Original Research Article

Correlation of D-dimer and progressive haemorrhagic injury: An institutional based observation study from Hyderabad

Momin Abdul Jaleel[1*], Shukla Amit Shyamsunder[2], R Hari Kishore Reddy[3], G Ananth[4], Shailendra Anjankar[5], Shighakolli Ramesh[6]

[1]Senior Consultant, Department of Neurosurgery, Kamineni Hospitals, Hyderabad, Telangana, India
[2]Senior Resident, Department of Neurosurgery, AIIMS, Raebarelli, Uttar Pradesh, India
[3]Consultant Neurosurgeon, Hari Kishore Neuro and Spine Center, Proddatur, AP, India
[4]Assosciate Professor, Department of Neurosurgery, Kamineni Hospitals, Hyderabad, Telangana, India
[5]Assistant Professor, Department of Neurosurgery, AIIMS, Raipur, Chhattisgarh, India
[6]Assistant Professor, Department of Neurosurgery, Kamineni Hospitals, Hyderabad, Telangana, India

Received:19-09-2021 / Revised: 13-10-2021 / Accepted: 30-11-2021

Abstract

Introduction: Progressive microvascular failure is one of the major complications occurring after head injury and is associated with increased morbidity and mortality as well as poorer neurological outcomes. **Aims:** Our aim of this study is to find out correlation of D-dimer at time of admission with progressive haemorrhagic injury. **Materials and Methods:** Prospective observational study of 208 patients above 18 years of age who sustained TBI from April 2015 to May 2019. **Results:** 17 out of 18 patients (94.4%) in PHI group and 18 out of 190 patients (9.5%) in non-PHI group had raised D-dimer levels and it was found to be statistically significant in occurrence of PHI. **Conclusion:** D-dimer is associated with increased risk of PHI, so such patients with raised value of D-dimer can be taken early for surgery for better outcome.

Keywords:D-dimer,correlation

Background

Progressive haemorrhagic injury (PHI) is defined as the appearance of new lesions or a conspicuous increase in the size of haemorrhagic lesions (i.e., a 25% increase or more compared to the first post-injury CT scan)[1]. [Figure 1] The incidence of PHI reported is 20–60%[1]. For the majority of patients with TBI, progression of injury is observed in the first 24–48 hours, although a few patients can show progression as long as 72 hours after injury. These events are associated with increased morbidity and mortality as well as poorer neurological outcomes[2]. D-dimer (or D dimer), a small protein fragment present in the blood after a blood clot is degraded by fibrinolysis, has been shown to be associated with such progressive haemorrhagic injury[3].

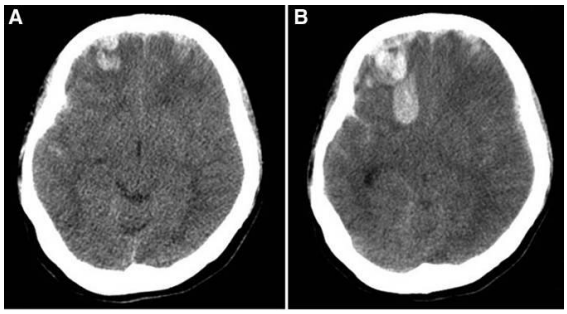

Fig 1.(A and B) Scans taken at 4 hours and at 12 hours respectively showing progression of bleed.

*Correspondence
Dr. Momin Abdul Jaleel
Senior Consultant, Department of Neurosurgery, Kamineni Hospitals, Hyderabad, Telangana, India
E-mail: momim@gmail.com

Aims

Our aim of this study is to find out correlation of D-dimer at time of admission with progressive haemorrhagic injury.

Materials and Methods

Prospective observational study of 208 patients above 18 years of age who sustained TBI from April 2015 to May 2019 admitted in Department of Neurosurgery, Kamineni Hospitals, L.B. Nagar, Hyderabad is the study group. Clinical, radiological and Laboratory parameters of these patients were studied. Sample size was calculated based on previous study by Yuan et al using the formula $N=Z^2PQ/L^2$, which was 130. Patients having long bone fractures, chest and abdominal injuries which can lead to increased D dimer levels has been excluded. We took sample size of 208 patients. Data was entered into Microsoft excel data sheet and was analysed using SPSS 22 version software. Chi-square test & Independent t test were used wherever appropriate. P value of <0.05 was considered as statistically significant.

