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PARAMETERS OF COAGULATION AND FIBRINOLYTIC PROFILE IN ISOLATED TRAUMATIC BRAIN INJURY

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Abstract

BACKGROUND & AIM- Traumatic brain injury (TBI) is the leading cause of death after trauma and major cause of long term physical and neurocognitive defects. TBI is linked with acute changes in the coagulation and fibrinolytic system which in turn is shown to have association with prognosis and clinical outcome of such patients. The study aimed to detect early coagulopathic changes and fibrinolytic profile after TBI and predict their relation to long term prognosis and outcome.

DESIGN- Prospective observational study

METHODS- The study included 300 admitted patients of isolated TBI. Coagulation and fibrinolytic profile was studied along with its association with clinical outcome. Blood samples were obtained for complete haemogram, prothrombin time (PT), activated partial thromboplastin time (APTT), fibrinogen and D-Dimers after injury. The clinical outcome was observed according to the Glasgow Outcome Scale (GOS). The data was analysed using statistical tests to establish the relation between early changes in coagulopathy and TBI.

RESULTS- The patients of TBI under study showed coagulation abnormalities whose values of the observed parameters co-related well with the severity of TBI. Platelet count was lower in patients with coagulopathy significantly and also found correlation with severity. PT and APTT were found to be higher significantly in coagulopathic patients and linked with severity of head injury. D-Dimers and fibrinogen concentration showed derangements in patients with coagulopathy but did not show any statistical significance as compared to patients without coagulopathy. Derangement in laboratory parameters was linked with GOS.

CONCLUSION- Coagulopathy is invariably present in the acute stage of isolated TBI. The laboratory parameters of coagulation and fibrinolytic profile were found to be reliable predictors of clinical outcome and long term prognosis of the TBI patients. Early diagnosis and management of coagulopathy can lead to improvement in morbidity and mortality in traumatic brain injury.

Key words: *Traumatic brain injury (TBI), coagulopathy, Fibrinoytic system..*

INTRODUCTION

Traumatic brain injury (TBI) is the principal cause of mortality after trauma or development of long standing physical and neuro-cognitive defects[1]. Primary harm to brain happens in the early phase of trauma while the secondary harm occurs because of continuing intracranial bleed and oedema with associated coagulopathy, which is one of the likely avertable source of morbidity/mortality. Retrospective observational researches have reported that associated coagulopathy is consistently observed in all traumatic brain injury patients[2]. TBI is usually linked with acute changes in the coagulation profile and fibrinolytic system[3]. Overall prevalance of TBI- associated coagulopathy was observed to be 32.7%-35.2% in a recent meta-analysis[4], which further proved the direct cor-relation between abnormal hemostasis and poor outcome of such patients.

Coagulopathy upon emergency room (ER) arrival in TBI still remains a powerful and
direct predictor of the immediate outcome and prognosis of the patient[5]. The laboratory parameters of coagulation have been considered as better predictors of the effect and mortality than the midline shift or pupillary reaction and directly linked ones are Platelet count, Fibrinogen, Prothrombin time ratio (PT/INR), Activated partial thromboplastin time (aPTT), D-Dimer etc[6].

Exact pathophysiology after TBI is unsatisfactorily recognised, although, studies report about coagulation derangements happen secondarily to tissue factor release (TF), which remains the physiological starter of regional and systemic coagulation/fibrinolytic pathways[7]. It is a vigorous process of hyper coagulability tailed by bleeding diathesis[8]. The hyper coagulable state can present with generalised disseminated intravascular coagulation (DIC) or in localised state such as micro thrombus formation around the contusion penumbra. Various suggested mode of actions are dysfunctioning of platelets and protein C activation pathways due to hypo perfusion[9,10]. Furthermore, DIC in isolated TBI along with hyper fibrinolysis modulates the patients outcome[11]. DIC when observed in the initial stage of TBI is one of the major factors in prediction of outcome of TBI[12].

