

Post-traumatic Early Cerebral Infarct: MRI-based Analysis of Incidence and Radiological Distribution

SHASHANK SAH¹, SUDARSHAN DESHMUKH², NEERAJ PRAJAPATI³

ABSTRACT

Introduction: Traumatic Brain Injury (TBI) is an alteration in brain function brought on by external trauma. Computed Tomography (CT) scanning is the mainstay diagnostic modality for evaluating the primary injury, as well as secondary events such as oedema, mass effect, herniation, infarction, etc., which are often catastrophic and responsible for morbidity and mortality. Early cerebral infarction, unless large and in a defined vascular territory, is quite likely to be missed on CT scans and can even be confused with cerebral oedema. In the diagnosis of early infarctions, especially the lacunar types, the detection rate of lesions with Magnetic Resonance Imaging (MRI) is significantly higher than that of CT.

Aim: To observe the incidence, distribution, and pattern of Post-traumatic Cerebral Infarction (PTCI) and its association with neurological deterioration.

Materials and Methods: In this cross-sectional study, 55 patients with head injuries admitted to the Department of Neurosurgery were evaluated between 72 to 96 hours post-trauma using Magnetic Resonance Imaging (MRI) of the brain (1.5 Tesla Siemens). Observations were made regarding the presence and pattern of any infarction, as well as its impact on the patients.

Results: Post-traumatic early cerebral infarction was detected in 19 out of 55 (34.5%) patients. Infarct distribution was observed in nearly all defined vascular territories, with the most common occurrence in the Middle Cerebral Artery (MCA) territory. Neurological deficit was observed in four out of 19 infarcted cases during the hospitalisation period.

Conclusion: Post-traumatic early cerebral infarction is common in head injuries and can lead to neurological deterioration. MRI is sensitive in detecting infarcts, especially the lacunar ones.

Keywords: Early cerebral infarction, Glasgow coma scale, Magnetic resonance imaging, Traumatic brain injury

INTRODUCTION

TBI is a common neurosurgical emergency and a leading cause of morbidity and mortality in young individuals, with an increasing incidence in the elderly [1]. The outcome of a TBI depends on several factors, including the patients' characteristics, disease severity at admission, and complications that arise during its clinical course. PTCI is a known complication of TBI in the acute stage of the disease and has been reported to occur in 1.9-32.9% of head injury cases [2,3]. Studies have reported it as a serious complication that adversely affects the prognosis and may even be associated with an increased risk of residual debility [4-6]. Various causes, such as direct vascular compression due to mass effect, arterial wall dissection, embolisation, cerebral vasospasm, vascular damage, and systemic hypoperfusion, have been proposed to explain this consequence. However, the exact pathogenesis of PTCI is still uncertain, and effective treatments are lacking [4].

TBI is inherently heterogeneous in nature, and patient outcomes vary across the range from no overt symptoms to life-altering or fatal outcomes. The variability in outcomes cannot be accounted for by heterogeneity in the injury alone, given that a subset of patients exhibit resilience against TBI symptoms even when similarly injured patients have persistent deficits. This divergence in recovery presents both a diagnostic challenge and a gap in the understanding of the mechanisms that contribute to TBI outcomes [7].

The CT scan is the mainstay of imaging in acute TBI as it is fast and accurate in detecting both primary and secondary injuries and guiding appropriate intervention [8]. However, at times, neurological deficits are difficult to explain as CT imaging may be negative, especially in cases of mild TBI [9] or Diffuse Axonal Injury [10]. Upto 30% of hospitalised TBI patients with a normal CT scan can have abnormalities on MRI [11], which makes it appropriate to use advanced imaging modalities like MRI to aid in the diagnosis.

Comparative studies between CT and MRI have shown a significantly higher detection rate for focal lesions when MRI is used as the imaging methodology, especially in cases of mild TBI [12]. MRI performs well in displaying the lesion morphology and is more sensitive for the detection of certain intracranial injuries (e.g., axonal injuries) and blood products 24-48 hours after the injury [8]. MRI, especially Diffusion Weighted Images (DWI), has a higher sensitivity for cerebral infarction. DWI is a promising tool for depicting post-TBI conditions and prediction outcomes in adults and paediatrics [13]. Neuroimaging, such as CT scan and, to an increasing extent, MRI, plays a critical role in the management and prognostication of TBI [14]. In fact, there is a class-I recommendation [15] to perform an MRI of the brain in TBI cases where non enhanced CT is normal and there are persistent unexplained neurological findings [14,16].