Results

Mean age of the patients was 38.58 years with standard deviation of 16.641 in PHI (Progressive haemorrhagic Injury) group and 40.64 years with standard deviation of 15.532 in Non- PHI (Non - Progressive haemorrhagic Injury) group. [Table 1] There were 2 females (11.1%) and 16 males (88.9%) in the PHI group, while 39 females (20.5%) and 151 males(79.5%) in non-PHI group.

Table 1: Age distribution in PHI and Non- PHI group

	GROUP	N	Mean	Std. Deviation	P value
AGE	PHI	18	38.58	16.641	0.610
	Non-PHI	190	40.64	15.532	

8 cases of GCS 3-8 (44.4%), 6 cases of GCS 9-12 (33.3%), 4 cases of GCS 3 to 8 (22.2%) respectively in PHI group, while 13 cases of GCS 3-8 (6.8%), 39 patients of GCS 9-12 (20.5%), 138 patients of GCS 3 to 8 (72.6%) in non-PHI group respectively. [Table 2]
In our study, 17 out of 18 patients (94.4%) in PHI group and 18 patients out of 190 (9.5%) in non-PHI group had raised D-dimer levels and it was found to be statistically significant in occurrence of PHI. [Figure 2]. The outcome was significantly better in Non-PHI group as compared to PHI group when compared on Glasgow outcome score .[Figure 3]

Table 2: Comparisons of various variables in PHI and Non-PHI group

Variables		PHI	Non-PHI
Gender	Males	16	151
	Females	2	329
GCS	3-8	8	13
	9-12	6	39
	13-15	4	138
D-dimer	≤740 ng/ml	1	171
	>740 ng/ml	17	18

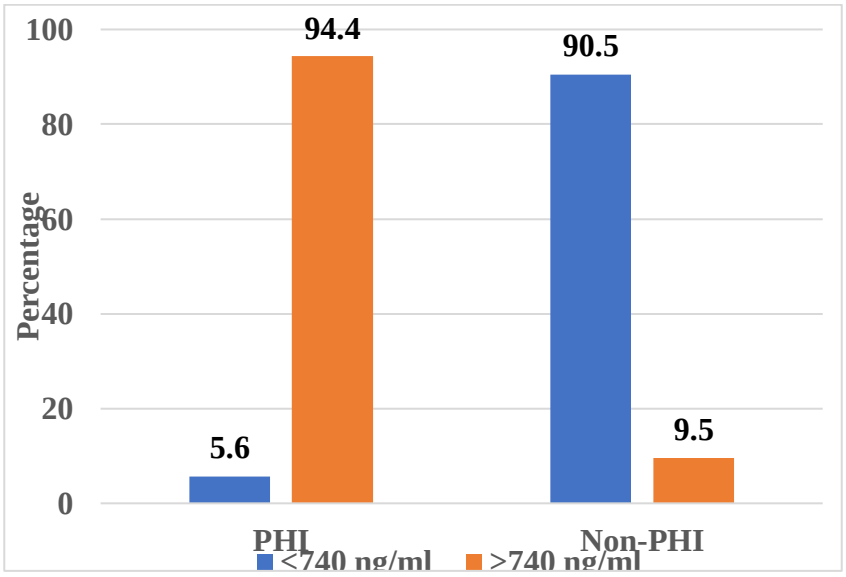

Fig 2: Graph showing Distribution of subjects according to D-DIMER level in PHI/non-PHI group