Prothrombin Time is an indicator of functioning of common and extrinsic pathways of coagulation cascade. Various studies have suggested prolonged PT as the most congruous deviation of coagulation in TBI[13]. APTT is another significant predicting factor for outcome and prognosis in TBI patients and reported as prolonged in multiple meta-analysis and observational studies[14,15]. D-dimers are fragments of degraded products of cross-linked fibrin. It is a measure of continuing fibrinolysis, and its concentration levels have been shown to be rising more in head injury as compared to the other traumatic injuries[16]. A notable cor-relation of coagulopathy in TBI has been found with reduced fibrinogen and high D-dimer levels in several studies[17]. D-dimer has been suggested as one of the top parameter to observe for outcome prediction in a study by Ryuta Nakae et al[18].
Coagulopathy is invariably linked with graveness of TBI, GCS, outcome and prognosis of the head trauma patients. The objective of our study was to prospectively analyse the role of associated coagulopathy in TBI, cor-relation of various coagulation & fibrinolytic variables in TBI post injury such as PT/INR, aPTT, fibrinogen, D-dimers and their influence on outcome and prognosis.

MATERIAL AND METHODS

This prospective study was peformed on 300 patients of traumatic brain injury admitted in the Trauma centre of SMS Medical College and attached hospital, Jaipur, Rajasthan, from January 2023 to December 2023. Ethical approval was obtained from the institutional ethical committee. Informed consent was duly obtained from all the patients under study. The inclusion criteria was isolated traumatic brain injury patients. The exclusion criteria were patients with associated multiple trauma/chest or abdominal injury or with known coagulation disorders/associated co-morbidities and patients who presented after 24 hours of injury. The coagulation and fibrinolytic profile of the patients who met the inclusion criteria was assessed. Other routine investigations and NCCT head for diagnosis of injury were also done.
The concerned patients were split up into three categories based on their GCS scores:-

- Mild head injury (GCS >13)
- Moderate head injury (GCS 9-13)
- Severe head injury (GCS <9)

Early resuscitation and successive handling was managed according to the Advanced Trauma Life Support (ATLS). Blood specimens for haemogram (CBC), prothrombin time (PT), partial thromboplastin time (PTK), D-Dimers & fibrinogen were collected in EDTA vials and PT tubes having anticoagulant sodium citrate and were evaluated instantly. On the basis of blood evaluation results, DIC score was computed and grading of DIC severity was done (Table 1). Coagulopathy was established as platelet count < 1 lac and PT > 15 seconds, APTT > 35 seconds, or a DIC score > 4. The outcome in every class was assessed according to the Glasgow Outcome Scale (GOS) and defined as discharged (GOS-5) or vegetative state (GOS-2) or dead (GOS-1).

