TBI, coagulopathy was observed in 68.03%–37.5% among adult and pediatric TBI group, respectively ( $P = -0.0016$ ). There was significant difference in the derangement of coagulation profile between adult and pediatric TBI group in case of severe TBI ( $P = -0.0016$ ) whereas difference was not significant among moderate TBI group [Table 1].

On comparing the individual coagulation test values (platelet count, BT, CT, aPTT, INR, FDP and D-dimer), there was no significant difference in the derangement between both

**Table 1: The frequency of coagulopathy among adult as well as pediatric traumatic brain injury patients**

Injury group	Coagulopathy	Adult patients (%)	Pediatric patients (%)	<i>P</i>
Moderate TBI	Yes	9 (30)	2 (12.5)	0.1851
	No	21 (70)	14 (87.5)	
	Total	30 (100)	16 (100)	
Severe TBI	Yes	83 (68.03)	12 (37.5)	0.0016
	No	39 (31.96)	20 (62.5)	
	Total	122 (100)	32 (100)	

TBI – Traumatic brain injury

adult and pediatric population in moderate TBI, whereas in severe TBI group, FDP and D-dimer were significantly deranged in adult TBI patients as compared to pediatric TBI patients ( $P = -0.0093\%$ ) [Table 2].

There was no statistically significant correlation found between midline shift and coagulopathy in the adult group ( $P = -0.065$ ; OR: 1.85) whereas there was significant correlation observed between midline shift and coagulopathy in the pediatric age group ( $P = -0.022$ ; OR: 4.58). Effaced cistern was significantly correlated with coagulopathy in both adult and pediatric groups ( $P < 0.0001$  and  $0.0008$ ).

There was significant correlation between coagulopathy and contusion on CT scan among the adult TBI patients ( $P = -0.007$ ; OR:  $-3.487$ ) whereas no such correlation was observed in pediatric TBI patients. There

was no correlation of other CT finding and coagulopathy in both groups.

Leukocytosis and hemoglobin (Hb)  $<10$  g/dl at the time of admission were significantly associated with coagulopathy among the adult TBI patients whereas this association was not observed among pediatric TBI group ( $P = -0.0473$  and  $0.0003$ , respectively, and OR  $3.346$  and  $4.234$ , respectively).

Mortality was  $63.04\%$  among the adult patients with coagulopathy (58 of 92) whereas it was  $50\%$  (7 of 14) among the pediatric TBI patients with coagulopathy. There was higher mortality rate among the coagulopathy group in both adult and pediatric population, but there was no statistically significant difference in the mortality among both groups ( $P = -0.350$ ) [Table 3].

**Table 2: Various coagulation parameters and their frequency in adult as well as pediatric patients with moderate and severe traumatic brain injury**

(A) Moderate TBI			
Coagulation profile	Adult TBI (n=30)	Pediatric TBI (n=16)	P
Platelet count	5	0	0.0837
Bleeding time	1	1	0.6441
Clotting time	2	0	0.2910
INR	4	0	0.1264
FDP	23	10	0.3095
D-dimer	23	10	0.3095
aPTT	2	1	0.9565
(B) Severe TBI			
Coagulation profile	Adult TBI (n=122)	Pediatric TBI (n=32)	P
Platelet count	40	8	0.3973
Bleeding time	19	3	0.3724
Clotting time	15	3	0.6472
INR	44	7	0.1290
FDP	114	25	0.0093
D-dimer	114	25	0.0093
aPTT	10	3	0.8310

TBI – Traumatic brain injury; INR – International normalized ratio; FDP – Fibrin degradation product; aPTT – Activated partial thromboplastin time

**Table 3: The outcome in the patients with coagulopathy among adult as well as pediatric traumatic brain injury patients**

Coagulopathy	Patient's outcome	Adult patients (n=152)	Pediatric patients (n=48)	P
Yes	Survived	34 (36.96)	7 (50)	0.3505
	Not survived	58 (63.04)	7 (50)	
	Total	92 (100)	14 (100)	
No	Survived	55 (91.67)	32 (94.12)	0.6636
	Not survived	5 (8.33)	2 (5.88)	
	Total	60 (100)	34 (100)	

### Discussion

There are several studies in literature showing coagulopathy among the adult as well as pediatric population,<sup>[11-14]</sup> but none of the studies has compared the coagulopathy between adult and pediatric age group in reference to their incidence, associated risk factors, and their impact on outcome. We report a series of patients with isolated TBI including 152 adult and 48 pediatric patients and compared both the age groups for the difference in incidence, risk factor associated, and their impact on outcome.