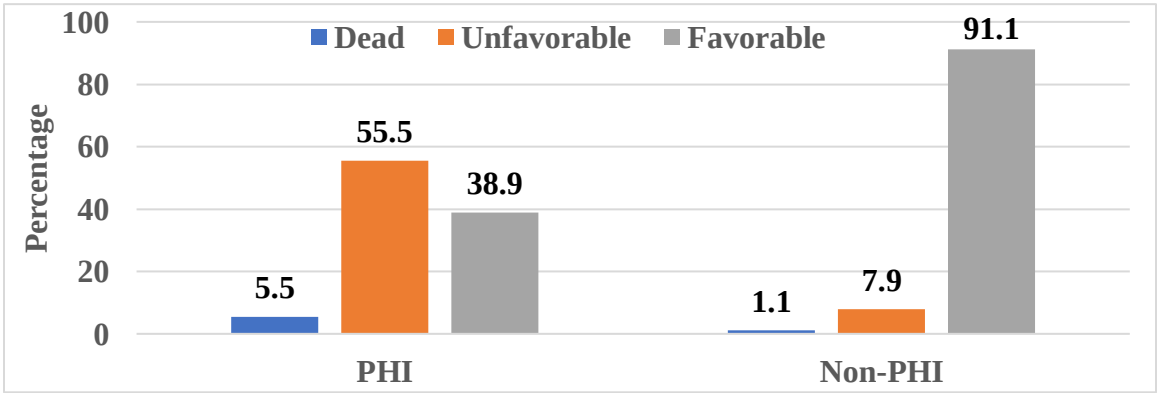

Fig 3:- Graph showing Distribution of subjects according to Glasgow outcome scale and PHI/non-PHI group.

Discussion

Traumatic brain injury (TBI) is defined as an insult to the brain caused by external physical force that may produce a diminished or altered state of consciousness resulting in an impairment of cognitive abilities or physical functioning. Profound disturbances of cognitive, emotional, and behaviour functioning after TBI may produce

permanent impairments that may result in partial or total functional disability and psychosocial maladjustment.(A) Head injury is one of the most important public health problems. The incidence of head injuries is rising all over the world. Its global incidence is rising, and is thought to surpass many diseases as a major cause of death and disability by the year 2020.TBI continues to cost millions of lives around the world on an annual basis.(B) TBI is responsible for causing one-third to one-half of all trauma deaths and is the leading cause of disability in people under forty, severely disabling 15–20/100,000 populations per year.(C) According to WHO, about 90% of deaths due to injuries occur in low- and middle-income countries (LAMICs), where 85% of population live, and this situation will continue to pose an important global health problem in the upcoming years.(D,E) TBI is a leading cause of mortality, morbidity, disability, and socioeconomic losses in India as well. It is estimated that nearly 1.5–2 million persons are injured, and 1 million die every year in India. India and other developing countries are facing the major challenges of prevention, prehospital care, and rehabilitation to reduce the burden of TBIs.(F)

According to the Centers for Disease Control, there is overall increase in TBI-related emergency department visits, hospitalizations, and deaths in the decade 2001–2010.(G)

However, taken individually, the total number of deaths related to TBIs has decreased over this same period of time due to increased awareness, evolving new guidelines and significant technological advancements in current treatment regimens.

Progressive hemorrhagic injury (PHI) was defined as the appearance of new lesions or a conspicuous increase in the size of hemorrhagic lesions (i.e., a 25% increase or more compared to the first post-injury CT scan) (H 14,I 15). Incidence of PHI has varied in different studies. It is one of the major complications occurring after head injury. Thus, it needs to be kept under check. There are certain variables which are associated with PHI but no cause-effect relationship has been elucidated. A hypothesis is proposed named "progressive microvascular failure" to explain the main cause of haemorrhagic progression of traumatic brain contusion[4,5]. The kinetic energy from a focal impact is delivered to the surface of the brain and follows a three-dimensional Gaussian-like distribution, with the epicentre receiving the peak amount of energy and a progressive dissipation of energy taking place as it moves away from the cortex[4,5].