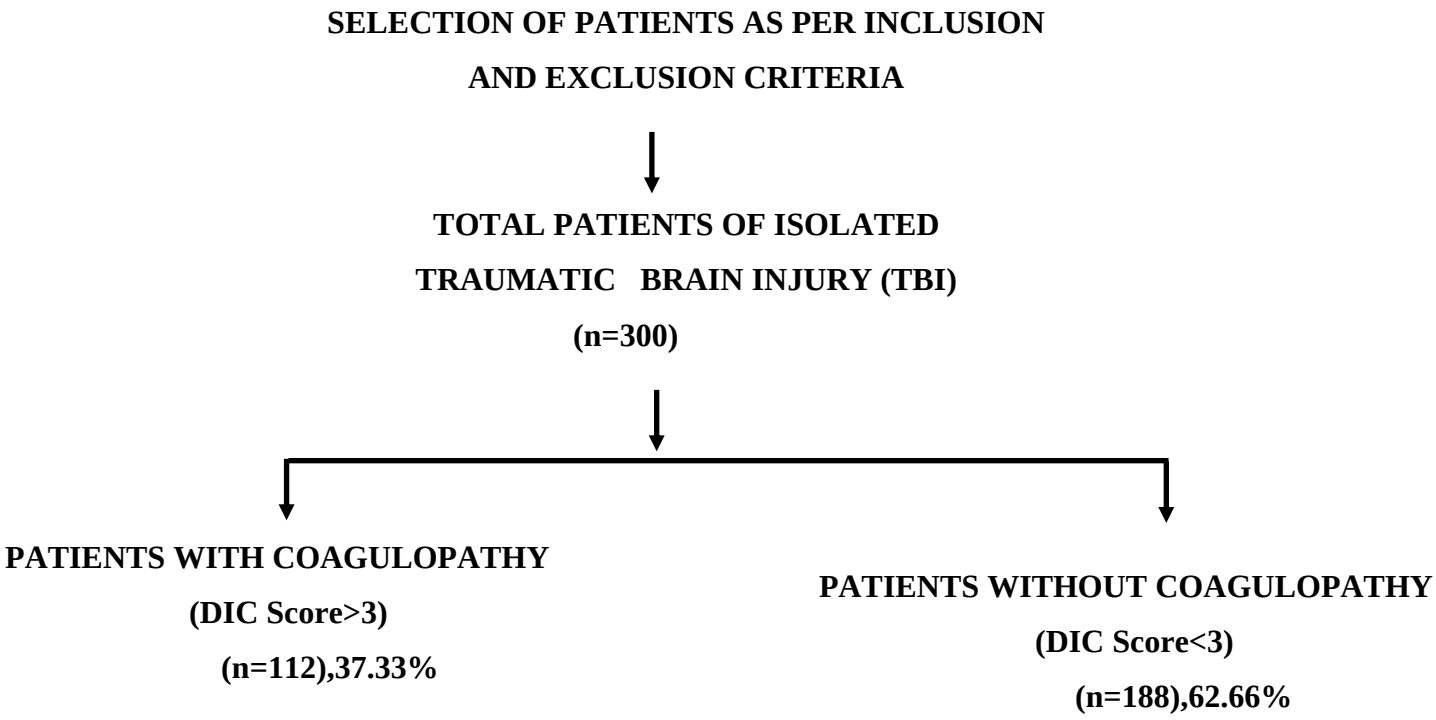

Fig.1. Flowchart of patient selection process

Table 1: Laboratory parameters with scoring system (DIC Score)

Severity	Platelet count(in lacs)	PT (in seconds)	APTT (in seconds)	D-dimers (ng/ml)	Fibrinogen(g/l)	Score for lab parameters	DIC score
Normal	>1.5	13.5	26-34	<1000	>2	0	0-3
Mild	1-1.5	13.5-15	>34	1000-2000	<2	1	3-6
Moderate	0.6-1.0	15-18	>39	2000-4000	<1.5	2	7-10
Severe	<0.60	>18	>54	>4000	<1	3	>10

Table 2 : Severity of DIC

DIC SCORE	INFERENCE
0-3	Normal
3-6	Mild derailment
7-10	Moderate derailment
>10	Severe derailment

STATISTICAL ANALYSIS

The data was computed and analysed in Microsoft Excel with SPSS v.29 software. The statistical analysis was finalised by chi square and independent t-test. The p-value of <0.05 was ascertained as statistically significant.

RESULTS

A sum of 300 patients of isolated TBI were involved in the study which were divided into mild, moderate and severe injury according to their GCS score. The patients with GCS >13 were labelled as Mild (n=124), with GCS 9-13 as Moderate (n =102) and with GCS <9 as Severe head injury (n=74). Amongst the severe group, 48/74 (64.8%) patients showed coagulopathy, among the moderate group 43/102 (42.1%) patients had coagulopathy while in mild injury group 21/124 (16.9 %) patients showed coagulopathy.

The demographic parameters i.e age & sex distribution of the TBI patients clearly depicted preponderence towards young adult males in comparison to other individuals as shown in Figure 2 . The mode of traumatic brain injury in study patients was assessed and shown in Figure 3, which showed roadside accidents (RSA) to be the leading cause of TBI (72%) while other causes being assault, fall from height etc.

The laboratory variables of severe TBI patients is depicted in Table 3. There was no significant difference observed in the Hb, Fibrinogen and D-Dimer values in the patients with or without coagulopathy. The platelet counts were found to be lower significantly in the patients having coagulopathy while PT & APTT values were higher significantly coagulopathic patients ($p<0.05$).