Literature on PTCI in acute TBI is scarce [4,6]. Considering the poor prognostic aspects, dedicated studies on PTCI are needed.

Present study was conducted on head injury patients with the primary objectives of observing the incidence, distribution, and pattern of PTCI, as well as its impact on the neurological status of patients.

MATERIALS AND METHODS

This cross-sectional study was conducted in the Department of Neurosurgery, Shri Ram Murti Smarak - Institute of Medical Sciences, Bareilly, Uttar Pradesh, India, between September 2021 and February 2023. Ethical clearance was obtained from the Ethics Committee of the institution (SRMSIMS/IEC/2020-21/049), and appropriate consent was obtained.

Inclusion criteria: Head injury patients coming to the hospital within 24 hours of injury and requiring admission were included in the study.

Exclusion criteria: Past history of ischaemic cerebrovascular accident, deep vein thrombosis, valvular heart disease, hypotension

(mean arterial pressure <70 mmHg) at or before admission, or patients on antiplatelets or anticoagulants were excluded from the study.

Sample size: Patients presenting with head injury in the Department of Neurosurgery and requiring admission were screened. A total of 55 patients meeting the inclusion criteria during the study period were enrolled in the study using a complete enumeration process.

Methodology: Between 72 to 96 hours post-injury, a non-contrast MRI of the brain was performed on a SIEMENS machine (1.5 tesla), and evidence of infarction was assessed.

Observations were made regarding: 1) Number of cases with acute infarctions; 2) Incidence of infarction in Mild (GCS 13-15), Moderate (GCS 9-12), and Severe (GCS 3-8) head injury categories [17]; 3) Pattern of infarction, such as lacunar infarcts or territorial infarcts affecting a vascular territory [18]; 4) Distribution of infarction, i.e., vascular territories involved; and 5) Association between infarction and neurological deficit.

STATISTICAL ANALYSIS

All analysis was performed using Microsoft Excel 2019 due to its usefulness in handling both qualitative and categorical data. Descriptive statistics were used to summarise the characteristics of the study sample, including frequency and percentage calculations. Percentages and proportions were calculated to assess the distribution. Subgroup analysis was conducted to explore specific aspects such as age, gender, and patterns of vascular territory involvement.

RESULTS

Out of the 55 patients evaluated, 19 patients (34.5%) had evidence of acute infarction. Among these patients with infarction, 57.9% (11 out of 19 patients) were less than 40 years of age [Table/Fig-1]. Fifteen out of 19 patients with infarct were male (78.95%). Road traffic accidents were the most common mode of injury (16 patients), followed by falls from height (3 patients).

Age (years)	n (%)	Patients with infarction, n (%)
<20	7 (12.7)	3 (5.5)
21-40	33 (60)	8 (14.5)
41-60	10 (18.2)	6 (10.9)
>61	5 (9.1)	2 (3.6)
Total	55 (100)	19 (34.5)

[Table/Fig-1]: Age distribution of head injury patients. Patients were randomly distributed into slabs of 20 year to observe the most frequently affected age group

Infarction occurred nearly equally frequently in patients with moderate head injury (40%, 8 out of 20 cases) and severe head injury (38.8%, 7 out of 18 cases), while 23.5% of patients (4 out of 17 patients) in the mild head injury category also suffered from infarct [Table/Fig-2].

GCS	No. of patients with infarct, n (%)	No. of patients without infarct, n (%)
Severe (3-8)	7 (12.7)	11 (20)
Moderate (9-12)	8 (14.5)	12 (21.8)
Mild (13-15)	4 (7.3)	13 (23.7)
Total	19 (34.5)	36 (64.5)

[Table/Fig-2]: Distribution of patients according to head injury severity. Patients were classified into 3 groups based on head injury severity, to observe most or the least affected patient group.

All major defined vascular territories were affected by infarct. In nine patients, only a single vessel territory was involved, and in 10 cases, more than one vascular territory was affected. The MCA territory was the most commonly affected territory, involved in 11 patients (57.89%). It was followed by PCA territory (31.6%) [Table/Fig-3].

Three patients had bilateral involvement of the same territories - one patient had bilateral ACA involvement, and two patients had bilateral MCA territory involvement.

