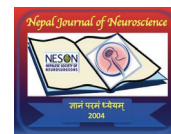


Determination of coagulopathy in acute traumatic brain injury and its effect on outcome

Safroz Ansari¹, Aditya Prakash Yadav², Masood Quazi³^{1,2,3} Neurosurgery Unit, Department of Surgery, National medical College and Teaching HospitalDate of submission: 5th May 2023Date of acceptance: 25th September 2023Date of publication: 15th October 2023

Abstract

Introduction: Coagulopathy after traumatic brain injury is quite a common finding. But its role associated with poor outcomes is still debatable. This study was designed to assess the frequency, and association of coagulopathy in outcome after TBI.

Materials and Methods: Single institute prospective study in isolated traumatic head injury was included and outcome was evaluated based Glasgow Outcome Scale recorded at the time of discharge. Coagulopathy was defined as deranged value of aPTT >39s, PT>14s, INR>1.2 and Platelets< 1.5lakhs.

Results: Among 405 subjects, mean age of the study population was 28.65 years, majority of the subjects were in the age group of 5-25 years 40.99%, 63.70% were males, mild condition 90.37%, whereas 8.39% presented with moderate and only 1.23% was having severe injury, The mean PT, INR & APTT were 13.69 seconds, 1.1 and 34.50 seconds respectively. The mean platelet count was 261231.9. Majority of the patients were having good recovery 93.1%, 5.5% had Moderate disability and 1% had severe disability, whereas two patients expired, patients with death and severe disability had higher proportions of coagulopathy, which was also statistically significant coagulopathy.

Conclusions: Coagulopathy is significantly associated with unfavorable outcome, though coagulopathy is not an independent factor for poor outcomes in isolated traumatic brain injury.

Key words: Traumatic Brain Injury, Glasgow Outcome Scale, Coagulopathy

Introduction

Traumatic brain injuries (TBI) result from external mechanical force applied to head. Majority of the TBI cases are result of RTA, followed by physical assault and occupational injuries, falls, and sports injury. Almost two thirds will not be able to return to their premorbid functional level¹. Male predominance with most often productive age group causes economic setback not for only one's family but also the country². The prognosis of TBI depends on

many factors. The major dependent factor for outcome depends on the severity of primary injury. However, secondary injury such as cerebral ischemia, raised ICP and coagulopathy have been shown to worsen survival after TBI.³ Prevention of secondary brain injuries is the mainstay of treatment in any head injuries which are potentially reversible. Coagulopathy is present in almost 25% of the traumatic cases at the time of admission⁴. Hypothermia, acidosis, consumption of clotting factors, plasma dilution from intravenous fluid and packed cell administration are widely believed as cause of coagulopathy. However, traumatic coagulopathy is present early in the postinjury phase before fluid administration and in normothermic patients⁶. Further, while acidosis per se affects coagulation protease function, clot time and maximum clot firmness are only impaired at very low pH (<6.8)⁷. Coagulopathy occurs when there is a failure of the blood to clot normally in response to tissue injury from trauma, surgery, or routine invasive procedures. Following head injury, there is release of tissue thromboplastin in circulation which leads to uncontrolled activation of clotting factors⁸. There is a strong association between severity of coagulopathy and density of intravascular coagulation. This insult, often aggravated by the infusion of large volume of colloids, crystalloids, and massive blood transfusion results into dilutional coagulopathy. Further acidosis and hypothermia contribute to vicious triad of coagulopathy, acidosis, and hypothermia.⁷ It has been estimated that TBI patients with

Access this article online

Website: <https://www.nepjol.info/index.php/NJN>DOI: <https://doi.org/10.3126/njn.v20i3.53896>

HOW TO CITE

Ansari S. Determination of coagulopathy in acute traumatic brain injury and its effect on outcome. NJNS. 2023;20(3):22-26.



Address for correspondence:

Dr. Safroz Ansari

Neurosurgery Unit, Department of Surgery,
National Medical College and Teaching Hospital,
E-mail: safrosh@hotmail.com

Copyright © 2023 Nepalese Society of Neurosurgeons (NESON)

ISSN: 1813-1948 (Print), 1813-1956 (Online)



This work is licensed under a Creative Commons Attribution-Non Commercial 4.0 International License.