The laboratory parameters of the patients with moderate TBI was shown in Table 4. There was no significant difference in the Haemoglobin, Fibrinogen and D-Dimer between the two groups, the platelet count was significantly lower in the patients with coagulopathy and the PT and APTT were significantly higher in the patients with coagulopathy in comparison to the patients without coagulopathy ($p<0.05$).

Table 5 shows laboratory variables of mild TBI patients and there was statistically significant difference in the values of PT and APTT in both the groups. The PT and APTT were found to be higher in coagulopathic patients ($p<0.05$; significant).

Table 6 shows the co-relation of DIC score with the Glasgow outcome scale (GOS) in the TBI patients in relation to their severity i.e mild, moderate and severe TBI. The patients with poor DIC scores had worse outcome and p-value of <0.001 was observed (statistically highly significant).

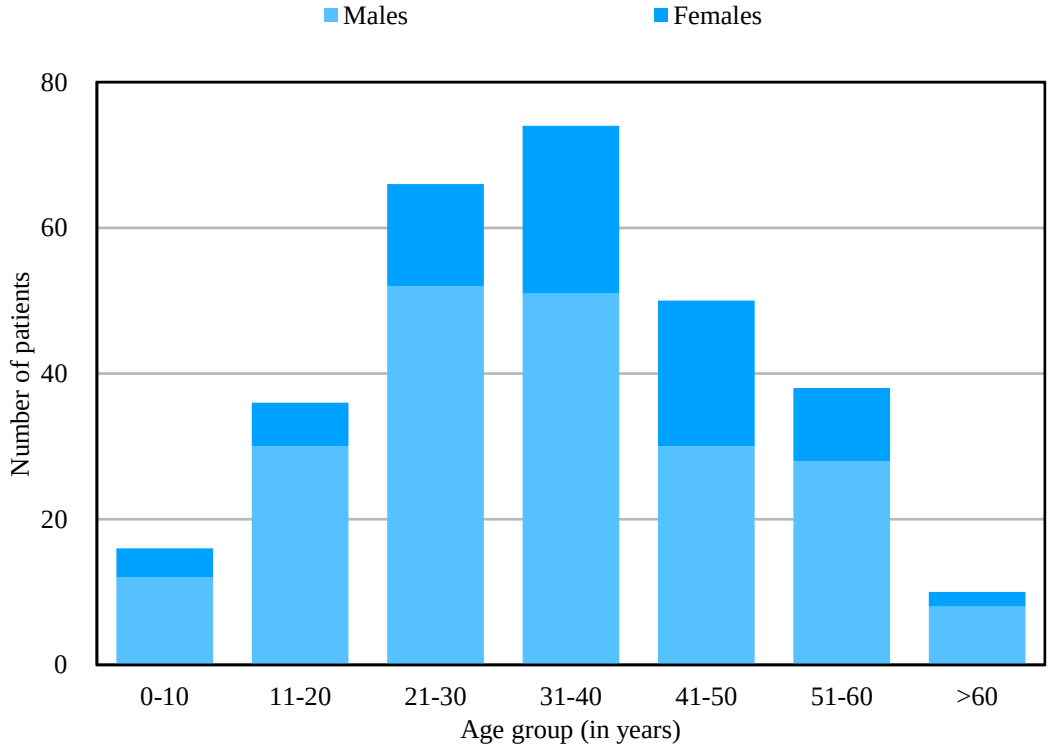

Fig.2 : Shows Age and Sex distribution of study population

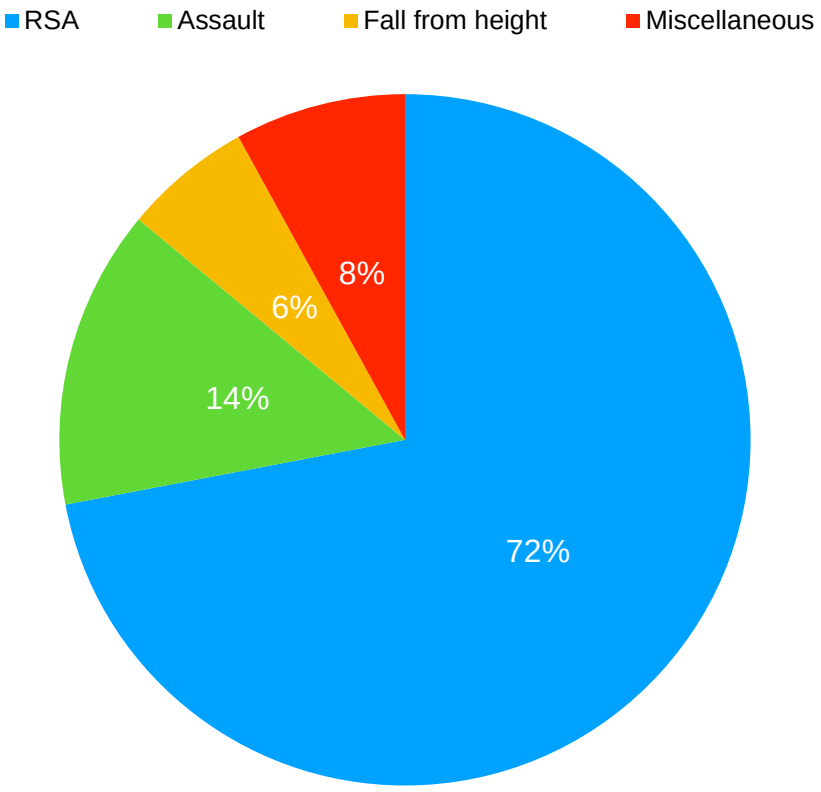

Fig. 3 : Data showing mode of injury (*RSA- Roadside accidents)

Table 3: Association of laboratory variables in Severe TBI in presence and absence of coagulopathy

Parameters	Patients with coagulopathy	Patients without coagulopathy	P-value
Haemoglobin(Hb)	10.3±2.1	11.8±2.4	>0.05
Platelet count	1.44±0.3	2.16±0.7	<0.05*
Prothrombin time(PT)	20.2±4.3	14.5±4.1	<0.05*
APTT	36.2±7.2	26.5±6.4	<0.05*
Fibrinogen	0.73±0.2	0.37±0.2	>0.05
D-Dimers	2764±883	2518±728	>0.05

*Statistically significant difference exists between the two groups

Table 4: Association of laboratory variables in Moderate TBI in presence and absence of coagulopathy

Parameters	Patients with coagulopathy	Patients without coagulopathy	P-value
Haemoglobin(Hb)	11.2±2.6	12.8±3.1	>0.05