Incidence of coagulopathy was  $60.52\%$  among the adult TBI group whereas it was  $29.16\%$  among the pediatric TBI group irrespective of the type of injury in our study. Among the patients with moderate TBI, coagulopathy was seen in  $30\%$  in adult TBI group whereas it was  $12.5\%$  in the pediatric TBI group ( $P = -0.185$ ). Likewise in patients with severe TBI, coagulopathy was observed in  $68.03\%$  and  $37.5\%$  among adult and pediatric TBI group, respectively. Incidence in our study comes in the range of reported incidence ( $10\%$ – $97\%$ ) of coagulopathy in literature in both age groups.<sup>[2-7]</sup>

On comparing the individual coagulation test values (platelet count, BT, CT, aPTT, INR, FDP and D-dimer), there was no significant difference found in the derangement between both adult and pediatric patients in moderate as well as severe TBI except that of FDP and D-dimer, which were significantly more deranged among the adult patients with severe TBI. There are several articles in literature showing the importance of individual coagulation parameter and their correlation with prognosis and outcome in adult as well as pediatric population.<sup>[6,14,15]</sup>

In our study, severe TBI (GCS  $<8$ ) is an independent risk factor for coagulopathy similar to the study by Macleod *et al.*<sup>[16]</sup> There are few studies showing the relationship between coagulopathy and CT finding.<sup>[3,17]</sup> In the study by Ueda *et al.*, patient with brain contusion had higher FDP levels. In our study, we found that there are significantly higher chances of coagulopathy in the adult patients with

TBI harboring contusion on CT scan in comparison with pediatric patients with TBI. There is no correlation found in SAH, acute SDH, and EDH with coagulopathy in our study among both the age groups. In our study, there is a strong correlation of midline shift with coagulopathy in pediatric TBI patients, but this correlation is not found true among the adult TBI group. Talving *et al.* had reported GCS <8, cerebral edema, SAH, and midline shift as a factor predicting the coagulopathy.<sup>[18]</sup> There is a significant correlation in effaced cistern and coagulopathy among both the age groups of our study. Chhabra *et al.* reported GCS <8, effaced cistern, Hb <10 g/dl, and D-dimer >1 mg/dl strongly predict the development of coagulopathy.<sup>[19]</sup> Similarly, we also found Hb <10 g/dl is a significant predictor of coagulopathy among the adult TBI group but not in the pediatric TBI group. In our study, we also observed that leukocytosis (total lung capacity >11,000) is strongly correlated with coagulopathy among the adult population, but same does not hold true for the pediatric group.

Overall mortality in our study is 36% which is comparable to mortality of 35% in the study by Chhabra *et al.* including both coagulopathy group and noncoagulopathy group of adult and pediatric population.

Albeit the difference is not statistically significant, the mortality was higher among adult TBI patients with coagulopathy (63.04%) in comparison to pediatric population (50%). This difference is probably due to the fact that immature brain has greater neuroplasticity in comparison to the mature brain. Several authors have reported a rise in mortality in the presence of coagulopathy, both in pediatric TBI patients as well as in adult TBI patients.<sup>[10,20-22]</sup> Hulka *et al.* reported that the patients who developed coagulopathy had nine times higher chances of mortality in a study of 159 adult patients with TBI.<sup>[10]</sup> Keller *et al.* reported in a study of 53 children with TBI that children who developed coagulopathy were at higher risk of death.<sup>[21]</sup> Chiaretti *et al.* found a significant correlation between the development of coagulopathy and poor outcome in a study of children with severe TBI.<sup>[23]</sup>

Despite our best effort, our study has certain limitations as the sample size of both groups is not equal, pediatric TBI group was smaller ( $n = 48$ ) as compared to adult TBI group ( $n = 152$ ); furthermore, ratio of severe TBI patients with moderate TBI patients was more in the adult population (4:1) than the pediatric population (2:1), that may be the cause of more coagulopathy among adult patients with severe TBI in comparison to pediatric patients with severe TBI. Among the pediatric population, TBI due to FFH is higher in younger age group whereas RTI is the major mode of injury among adolescents. We have taken both above-mentioned groups together in the pediatric

population, but there may be variability in the coagulation profile among both age groups. To add, to the best of our knowledge, our study is the first study in which we have compared the coagulopathy among adult and pediatric TBI patients for difference in incidence, associated risk factor, and their effect on the outcome.

## Conclusion

Coagulopathy is significantly higher among the adult patients with severe TBI in comparison with pediatric patients with severe TBI. There is no statistically significant difference in the mortality among both the age group patients with coagulopathy. Apart from low GCS, contusion on CT scan, midline shift, effaced cistern, and Hb <10 g/dl, we found leukocytosis is also significantly associated with coagulopathy in adult patients with TBI as compared to pediatric patients with TBI. Moreover, further researches with comparable number of patients in both adult and pediatric TBI groups are required to draw better conclusion.

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## Conflicts of interest

There are no conflicts of interest.

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