Determination of coagulopathy in acute traumatic brain injury and its effect on outcome

coagulopathy have mortality four times higher than those with normal coagulation profile⁹. This study was designed to determine incidence of coagulopathy and whether the acute traumatic coagulopathy has effect on outcome in isolated acute traumatic brain injury.

Materials and Methods

This is a prospective study conducted at National Medical College and Teaching Hospital, Birgunj, Nepal over a period of one year. After ethical clearance from Institutional Review Committee [F-NMC/535/077-078] all patients with head injury were included in the study except those under exclusion criteria. Informed consent was taken, and blood samples were collected at the time of admission, GCS, and data such as age, sex, timing of injury were taken according to the proforma. Exclusion criteria included history of prior coagulopathy, patients using anticoagulants, polytrauma patients or long bone fractures, Brain Dead at time of presentation, any other severe co-morbidity, such as liver disease, diabetes mellitus, known history of hypertension, which is likely to influence outcome, patients or legal guardian declining to participate in the study and the patients requiring urgent surgery. Outcome was evaluated based on Glasgow coma scale (GOS) recorded at the time of discharge and follow up was done for 3 months. Coagulopathy was defined as deranged value of aPTT >39s, PT>14s, INR>1.2 and Platelets< 1.5lakhs. These values were taken in reference to institutional practice which were also congruent to international standard values.

Statistical analysis

Sample size was calculated using formula $N = Z^2 pq / e^2$. Where, N= sample size, Z= 1.96 (at 5% type 1 error,

$p < 0.05$), $p =$ occurrence of coagulopathy = 0.5 (the possibility of occurrence of coagulopathy among TBI varied from 25% to 75%, no any data was available from our region, so to get better result 50% chance of occurrence of coagulopathy was used in this study to calculate the sample size), $q = 1 - p = 0.5$, $e =$ margin of error = 5%, Keeping all the values in the formula the sample size obtained was 384. Collected data was analyzed using IBM SPSS version 28.

Results

The present study was conducted among 405 patients with traumatic head injury to determine the correlation between coagulopathy and outcome in acute traumatic brain injury at Neurosurgery Unit of Department of Surgery, National Medical College and Teaching Hospital (NMCTH), Birgunj, Nepal. The mean (SD) age of the study population was 28.65 (18.31) years. The majority of the subjects were in the age group of 5-25 years (40.99%). Most of the patients were males (63.70%) and 36.3% were females. Most of the patients were having mild conditions (90.37%), whereas 8.39% presented with moderate and only 1.23% was having severe injury at the time admission. Majority of the patients presented with <24 hours duration, while 2.7% presented in between 24-72 hours and 1.5% presented after 72 hours since the occurrence of injury. The mean (SD) PT, INR & APTT were 13.69 (1.32) seconds, 1.1 (0.7) and 34.50 (11.37) seconds respectively. The mean (SD) platelet count was 261231.9 (262094.9). Majority of the patients were having good recovery (93.1%), 5.5% had Moderate disability and 1% had severe disability, whereas two patients expired. The patients with death and severe disability had higher proportions of coagulopathy, which was also statistically significant coagulopathy.