Platelet count	1.51±0.4	2.38±0.7	<0.05*
Prothrombin time(PT)	20.9±4.4	14.2±3.7	<0.05*
APTT	35.7±7.2	25.8±6.9	<0.05*
Fibrinogen	0.67±0.1	0.36±0.1	>0.05
D-Dimers	2849±894	2450±702	>0.05

*Statistically significant difference exists between the two groups

Table 5: Association of laboratory variables in Mild TBI in presence and absence of coagulopathy

Parameters	Patients with coagulopathy	Patients without coagulopathy	P-value
Haemoglobin(Hb)	12.5±2.7	12.9±3.1	>0.05
Platelet count	2.42±0.4	2.37±0.8	>0.0.5
Prothrombin time(PT)	18.7±4.5	12.6±3.7	<0.05*
APTT	33.8±7.2	24.8±6.7	<0.05*
Fibrinogen	0.41±0.2	0.43±0.1	>0.05
D-Dimers	2830±892	2480±707	>0.05

*Statistically significant difference exists between the two groups

Table 6: Result of DIC score and GOS in relation with severity of TBI

	DIC score	GOS	*p*-Value
Severe head injury	6.34 ± 2.16	1.36 ± 1.78	< 0.001
Moderate head injury	4.43 ± 1.57	3.42 ± 1.60	< 0.05
Mild head injury	2.34 ± 2.29	4.4 ± 1.6	< 0.001

DISCUSSION

The incidence of traumatic brain injury has been increasingly on the rise nowadays, mainly due to an increase in the number of roadside motor vehicle accidents[19]. Road side accidents (RSA), physical violence and fall from height are primary cause of TBI. Many researches have reported RSA as the most consistent cause of injury[20] and our study observed RSA as the major means of TBI in approx 72% of casualties. Most of the patients in our study were found to be of young age i.e between 20-40 years and mainly males as they are more involved in outside pursuits, alcohol inebriation, driving etc. In review & meta-analysis of 82 researches, Nguyen et al[21] depicted major TBI cases in the adult male population. Another close result has been depicted by Frost et al[22] in meta-analysis and same results have been observed in many other studies[23].