Vascular territory	n (%)
Anterior cerebral artery	3 (15.8)
Middle cerebral artery	11 (57.9)
Posterior Cerebral Artery (PCA)	6 (31.6)
Lenticulo striate artery	3 (15.8)
Basilar artery	2 (10.5)
Posterior inferior cerebellar artery	1 (5.3)
Anterior choroidal artery	1 (5.3)

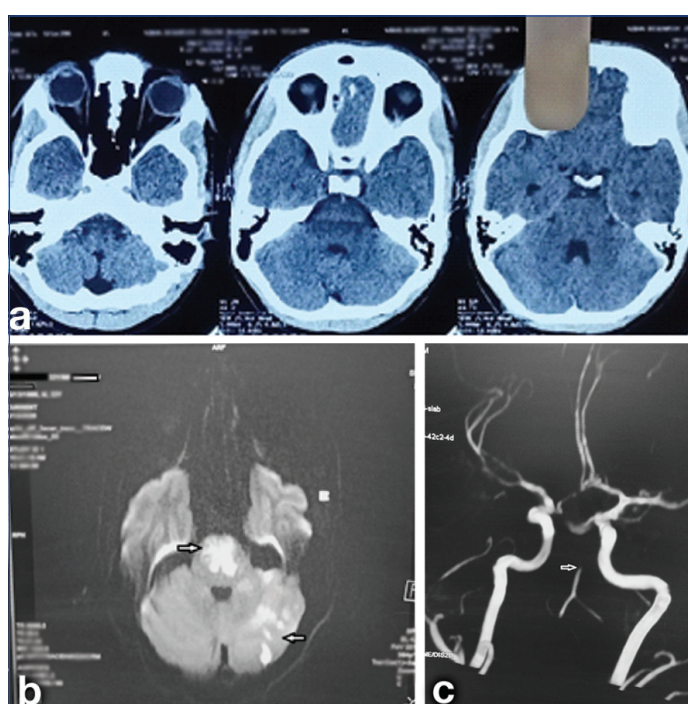
[Table/Fig-3]: Distribution of vascular territories affected by infarct n=19.

Lacunar infarcts were seen in 14 patients, while territorial infarcts were seen in five patients. The distribution of territorial infarcts was as follows: MCA territory 2, Branch of Posterior Cerebral Artery (PCA) territory 1, Posterior Inferior Cerebellar Artery (PICA) territory 1, Basilar Artery (BA) 1.

Neurological worsening was observed in four patients [Table/Fig-4] - one patient had an infarct in the pons and adjoining cerebellum. He presented with altered sensorium and cranial nerve palsy. His initial CT scan did not reveal any infarct [Table/Fig-5a]. An MRI Brain with MR Angiography suggested an infarct in the territory of the basilar artery [Table/Fig-5b] and thrombosis of the basilar artery [Table/Fig-5c]. The second patient, a 54-year-old female, developed vertigo and imbalance on the 3rd day of injury. Her MRI revealed an infarct in the territory of PICA. The third patient had hemiparesis secondary to

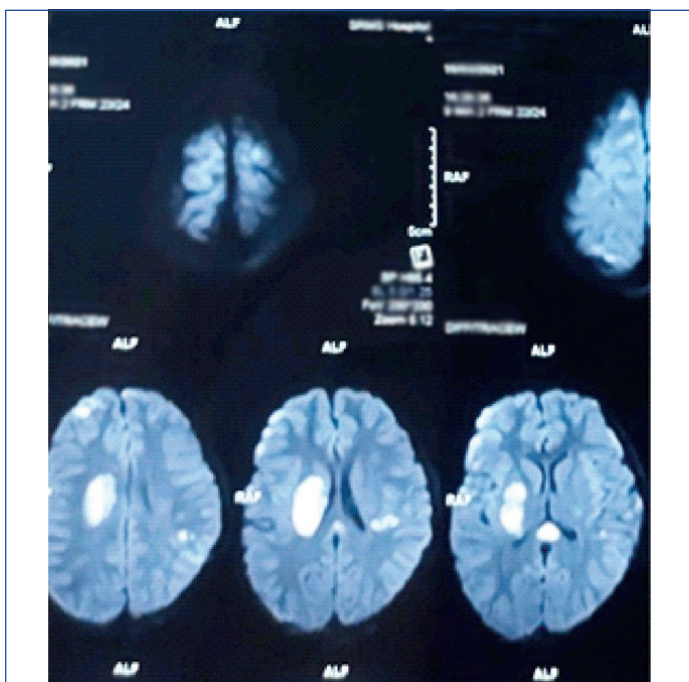
Age/ Sex	GCS	CT findings (at time of admission)	MRI findings (with regards to infarct)	Neurological deficit
22/M	11	Right frontal contusion	Infarct in pons and inferior cerebellum	Cranial nerve palsy and ataxia
54/F	13	Left fronto temporal acute SDH	Acute infarct in territory of left PICA	Ataxia
39/M	6	Diffuse axonal injury	Lacunar infarct in pons	Hemiparesis
50/M	10	Right temp contusion	Infarct in region of internal capsule	Hemiparesis