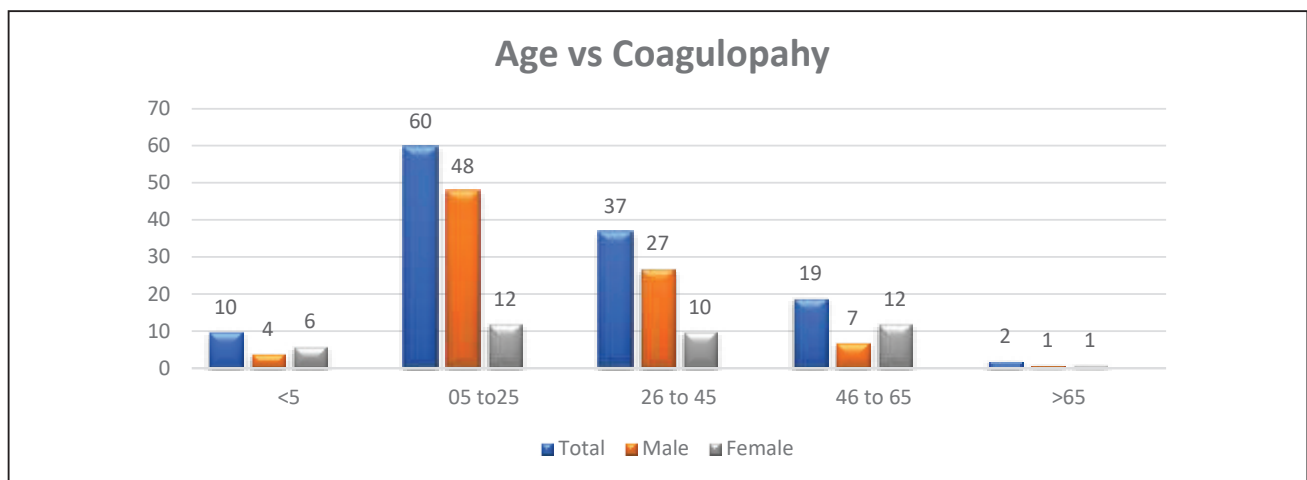


Table 1: Distribution of study subjects according to age groups (n=405)

Table 7: Distribution and association of presence of coagulopathy according to age, sex, severity, duration, and outcome of study subjects (n=405)

Variables	Coagulopathy n (row %)		Chi square value, p value
	Present	Absent	
Gender			
Male	87	171	1.215, 0.270
Female	41	106	
Glasgow outcome scale			
Good	121	275	9.0781, 0.00258
Poor	7	2	
Severity			
Mild	118	248	3.8248, 0.1464
Moderate	7	27	
Severe	3	2	
Duration (hours)			
<6	95	212	2.7029, 0.4395
6-24	30	51	
24-72	2	9	
>72	1	5	

Discussion

Coagulopathy after traumatic brain injury is multifactorial and represents predictor of outcome and prognosis^{10,11,12}. In the present study we had 2 mortalities of patients with coagulopathy. This is statistically significant, but these patients had severe head injury. Patients with severe head injuries have itself high risk of mortality, which has been proved by Lefering et. al.¹³ Classifying the Glasgow Outcome Scale into, GOS 1(death), 2(vegetative), 3(severe disability) as poor and 4(moderate disability), 5(Good recovery) as good outcomes, 97.78% of the subjects had good outcome whereas only 2.2% had poor outcome. Point seven percent of the subjects without coagulopathy had poor outcome while 5.4 % of those with coagulopathy giving p-value of 0.0025 which is statistically significant.

The majority of the patients (90.37%) had mild head injury with incidence of coagulopathy 32.24% in isolated mild head injury. This is similar to a study published by Hebert et. al in “Coagulopathy in the Setting of Mild Traumatic Brain Injury: Truths and Consequences”¹⁴. Hebert et. al also stated that Incidence of coagulopathy in severe head injury was 60%,¹⁵ which resembles to our study. Overall incidence of coagulopathy in traumatic brain injury was 31.60%. A meta-analysis of 34 studies also showed prevalence of coagulopathy after TBI close to ours 32.7%¹⁵.

Nekludov et. al suggested that coagulation system activates when blood passage through the damaged brain tissue¹⁶. In his study all sample patients had traumatic intracranial hemorrhage and GCS ≤ 8. This only

enlightens us coagulopathy in severe head injury but not on coagulopathy in isolated mild head injury with normal CT scan. In our study among 405, radiological and clinical diagnosis revealed Normal CT (n=236), Skull Fractures (n=37), Diffuse Axonal Injury (n=5), Epidural hematoma (n=33), Subdural Hematoma (n=23), Brain Contusion (n=60), Subarachnoid Hemorrhage (n=11). Here, cumulatively isolated traumatic intracranial hematoma patients had 33.07% coagulopathy whereas normal CT patients 30.51%. Unlike coagulopathy in moderate to severe TBI, mechanism in mild TBI is different. Brain Derived Microparticles (BDMPs) are circulating phospholipids derived from neuronal cells and glial cells. These particles are elevated after trauma. Release of these BDMPs induce coagulopathy in mild TBI, eliminating the systemic hypoperfusion which is thought to be hallmark of trauma induced coagulopathy¹⁵.