The irregularities of coagulation in TBI have been approached extensively and it is linked with coagulation cascade activation via release of cerebral tissue factor which further leads to DIC & formation of micro thrombi in cerebral circulation. The resulting abnormality in clotting and fibrinolytic activity along with coagulopathic disorder can raise the chances of secondary bleed and morbidity.

Platelet dysfunction in TBI has been well established. Many researches have shown a predominant platelet dysfunction in severe TBI[24]. In our study, we found significant reduction of platelet count in coagulopathic patients as compared to patients not having coagulopathy and shows significant difference in relation to severity of TBI. It was observed that the mean platelet count in the severe and moderate TBI group was lower than in mild TBI group. This result was backed up in a study by Engstrom et al[25], in which reduced platelet count was reported as most consistent risk parameter in TBI.

In our study, the mean PT and APTT in the severe, moderate and mild TBI groups was higher in coagulopathic patients as compared to non-coagulopathic patients. The PT and APTT values were observed as statistically significant parameters in our study for all TBI patients. Derangement in these parameters were found to be higher in severe head injury in comparison to mild head injury. Saggar et al[26] reported similar findings in their study. Many more studies have found PT as the most consistent coagulation abnormality in patients of TBI[27,24,13]. The APTT values have been reported as prolonged in various studies[14,19,28]. A multivariate logistic regression analysis by Yuan et al[15] depicted INR>1.25, and APTT > 36 seconds as invariably associated factors with mortality in TBI. In present study, plasma fibrinogen levels were higher in the patients who showed coagulopathy but no relation was observed with severity of TBI. Same results were obtained in another study by Jovan et al[29].

D-dimer is a segment of degraded products of cross-linked fibrin and is a measure of progressive fibrinolysis. In our study, D-Dimers were observed having higher values in the TBI patients with coagulopathy, however showed no statistically significant value according to severity of TBI. Kuo et al[30] showed that D-dimers > 1,496 mcg/dL were linked with bad prognosis in TBI patients. Same results were observed in a research by Scherer et al[16].

DIC score was observed as major predictor of patients outcome (GOS). In our study, by analysis of DIC score with GOS, highly significant p-value of < 0.001 was reported. We observed that patients having poor DIC scores (> 4) during first 24 hours showed worst prognosis (GOS 1). Pahatouridis et al[31] depicted a correlation of head injury severity along with severity of coagulation disorder & found out that patients with lower GCS were at higher possibility of coagulation derangement. Van Gent et al[32] reported lower GCS score along with bad outcome in patients having coagulopathy during first 24 hours in comparison to patients with no coagulopathy. Talving et al[33] observed that GCS score < 8 is an independent variable in coagulopathy in TBI and coagulopathy was linked with more ICU stays and mortality. The research data suggests that coagulopathic disorder and GCS are inter-linked variables. Affonseca et al[20] and Greuters et al[14] found that presence of coagulopathy was directly linked to a bad outcome and had clear co-relation with prognosis. Macleod et al[27] showed initial coagulopathy as risk factor for mortality in trauma.

CONCLUSION

This study concluded that the patients of traumatic brain injury (TBI) have higher probability of progressive coagulation disorder. Coagulopathy is found invariably linked with the severity of TBI, GCS score and poor prognosis. DIC score is very valuable parameter in the depiction of outcome in TBI. The well timed interposition by early diagnosis and prompt management in TBI patients can lead to improvement in outcome and survival rate. The coagulation parameters are useful predictors of clinical outcome and course of the patient in the hospital.

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