[Table/Fig-4]: Neurological deficits attributable to infarction and MRI findings.

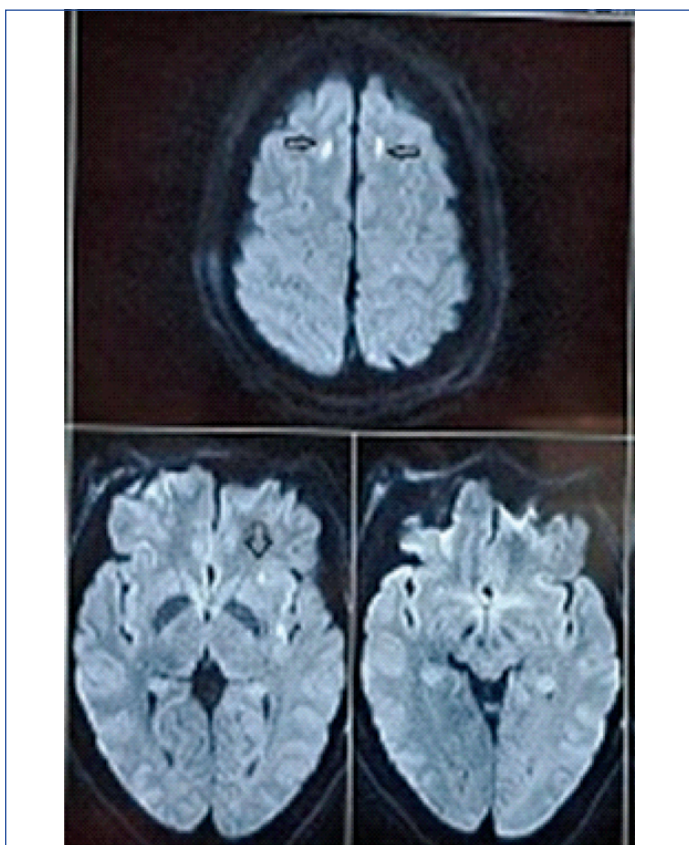


[Table/Fig-5]: a) Normal appearing CT scan in head injury; b) MRI of same patient reveals infarction in territory of basilar artery; c) MR Angiography- shows thrombosed basilar artery.

a lacunar infarct in the pons, and the fourth patient had hemiparesis secondary to a large infarct in the right paraventricular area [Table/Fig-6]. In the remaining patients, it was difficult to observe any change in neurology, possibly because the size of the lacunar infarcts in non eloquent areas did not produce any deficit [Table/Fig-7].



[Table/Fig-6]: Multiple infarcts involving territories of ACA, MCA and PCA.



[Table/Fig-7]: Multiple lacunar infarcts.

DISCUSSION

The present study aimed to evaluate the incidence and radiological distribution of post-traumatic early cerebral infarction based on MRI. The study outcome revealed that infarctions were present in 34.5% of head injury patients and were mostly lacunar in nature. Infarcts involved almost all vascular territories but were most common in the MCA territory. A subset of patients developed neurological deficits attributable to infarct.

Head trauma is a common reason for emergency department visits. Many patients who suffer blunt head trauma are at risk of TBI, which affects a large number of individuals each year [8]. As a leading cause of mortality and morbidity among young people, head injury is now becoming more frequent in older people [4]. The outcome of a TBI depends on several factors, including patient characteristics, the extent of cranio-cerebral damage, and complications that arise during its clinical course. PTCI is a complication that may lead to a poor neurological outcome and high mortality [4].

