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Original Article

Surgery Section

Clinicoradiological Study of Diffuse Axonal Injury: A Longitudinal Study

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ABSTRACT

Introduction: Damage to the axons in neural brain tracts, corpus callosum, and brainstem, known as Diffuse Axonal Injury (DAI), can result in considerable morbidity and mortality in patients with head injuries. This type of injury involves microscopic damage and can have severe consequences.

Aim: To investigate the incidence, clinical features, and radiological findings of DAI on Magnetic Resonance Imaging (MRI) and to associate MRI grading with neurological outcome using the Glasgow Outcome Scale (GOS).

Materials and Methods: A longitudinal study was conducted in the Department of Neurosurgery, Jayarogya group of Hospitals, Gajra Raja Medical College, Gwalior,Madhya Pradesh, India, from December 2017 to November 2019. All the patients with Glasgow coma scores of eight or less with Computed Tomography (CT) and MRI brain findings consistent with DAI were included. The study collected data on patients including sociodemographic information, clinical variables related to trauma, details of hospital admission and stay, and variables related to the severity and consequences of DAI. Glasgow Coma Scale (GCS) was noted after resuscitation, MRI brain was done in stable patients. The neurological outcome was assessed after six months using the GOS and associated with MRI brain grading. The analyses were done using Statistical Package for Social Sciences (SPSS) version 26.0 and the frequencies were reported as percentages.

Results: Total patients with head injury were N=694 and out of which patients with DAI n=94. The mean age was 33.97 years with a male:female ratio of 4.33:1. Grade 1, grade 2, and grade 3 MRI brain findings were present in 50% (N=50), 31.25% (N=20), and 18.75% (N=12) of cases. Most common site for contusions was parietal-temporo-occipital region found in 85.93% cases. Regarding functional outcome, poor outcome was observed in 26.67% (n=4) of grade II DAI and 75% (n=9) of patients of grade III DAI.

Conclusion: DAI is major mechanism involved in Traumatic Brain Injury (TBI). In affected patients, long term hospitalisation is necessary. Patients with MRI grade I and II had a good outcome.

Keywords: Computed tomography scan, Head injuries, Magnetic resonance imaging

INTRODUCTION

Microscopic damage to the axons in the neural brain tracts, corpus callosum, and brainstem, referred to as DAI, can lead to substantial morbidity and mortality in individuals who have suffered head injuries. DAI typically results from diffuse shear injuries to white matter structures caused by rotational acceleration-deceleration forces. This type of injury is more frequently observed in instances of higher energy trauma, such as traffic accidents [1-3]. The DAI is clinically defined as coma lasting for ≥6 hours after TBI, excluding cases of swelling or ischaemic brain lesions [2]. DAI is considered the most important factor in determining morbidity and mortality in victims of TBI and is the most common cause of post-traumatic coma, disability, and a persistent vegetative state [1,2]. DAI can have a significant impact on patients and their families, leading to cognitive, physical, and behavioural changes that can hinder social reintegration, return to productivity, and overall quality of life. These changes can persist for an extended period even after the acute phase of treatment. While the brain tissue may not be destroyed, it is functionally impaired. However, the brain may gradually recover normal function over time as neural connections are remodelled through plasticity and as the clinical condition stabilises [4]. DAI is presently considered one of the most common types of primary lesion in patients with severe closed head injury, and its sequelae are recognised as among the most common causes of unfavourable outcome [1-3].

In a hallmark study, Gennarelli TA demonstrated that DAI can be the only contributor to post-traumatic unconsciousness [2]. They observed that, non human primates developed immediate and prolonged coma in the absence of focal lesions when subjected to non impact rotational acceleration [1]. DAI was the only type of tissue injury noted in pathological examination of these animals. In subsequent studies, other scientists used Adam's classification [5,6] to categorise DAI as mild, moderate, or severe. They proposed that any acceleration or deceleration could cause a mild case of DAI, in which brief loss of consciousness occurred.

Since, Strich SJ published the initial report, many studies have examined DAI's pathogenesis and clinical outcomes [7]. The evolution of the radiological imaging system has led to significant changes in the diagnosis of DAI. Because, patients with DAI require more extended periods of recovery and rehabilitation and have an economic and psychological burden on the family, neurosurgeon needs to make accurate predictions about the clinical course [8]. CT is the initial investigation of choice for head injury patients; however, it is less sensitive for detecting DAI. CT scan is the imaging tool, still the initial study of choice for head injury patients because CT scan is readily available, fast, and cheaper than MRI for detecting haemorrhage. However, there are some findings on CT which are suggestive of DAI. Individuals who had intraventricular haemorrhage, Subarachnoid Haemorrhage (SAH), gliding contusion, or diffuse swelling with deletions of the basilar cisterns or grooves (which are indirect signs of injury) were included in the study for the purpose of detecting DAI through cranial CT scans within the first 72 hours of hospital admission [9]. MRI is a more accurate and sensitive imaging tool than a CT scan for diagnosing and classifying DAI into grades according to the structure involved in DAI related lesions, although both methods are widely used [10]. However, MRI is always superior to a CT scan in detecting the lesions when used for diagnosis and evaluating DAI. T1, T2, Fluid-attenuated Inversion Recovery (FLAIR), Diffusion Weighted Imaging (DWI), Gradient Recalled Echo (GRE) and Susceptibility Weighted Imaging (SWI) sequences are used for diagnosing and grading DAI.