Of the total participants, 21.48% male patients had coagulopathy whereas only 10.12% of female patients. This difference could only be due to the fact that male patients outnumbered female patients. However, the prevalence of coagulopathy in males was 33.72% and 27.9% in females respectively, which is statistically non-significant. Hence, we can say that sex doesn't affect coagulopathy is TBI.

Time is very crucial in TBI, timely intervention has a direct effect on outcome. In the present study majority (75.80%) of the patients presented to emergency within 6 hours of injury. Whereas 20% between 6 to 24hrs and 4.1% more than 24 hours after post trauma. Coagulopathy in patients presenting within 6 hours of injury was 30.94%, however, patients reaching hospital between 6 – 24 hours

Determination of coagulopathy in acute traumatic brain injury and its effect on outcome

had slightly more 37.04%. Patients presenting late post injury in the emergency are usually managed outside and receive higher amount of IV fluids which may interfere with the coagulopathy results which may be the cause of above discrepancy. There was 17.64% coagulopathy in patients presenting after 24 hours of injury. Though statistically ($p=0.439$) insignificant, it appears that coagulation disorders were more prominent in the early hours after trauma. Most of the patients had reached hospital within 6 hours. This is intriguingly surprising for this part of the world, as it shows improvement and awareness of health services. Again, this could be the fact that the majority of the patients had cause of trauma road traffic accident, where the development of roads has improved the ambulance services. According to Van Gent et. al. risk of developing coagulopathy after traumatic intracranial hemorrhage remains 72 hours¹⁷. Contrary to ours (32%) Van Gent et. al. had only 12% coagulopathy within 24 hours after trauma. However, their retrospective observational study sampled only traumatic ICH patients.

Younger people are more prone for trauma which may result in TBI, as they must mobilize for their work or schools. This may be the only explanation for the large number of younger patients in our study. This is similar to other various studies^{3,4}. In the present study we classified age into <5, 6-25, 26-45, 46-65 and more than >65 years. More patients were from age group 6-25 followed by 26-45 with coagulation disorder 41% and 30% respectively. Coagulopathy in these age groups were 24, 36, 27, 29 and 16 percent respectively. The relationship between age and coagulopathy remains unclear however, some believe that older patients are more likely to have coagulopathy^{18,19}. On contrary, in the present study coagulation disorder was more profound in younger subjects.

Conclusion

Coagulopathy is frequently associated with traumatic brain injuries. But coagulopathy is not an independent factor for poor outcomes. The frequency of coagulation disorder is high in early hours of postinjury and younger age groups whilst there is no association with gender. The risk of coagulation disorder in patients with intracranial hematoma is higher than those with normal CT scan of brain after injuries. We did not have any mild head injuries patient having coagulopathy with unfavorable outcomes. However, coagulopathies in TBI associated with severe head injuries and poor GCS may result in poor outcomes.

Limitations of the study

- (1) Different reagents used for detecting coagulopathy may produce different results.

- (2) Prehospital managed patients with higher volume of fluids will interfere results.
- (3) Improper technique for blood sampling and transportation to the laboratory.