The incidence of PTCI has been reported with variability in the literature. Bae DH et al., reported an incidence of 2.1% [19], Marino R et al., reported an incidence of 19.1% [6], while Latronico N et al., in a multicentric study, reported an incidence of 32.9% among 143 patients with head injury [3]. This variability might reflect differences in the timing of evaluation, the intensity of work-up, and the quality of available images. In comparison to the aforementioned series, a higher incidence of 34.5% was found in this study.

A study by Ham HY et al., reported a mean age of patients as 43.8 ± 17.2 years, and the majority of them were male (80.8%) [20]. In this study, subgroup analysis for age shows that PTCI was most common in young patients, with 57.9% of reported infarcts occurring in patients less than 40 years of age. Road traffic accidents emerged as the most common mode of head injury in 81.2% of patients, while falls from height and falls on the ground were the other modes of injury in patients with infarction.

Latronico N et al., in their study, reported territorial infarctions (in decreasing order of incidence) in the PCA, ACA, and MCA territories, followed by lenticulo striate arteries, thalamo perforators, the basilar artery, the superior cerebellar artery, PICA, and the Anterior communicating Artery (AcoA) [3]. In another study by Ham HY et al., infarction was most commonly observed in the PCA distribution in 80% of patients [20]. Whole territory infarction was observed in 40% of patients. Territorial infarction was relatively less common in the present study (26.3% in present study vs 86.2% in the study by Latronico N et al.). Bae DH et al., reported that infarction was most common in the PCA distribution in 38.09% of patients, and MCA territory was observed in 23.8% of patients [19]. In contrast, in this study, the MCA territory was affected in 57.89% of cases, and the PCA territory was affected in 31.6% of patients.

Lacunar infarcts were the most common pattern (73.7%) in this study, followed by territorial infarcts in a defined vascular territory (26.3%). Infarcts were observed in almost all defined vascular territories, either in a single vascular territory (52.63%) or in more than one vascular territory (47.37%). Overall, the territory supplied by the MCA was the most affected area. This is possibly because the MCA feeds the largest area of the brain.

Malignant MCA infarction was first described by Hacke W et al., [21]. MCA territory infarction occurs due to a gross mass effect and herniation or severe brain swelling/oedema [22]. Potential contributing factors include stretching and attenuation of the MCA, increased intracranial pressure, and a direct pressure effect of a haematoma [23]. It is worth mentioning here that four patients, not included in present study group, had large infarcts in the distribution of the MCA territory (two cases), ICA+PCA territory (hemispherical infarct in one case), and PCA territory in one case. These were diagnosed on a CT scan within 48 hours of injury, and the patients died soon after due to a large intracranial haematoma and mass effect.

Associating with the admission GCS score, this study found that infarction was seen with nearly equal frequency in moderate (38.8%) and severe injury (40%) grades. The study by Latronico N et al., reported that 21.3% of patients with moderate head injury developed cerebral infarction [3]. In a study by Bae DH et al., it was found that on admission, 52.4% of patients had a GCS score of 3-6, 9 patients (42.9%) had a GCS score of 7-11, and only one (4.8%) had GCS scores over 12. The initial GCS score was an

important factor for prediction survival and complications [19]. Tian HL et al., showed that a lower GCS score (i.e., a more severe injury) corresponds to a higher probability of PTCI [24].

PTCI is a common complication in patients suffering from a moderate or severe head injury and can be an independent risk factor for long-term disability. Bae DH et al., in their study, suggested that increasing age (p-value=0.037), GCS score at admission (p-value <0.01), brain herniation (p-value=0.044), and decompressive craniotomy (p-value=0.012) were risk factors for PTCI in patients with TBI. There was no statistical significance between cerebral infarction and gender (p-value=0.495) or abnormalities of laboratory findings. Neurological deterioration was observed in 21.05% of cases with infarct in this study. However, long-term studies can shed light on the impact of lacunar infarct on neurological recovery.

Limitation(s)

Severe head injury patients with identifiable large infarcts on a CT scan who died within 72 hours of injury could not be included in the study. Hence, the actual incidence might be higher.

CONCLUSION(S)

The present study, an MRI-based evaluation of head injury patients, observed post-traumatic cerebral infarct in more than one-third (34.5%) of TBI cases. Mostly, infarcts were lacunar in nature (73.7%) and most frequent in the territory of the MCA. Clinically identifiable neurological deficits attributable to infarct were seen in 21% of PTCI cases. The greater sensitivity of MRI helped in picking up acute infarcts. It needs to be established whether finding the additional lesions that MRI detected would significantly change the acute management of head trauma. Hence, dedicated long-term studies are needed to assess the impact of minor infarcts on neurological recovery.