Yuan et al showed that there are various factors in predicting progressive hemorrhagic injury after traumatic brain injury. They were old age, male patients, low platelet count, PT/INR, APTT, Blood glucose levels, D-dimer. They studied these factors and concluded that they are significant in predicting PHI[1]. In the present study we have focussed on the role of D-dimer as an early marker for PHI. J Zhang et al in their review article showed that they studied eight articles and examined the predictive role of D-dimer for the risk of PHI. The pooled OR was 1.71 (95% CI, 1.23-2.42)[3]. Tian and the colleagues studied 194 patients and 41.8% demonstrated PHI on the second CT scan. High D-dimer level was found in 71.4% patients having PHI[6]. Juratli et al in their study showed that 42.1% in non-PHI and 64%-81% in PHI group had raised D-dimer levels[7]. Yuan et al showed that patients with higher D-dimer levels had higher odds ratio (9.95) in PHI group as compared to non-PHI group, yet no significant relationship was found between D-dimer level and the risk of poor functional outcome at 3 months (3M GOS $\leq$3)[1]. In our study, 17 out of 18 patients (94.4%) in PHI group and 18 out of 190 patients (9.5%) in non-PHI group had raised D-dimer levels and it was found to be statistically significant in occurrence of PHI. There is usually a dilemma on whether to operate a small contusion or not. Authors found out that if D-dimer is raised there is more chances of progressive haemorrhagic injury and hence such patients must be monitored vigilantly in intensive care units and surgery should be considered with correction of coagulation parameters if required. The contusion should be evacuated to avoid increased intracranial pressure and further irreversible neurological damage.

Conclusion

D-dimer is associated with increased risk of PHI, consequently leading to failure of conservative management. Such patients can be taken early for surgery for better outcome, irrespective of the initial small size of contusion. Coagulation abnormalities can be corrected to intercept the formation of PHI. Abnormality of such variables can make one more vigilant towards these patients and can do intervention at right time in order to improve outcome of the patient.

Conflict of Interest: Nil Source of support: Nil

References

1. Yuan F, Ding J, Chen H, Guo Y, Wang G, Gao WW, et al. Predicting Progressive Hemorrhagic Injury after Traumatic Brain Injury : Derivation and Validation of a Risk Score Based on Admission Characteristics. J Neurotrauma. 2014;29(12):2137–42.
2. Vedantam A, Yamal JM, Rubin ML, Robertson CS, Gopinath SP. Progressive hemorrhagic injury after severe traumatic brain injury: effect of hemoglobin transfusion thresholds. Journal of neurosurgery. 2016 Nov 1;125(5):1229-34.
3. Zhang J, He M, Song Y, Xu J. Prognostic role of D-dimer level upon admission in patients with traumatic brain injury. Medicine. 2018 Aug;97(31)..
4. Simard JM, Kilbourne M, Tsymbalyuk O, Tosun C, Caridi J, Ivanova S, Keledjian K, Bochicchio G, Gerzanich V. Key role of sulfonylurea receptor 1 in progressive secondary hemorrhage after brain contusion. Journal of neurotrauma. 2009 Dec 1;26(12):2257-67.
5. Patel AD, Gerzanich V, Geng Z, Simard JM. Glibenclamide reduces hippocampal injury and preserves rapid spatial learning in a model of traumatic brain injury. Journal of Neuropathology & Experimental Neurology. 2010 Dec 1;69(12):1177-90.
6. Tian HL, Chen H, Wu BS, Cao HL, Xu T, Hu J, et al. D-dimer as a predictor of progressive hemorrhagic injury in patients with traumatic brain injury: Analysis of 194 cases. Neurosurg Rev. 2010;33(3):359–65.
7. Juratli TA, Zang B, Litz RJ, Sitoci KH, Aschenbrenner U, Gottschlich B, , Sobottka SB. Early hemorrhagic progression of traumatic brain contusions: frequency, correlation with coagulation disorders, and patient outcome: a prospective study. Journal of neurotrauma. 2014;31(17):1521-7.
8. Kamal VK, Agrawal D, Pandey RM. Epidemiology, clinical characteristics and outcomes of traumatic brain injury: Evidences from integrated level 1 trauma center in India. Journal of neurosciences in rural practice. 2016 Oct;7(4):515.
9. Murray C, Lopez A. Global health statistics: A compendium of incidence, prevalence, and mortality estimates for over 200 conditions. Global burden of disease and injury series 2. 1996.
10. Gururaj G. Epidemiology of traumatic brain injuries: Indian scenario. Neurological research. 2002;24(1):24-8.
11. Taylor CA, Bell JM, Breiding MJ, Xu L. Traumatic brain injury–related emergency department visits, hospitalizations, and deaths—United States, 2007 and 2013. MMWR Surveillance Summaries. 2017;66(9):1