References

1. Shepard S. Head Trauma. *J. Neuroscience* 2004; 20(8):2825-34.
2. Timilsina DS. General Surgeons in the management of head injuries. *JSSN*. 2005;8:3-10.
3. Kumura E, Sato M, Fukuda A, Takemoto Y, Tanaka SH, Kohama A. Coagulation disorders following acute head injury. *Acta neurochirurgica*. 1987 Mar;85:23-8. [doi.org/10.1007/BF01402365]
4. Brohi K, Singh J, Heron M, Coats T. Acute traumatic coagulopathy. *Journal of Trauma and Acute Care Surgery*. 2003 Jun 1;54(6):1127-30.[DOI: 10.1097/01.TA.0000069184.82147.06]
5. Arnold H, Head injury, Pathophysiology and management. 2ed; 2005;1-501.
6. Sakowitz OW, Sharma MR, Kiening KL. Current Concepts in Diagnosis and Treatment of Traumatic Brain Injury: Implications for Healthcare in Nepal. *Nepal Journal of Neuroscience*. 2005 Jan 31;2(1):29-51.[DOI: 10.3126/njn.v2i1.19994]
7. Haggga JR, Lanzieri CF, Sartoris DJ, Zerhouni EA. CT and MRI of the whole body. 4th ed. St Louis : Mosby, 2003:317-50
8. Engström M, Schött U, Romner B, Reinstrup P. Acidosis impairs the coagulation: a thromboelastographic study. *Journal of Trauma and Acute Care Surgery*. 2006 Sep 1;61(3):624-8.[PMID: 16966998]
9. Kaufman HH, Mattson JC. Coagulopathy in head injury. *Central nervous system trauma status report*. 1985:187-206.
10. Lapointe LA, Von Rueden KT. Coagulopathies in trauma patients. *AACN Advanced Critical Care*. 2002 May;13(2):192-203. [PMID: 12011592]
11. Olson JD, Kaufman HH, Moake J, O’Gorman TW, Hoots K, Wagner K, Brown KC, Gildenberg PL. The incidence and significance of hemostatic abnormalities in patients with head injuries. *Neurosurgery*. 1989 Jun 1;24(6):825-32.[PMID: 2747858]
12. Piek J, Chesnut RM, Marshall LF, van Berkum-Clark M, Klauber MR, Blunt BA, Eisenberg HM, Jane JA, Marmarou A, Foulkes MA. Extracranial complications of severe head injury. *Journal of neurosurgery*. 1992 Dec 1;77(6):901-7. [PMID: 1432133]
13. Stein SC, Young GS, Talucci RC, Greenbaum BH, Ross SE. Delayed brain injury after head trauma: significance of coagulopathy. *Neurosurgery*. 1992 Feb 1;30(2):160-5. [PMID: 1545882]

14. Lefering R, Paffrath T, Linker R, Bouillon B, Neugebauer EA, Deutsche Gesellschaft für Unfallchirurgie/German Society for Trauma Surgery. Head injury and outcome—what influence do concomitant injuries have?. *Journal of Trauma and Acute Care Surgery*. 2008 Nov 1;65(5):1036-44. [PMID: 19001971]
15. Herbert JP, Guillotte AR, Hammer RD, Litofsky NS. Coagulopathy in the setting of mild traumatic brain injury: Truths and consequences. *Brain sciences*. 2017 Jul 22;7(7):92. [doi: 10.3390/brainsci7070092]
16. Harhangi BS, Kompanje EJ, Leebeek FW, Maas AI. Coagulation disorders after traumatic brain injury. *Acta Neurochir (Wien)*. 2008;150(2):165-175. [PMID: 18166989]
17. Nekludov M, Antovic J, Bredbacka S, Blombäck M. Coagulation abnormalities associated with severe isolated traumatic brain injury: cerebral arterio-venous differences in coagulation and inflammatory markers. *Journal of neurotrauma*. 2007 Jan 1;24(1):174-80. [PMID: 17263681]
18. van Gent JA, van Essen TA, Bos MH, Cannegieter SC, van Dijck JT, Peul WC. Coagulopathy after hemorrhagic traumatic brain injury, an observational study of the incidence and prognosis. *Acta neurochirurgica*. 2020 Feb;162:329-36. [PMID: 31741112]
19. Nakae R, Takayama Y, Kuwamoto K, Naoe Y, Sato H, Yokota H. Time course of coagulation and fibrinolytic parameters in patients with traumatic brain injury. *Journal of neurotrauma*. 2016 Apr 1;33(7):688-95. [PMID: 26414158]