REFERENCES

- Maas AIR, Menon DK, Adelson PD, Andelic N, Bell MJ, Belli A, et al. Traumatic brain injury: Integrated approaches to improve prevention, clinical care, and research. *Lancet Neurol.* 2017;16(12):987-1048. Doi: 10.1016/S1474-4422(17)30371-X.
- Hartwell JL, Spalding MC, Fletcher B, O'mara MS, Karas C. You cannot go home: Routine concussion evaluation is not enough. *The American Surgeon.* 2015;81(4):395-403.
- Latronico N, Piva S, Fagoni N, Pinelli L, Frigerio M, Tintori D, et al. Impact of a posttraumatic cerebral infarction on outcome in patients with TBI: The Italian multicenter cohort INCEPT study. *Crit Care.* 2020;24(1):33. Doi: 10.1186/s13054-020-2746-5.
- Zhi-Ling C, Qi L, Jun-Yong Y, Bang-Qing Y. The prevalence and risk factors of posttraumatic cerebral infarction in patients with traumatic brain injury: A systematic review and meta-analysis. *Bioengineered.* 2022;13(5):11706-17. Doi: 10.1080/21655979.2022.2070999.
- Wu YG, Chao Y, Gao G, Bao D, Dong Y, Wei X, et al. Risk factors for cerebral infarction after moderate or severe traumatic brain injury. *Ther Clin Risk Manag.* 2021;17:433-40. Published 2021 May 21. Doi: 10.2147/TCRM.S309662.
- Marino R, Gasparotti R, Pinelli L, Manzoni D, Gritti P, Mardighian D, et al. Post-traumatic cerebral infarction in patients with moderate or severe head trauma. *Neurology.* 2006;67(7):1165-71. Doi: 10.1212/01.wnl.0000238081.35281.b5.
- Weil ZM, Karelina K. Lifelong consequences of brain injuries during development: From risk to resilience. *Front Neuroendocrinol.* 2019;55:100793. Doi: 10.1016/j.yfrne.2019.100793.
- Schweitzer AD, Niogi SN, Whitlow CT, Tsiouris AJ. Traumatic brain injury: Imaging patterns and complications. *Radiographics.* 2019;39(6):1571-95. Doi: 10.1148/rg.2019190076.
- Toth A. Magnetic Resonance Imaging Application in the Area of Mild and Acute Traumatic Brain Injury: Implications for Diagnostic Markers? In: Kobeissy FH, editor. *Brain Neurotrauma: Molecular, Neuropsychological, and Rehabilitation Aspects.* Boca Raton (FL): CRC Press/Taylor & Francis; 2015. Chapter 24. PMID: 26269902.
- Lindsey HM, Wilde EA, Caeyenberghs K, Dennis EL. Longitudinal neuroimaging in pediatric traumatic brain injury: Current state and consideration of factors that influence recovery. *Front Neurol.* 2019;10:1296. Published 2019 Dec 13. Doi: 10.3389/fneur.2019.01296.
- Steyerberg EW, Wiegers E, Sewalt C, Buki A, Citerio G, De Keyser V, et al. Case-mix, care pathways, and outcomes in patients with traumatic brain injury in CENTER-TBI: A European prospective, multicentre, longitudinal, cohort study. *Lancet Neurol.* 2019;18(10):923-34. Doi: 10.1016/S1474-4422(19)30232-7.
- Lee H, Wintermark M, Gean AD, Ghajar J, Manley GT, Mukherjee P. Focal lesions in acute mild traumatic brain injury and neurocognitive outcome: CT versus 3T MRI. *J Neurotrauma.* 2008 Sep;25(9):1049-56. Doi: 10.1089/neu.2008.0566.
- Hou DJ, Tong KA, Ashwal S, Oyoyo U, Joo E, Shutter L, et al. Diffusion-weighted magnetic resonance imaging improves outcome prediction in adult traumatic brain injury. *J Neurotrauma.* 2007;24(10):1558-69. Doi: 10.1089/neu.2007.0339.
- Wintermark M, Sanelli PC, Anzai Y, Tsiouris AJ, Whitlow CT; ACR Head Injury Institute; ACR Head Injury Institute. Imaging evidence and recommendations for traumatic brain injury: Conventional neuroimaging techniques. *J Am Coll Radiol.* 2015;12(2):e1-e14. Doi: 10.1016/j.jacr.2014.10.014.
- Kara A, Celik SE, Dalbayrak S, Yilmaz M, Akansel G, Tireli G. "Magnetic resonance imaging finding in severe head injury patients with normal computerized tomography." *Turkish Neurosurgery.* 2008;18(1):01-09.
- Lee H, Yang Y, Xu J, Ware JB, Liu B. Use of magnetic resonance imaging in acute traumatic brain injury patients is associated with lower inpatient mortality. *J Clin Imaging Sci.* 2021;11:53. Doi: 10.25259/JCIS_148_2021. PMID: 34754593; PMCID: PMC8571198.
- O'Neil ME, Carlson K, Storzbach D, Brenner L, Freeman M, Quiñones A, et al. Complications of mild traumatic brain injury in veterans and military personnel: A systematic review [Internet]. Washington (DC): Department of Veterans Affairs (US); 2013 Jan. Table A-1, Classification of TBI Severity. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK189784/table/appc.t1/>.
- Jose J, James J. An MRI based ischemic stroke classification- A mechanism oriented approach. *Ann Indian Acad Neurol.* 2022;25(6):1019-28. Doi: 10.4103/aian.aian_365_22.
- Bae DH, Choi KS, Yi HJ, Chun HJ, Ko Y, Bak KH. Cerebral infarction after traumatic brain injury: Incidence and risk factors. *Korean J Neurotrauma.* 2014;10(2):35-40. Doi: 10.13004/kjnt.2014.10.2.35.
- Ham HY, Lee JK, Jang JW, Seo BR, Kim JH, Choi JW. Post-traumatic cerebral infarction: Outcome after decompressive hemicraniectomy for the treatment of traumatic brain injury. *J Korean Neurosurg Soc.* 2011;50(4):370-76. Doi: 10.3340/jkns.2011.50.4.370.
- Hacke W, Schwab S, Horn M, Spranger M, De Georgia M, von Kummer R. 'Malignant' middle cerebral artery territory infarction: Clinical course and prognostic signs. *Arch Neurol.* 1996;53(4):309-15. Doi: 10.1001/archneur.1996.00550040037012.
- Tawil I, Stein DM, Mirvis SE, Scalea TM. Posttraumatic cerebral infarction: Incidence, outcome, and risk factors. *J Trauma.* 2008;64(4):849-53. Doi: 10.1097/TA.0b013e318160c08a.
- Server A, Dullerud R, Haakonsen M, Nakstad PH, Johnsen UL, Magnaes B. Post-traumatic cerebral infarction. Neuroimaging findings, etiology and outcome. *Acta Radiol.* 2001;42(3):254-60. Doi: 10.1080/028418501127346792.
- Tian HL, Geng Z, Cui YH, Hu J, Xu T, Cao HL, et al. Risk factors for posttraumatic cerebral infarction in patients with moderate or severe head trauma. *Neurosurg Rev.* 2008;31(4):431-37. Doi: 10.1007/s10143-008-0153-5.

