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Prospective study of the association of coagulopathy and isolated traumatic brain injury

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ABSTRACT

The purpose of this study is to evaluate the association of coagulopathy and isolated traumatic brain injury as regard its frequency and outcome for patients who developed coagulopathy. This prospective study was conducted to include sixty patients with isolated traumatic brain injury admitted to attending the Emergency Department of Alexandria main university hospital. Primary survey and secondary survey done for those patients, radiological investigations done including CT brain and other radiological investigations to exclude other sources of coagulopathy. This also includes laboratory tests to asses coagulation as INR, platelet count, PTT and FDP for those who showed abnormality with the previous three tests. The frequency of coagulopathy in patients with isolated TBI is 8.3%. Brain edema is the most common CT finding in patients with coagulopathy following TBI as it is present in (80%) of case .SDH is the second most common CT finding in those who develop coagulopathy occurring in (60%) of patients. . All patients with coagulopathy had FDP >10 mic/ml and INR>1.3 ,while PTT >34 seconds in (80%) of patients who develop coagulopathy while platelets <100,000 cell/mm3present in (40%) of patients who developed coagulopathy .80%of cases who developed coagulopathy had deterioration of GCS, while (40%) developed DIC .Also (80%) had progressive hemorrhagic lesion. . Not all cases of TBI that has high levels of FDP had disseminated intra vascular coagulopathy.

Key words: isolated traumatic brain injury, coagulopathy disseminated intravascular coagulopathy

INTRODUCTION

Traumatic brain injury is a leading cause of traumatic death in patients younger than 25 years and accounts for nearly one third of all trauma deaths and disability worldwide. Every year, about 1.5 million affected people die and several millions receive emergency treatment worldwide, most of the burden 90 %is in low and middle income countries (Bruns et al 2003).

The ultimate survival and neurologic outcome of head trauma patient depend on the extend of brain injury occurring at time of injury with secondary systemic insult that worsen the resulting neurochemical and neuroanatomic pathophysiology (William 2006). The complex pathophysiological mechanisms behind the coagulopathy of TBI are multifactorial and remain poorly defined, but there are theories as:

Tissue factor hypothesis. It is assumed that TBI induces massive release of TF into the systemic circulation, which results in a widespread activation of the extrinsic coagulation cascade with possible

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consumptive coagulopathy and a depletion of coagulation factors and platelets. TF, the main physiological initiator of coagulation, is expressed, to a high degree, as a trans-membrane protein in different cell types of the central nervous system. Protein C pathway thus promoting hyper fibrinolysis and also inhibits the coagulation factors Va and VIIIa. Decreased platelet counts and or platelet function after TBI early after injury have been associated with increased coagulopathy.

Many studies have shown progression of parenchymal lesions, particularly in patients with coagulopathy (Chang et al 2006, Tan 2004). More-over, the presence of coagulation abnormalities is related to poorer outcome .Disorders of coagulation may be amenable to treatment, and adequate and prompt intervention may prevent secondary complications and poorer outcome.

PATIENTS AND METHODS

Patients:

The study was conducted on 60 patients with traumatic brain injury admitted to Emergency Department of Alexandria Main University Hospital. This study includes blunt isolated traumatic brain injured patients admitted within 24 hours of trauma. Patients with known coagulopathy, on anticoagulant therapy, Patients with injuries that affects coagulation as intra-abdominal collection, hemothorax etc were excluded from the study.

Methods:

Primary survey and secondary survey done for patients, radiological investigations done including CT brain and other radiological investigations to exclude other sources of coagulopathy. This also includes laboratory tests to asses coagulation as INR, platelet count, PTT and FDP for those who showed abnormality with the previous three tests.

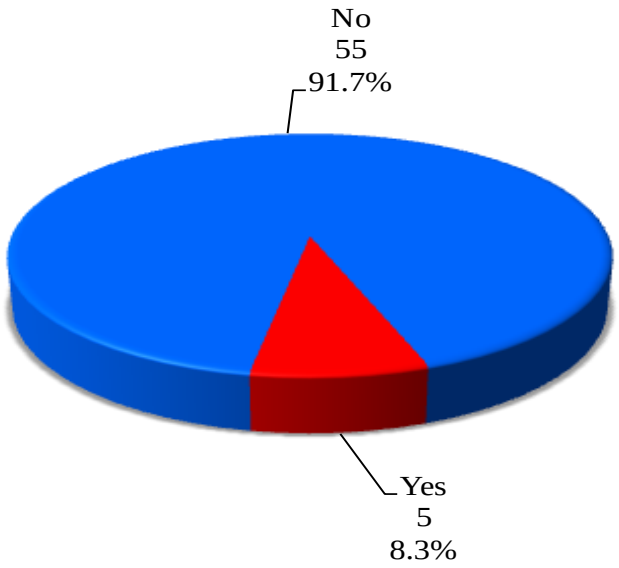
Statistical analysis:

The results were expressed as means, standard deviation (SD), counts and percentages. Univariate analysis was performed using a $\chi 2$ test for categorical data. Fisher's exact test was used when a data table had at least one cell with an expected frequency of < 5 .Differences were considered to be significant at the ($p \leq 0.05$) probability level. Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS 14) for Windows (SPSS,2005)

RESULTS AND DISCUSSION

Uncontrolled hemorrhage is a leading and preventable cause of death in patients with traumatic injury, accounting for 30-40% of all trauma fatalities. The present study was conducted to assess the overall frequency of acute post-traumatic coagulopathy upon hospital admission in patients with isolated blunt TBI, to evaluate the potential impact of acute coagulopathy on outcome. In this study the frequency of coagulopathy in patients with isolated TBI was 8.3% in agreement with retrospective and observational studies that shows that trauma associated coagulopathy is more common in patients with TBI (Stein et al 2004, Harhangi et al 2008) but its incidence varies considerably in the literature ,ranging from 10 to 97.2%. Many factors contribute to this variation including :heterogeneity of the patients ,types of laboratory tests used to define coagulopathy, the timing of performing these tests and the lack of clear consensus to define TBI associated coagulopathy (Salehpour et al 2011). Also Wafaisade and coworkers have recently assessed retrospectively the TR-DGU (Trauma Registry of the Deutsche Gesellschaft fur Unfallchirurgie) Trauma-Registry of the German Society for Trauma Surgery data-base for frequency, outcome, and risk factors of acute coagulopathy in isolated TBI.

Figure-1. Frequency of coagulopathy in patients with isolated traumatic brain injury.



Out of 3114 patients, 706 (22.7%) were coagulopathic upon emergency arrival. Also the study done by Epstein et al showed that the incidence of coagulopathy was (7.7%) %), he used initial INR ≥ 1.3 to define coagulopathy associated with TBI (Daniel et al 2014) this study disagree with the study done by (Cohen et al 2007) that showed that TBI alone does not cause early coagulopathy, but must be coupled with hypo perfusion to lead to coagulation derangement.

Table-1. Distribution of the studied cases according to Severity of head injury

	Development of coagulopathy				χ^2	^{FE}p
	No (n = 55)		Yes (n = 5)			
	No.	%	No.	%		
Severity of head injury						
Mild TBI	28	50.9	0	0.0	4.773	0.055
Moderate	15	27.3	1	20.0	0.124	1.000
Severe	12	21.8	4	80.0	7.934*	0.015*

Table-2. Distribution of the studied cases according to CT finding

	Development of coagulopathy				χ^2	^{FE}p
	No (n = 55)		Yes (n = 5)			
	No.	%	No.	%		
CT brain						
EDH	19	34.5	0	0.0	2.528	0.168
SDH	12	21.8	3	60.0	3.564	0.094
Contusion	32	58.2	2	40.0	0.617	0.644
SAH	12	21.8	1	20.0	0.009	1.000
Edema	16	29.1	4	80.0	5.345*	0.038*
IVH	1	1.8	2	40.0	14.067*	0.016*
Depressed Fracture	3	5.5	0	0.0	0.287	1.000
Fissure Fracture	15	27.3	1	20.0	0.124	1.000

As regard the severity of head injury the GCS was used to define the severity of TBI this in agreement with the study done by Wafaisade et al which showed that the GCS has been applied by several investigators to define the severity of TBI (Affonseca et al 2007). In this series (80%) of cases who developed coagulopathy had severe TBI and (20%) had moderate (TBI) but no cases who developed coagulopathy had mild TBI .Study done by (Talving et al 2009) showed that GCS < or equal 8 is independent risk factor for coagulopathy after TBI.