PARTICULARS OF CONTRIBUTORS:

- Assistant Professor, Department of Neurosurgery, Shri Ram Murti Smarak-Institute of Medical Sciences, Bareilly, Uttar Pradesh, India.
- Senior Resident, Department of General Surgery, Shri Ram Murti Smarak-Institute of Medical Sciences, Bareilly, Uttar Pradesh, India.
- Professor, Department of Radiodiagnosis, Shri Ram Murti Smarak-Institute of Medical Sciences, Bareilly, Uttar Pradesh, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:

Dr. Shashank Sah,
Assistant Professor, Department of Neurosurgery, Shri Ram Murti Smarak-Institute of Medical Sciences, Nainital Highway, Bareilly-243202, Uttar Pradesh, India.
E-mail: shashsah@gmail.com

AUTHOR DECLARATION:

- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. No

PLAGIARISM CHECKING METHODS: [Jain H et al.]

- Plagiarism X-checker: Aug 09, 2023
- Manual Googling: Sep 08, 2023
- iThenticate Software: Oct 12, 2023 (13%)

ETYMOLOGY: Author Origin

EMENDATIONS: 8

Date of Submission: Aug 09, 2023
Date of Peer Review: Aug 25, 2023
Date of Acceptance: Oct 14, 2023
Date of Publishing: Nov 01, 2023