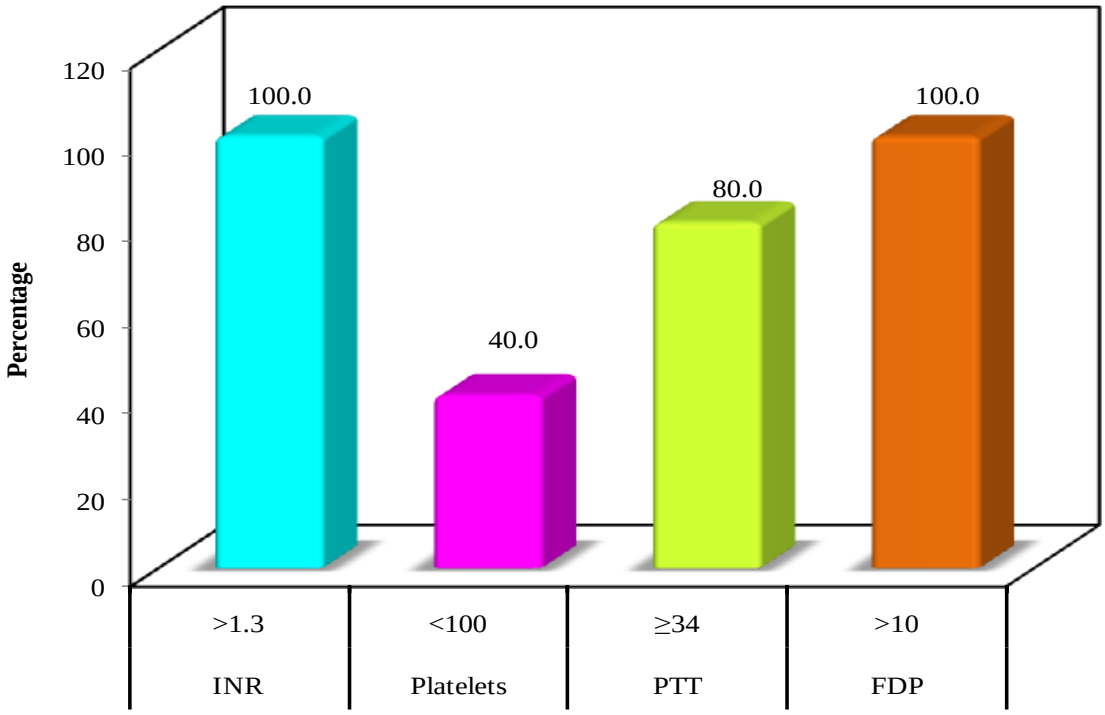
In this series, brain edema, subdural hemorrhage hemorrhagic contusions occurs more frequently in patients with coagulopathy. Several studies reported coagulopathy to occur most frequently with acute subdural hematoma (SDH), sub-arachnoid hemorrhage, or parenchymal contusions (Talving et al 2009) ,but in study done by Arasch et al incidence of SDH was significantly higher in coagulopathic patients, but none of the different types of intracranial pathologies were calculated to be independently associated with coagulopathy after TBI.

In the last decade, disseminated intravascular coagulation (DIC) has been proposed as an indicator of early TBI-related coagulopathy by the International Society on Thrombosis and Haemostasis, and the diagnostic criteria for DIC have recently been simplified (Sagger et al 2009 and Radha Krishnan D and Aditya M.G.V (2015). However, the DIC score has only been scarcely used to diagnose isolated TBI-related coagulopathy, and most studies rely on classical laboratory parameters like activated partial thromboplastin time (aPTT), the prothrombin time (PT), the international normalized ratio (INR) in the PT, fibrinogen levels and platelet count.

As regard laboratory investigations used to asses coagulopathy the standard laboratory tests used to measure hemostasis and bleeding risk in TBI patients include PT ,PTT and platelet count, PT and PTT was originally designed to asses activity of specific coagulation factors however, they are currently used to predict the bleeding risk in preoperative neurosurgical patients (West et al 2011) .The PT in Quick-% is preferred by the majority of German physicians and medical institutions, where a value of <70% is equivalent to an INR > 1.3 (Van Beek 2007)In this series INR was (>1.3) in 100% patients who develop coagulopathy. PTT in this series >36 seconds in (80%) of cases in agreement with M. A .Kumar which found that PTT is less affected than INR (23).

In this study , FDP was high in all cases who developed coagulopathy and (80%) of them died ,moreover studies done by Selladurai and colleagues 1997 found that high FDP levels predict poor outcome independently of other variables. that prognosis worsens as the level of FDP increases .Another retrospective study made in 2001 by

Figure-2. Distribution of the cases who developed coagulopathy according to laboratory findings to asses' coagulation



Vavilala and coworkers. extended the array of coagulopathy markers to fibrin degradation products FDP and examined the relationship between (FDP) and outcome in children with isolated head injury by reviewing the records of 69 patients. The authors concluded that FDP have strong prognostic value in children when GCS is between 7 and 12.

Table-3. Distribution of cases who developed coagulopathy according to outcome

	N=5	%
Deterioration of GCS	4	80%
Development of DIC	2	40%
Increase Hemorrhage on CT	4	80%
Death within 48 hours		
Development of multi organ	4	80%
failure	1	20%
Surgical intervention	1	20%

CONCLUSION

Coagulopathy occurs frequently in TBI. Coagulopathy is much more pronounced in patients with severe traumatic brain injury than in patients with mild or moderate TBI. Routine determination of the coagulation status should therefore be performed in all patients with traumatic brain injury. Cerebral edema and subdural hematoma are the most common CT findings in patients with coagulopathy after TBI. Not all cases of TBI that has high levels of FDP had disseminated intra vascular coagulopathy. Coagulopathy following TBI is frequent and important independent risk factor related to prognosis. Coagulopathy following TBI may be amenable to treatment.

Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

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