The present study was designed to investigate the epidemiological profile and outcome of patients with primary diagnosis of DAI and to identify clinical and sociodemographic factors associated and the functional outcome at six months after the injury at tertiary centre Gwalior region.

MATERIALS AND METHODS

The present study was a longitudinal study conducted in the Department of Neurosurgery, Jayarogya Group of Hospitals, Gajra Raja Medical College, Gwalior, Madhya Pradesh, India, from December 2017 to November 2019. The Institutional Ethical Committee (D.No 591/Bio/MC/Ethical) approved the study protocol. The nature and purpose of the study were explained to the participant, and written informed consent was obtained.

A total of 694 patients with TBI were admitted to the Neurosurgery Ward through the Trauma Centre and Out-patient Department (OPD). 94 cases were diagnosed as DAI, consisting of clinical and radiological findings. In the present study, 94 patients fulfilled Non-contrast Computerised Tomography (NCCT) head criteria of DAI, out of which 30 patients expired without MRI due to their clinical condition whereas, 64 patients underwent MRI.

Inclusion criteria: Patients between 18 to 65 years, with TBI with a GCS score of ≤8 at admission [11]. NCCT head should be normal or show haemorrhagic contusion less than 2 cm in size (CT Diagnostic criteria of DAI) were included [12].

Exclusion criteria: Patients with associated chest, abdominal and orthopaedic injuries, previous history of seizure disorders, Intraparenchymal haemorrhage more than 2 cm in diameter, or any associated Extradural Haemorrhage (EDH), Subdural Haemorrhage (SDH), or SAH were excluded.

The clinical definition of DAI excludes cases of brain swelling or ischaemic brain lesions and is characterised by a coma that lasts for six hours or more following a TBI [2]. DAI was categorised in three grades based on MRI findings [5].

Grade I: Axonal injury limited to white matter (grey-white matter interfaces).

Grade II: Grade I + involvement of corpus callosum.

Grade III: Grade II + involvement of brainstem.

Study Procedure

At the time of admission, resuscitation was done. The study gathered information on patients from their relatives, which included sociodemographic data, clinical variables related to the trauma, admission and hospitalisation details, as well as, variables related to the severity and consequences of DAI. GCS was noted and dichotomised. NCCT head was done. X-rays of the cervical spine, chest, pelvis and long bone were done to rule out bony injuries. Ultrasonography (USG) abdomen was done to rule out intra-abdominal injury. Those patients who had features of DAI on the NCCT head and who were haemodynamically stable underwent MRI (T1, T2, FLAIR, DWI, and GRE) for confirmation and grading of DAI.

Patients were managed in the trauma Intensive Care Unit (ICU) according to the protocol of management of DAI patients, and after stabilisation, they were shifted to the neurosurgical ward and then discharged. Patients were followed-up at one month and six months after discharge. During the first month and six months follow-up interval, sociodemographic data and data related to the traumatic event were confirmed, and information regarding the functional outcome of victims was recorded using the GOS [13]. The relationship between DAI and the outcome in the patients with a head injury was analysed at six months, and the association of outcome with MRI brain grading was done. The criteria for determining good and poor outcomes were based on this scale. Patients who were classified as having good recovery or moderate disability were categorised as having a good outcome, while those with severe disability, in a persistent vegetative state, or who had passed away were classified as having a poor outcome.

STATISTICAL ANALYSIS

The analyses were done using SPSS version 26.0. The frequencies were reported as percentages. Chi-square test was used. The differences were considered statistically significant at a 95% confidence level, i.e., when the (p-value≤0.05).

RESULTS

Out of 694 patients with TBI, 94 cases were diagnosed as diffuse axonal injuries with clinical, radiological, and NCCT head findings. A total of 64 patients underwent MRI brain with T1, T2, FLAIR, DWI and GRE sequences. DAI was found in 13.55% of head injury patients [Table/Fig-1]. Half of the patients belonged to grade 1, 31.25% to grade 2, and 18.75% to grade 3 [Table/Fig-2].

Variables	Number (n)	Percentage (%)
Gender		
Male	76	80.85
Female	18	19.14
Total	94	100
Age (years)		
18-30	42	44.680
31-40	27	28.723
41-50	15	15.957
51-65	10	10.638
Total	94	100
Type of injury		
Two wheeler TA	50	53.191
Four wheeler TA	22	23.404
Pedestrian	08	08.510
Fall from height	14	14.893
Total	94	100
GCS		
3-4	29	30.85
5-8	65	69.14
Total	94	100
DAI findings on NCCT head		
Present	54	57.45
Absent	40	42.55
Total	94	100
Time to regain consciousness according to MRI Grades	Mean±SD (in days)	
Grade 1	7.13±4	
Grade 2	13.67±5.4	
Grade 3	34.7±14.6	

[Table/Fig-1]: Demographic profile of Diffuse Axonal Injury (DAI) patients.
GCS: Glasgow coma scale

MRI grading	Number (n)	Percentage (%)
Grade 1	32	50.0
Grade 2	20	31.25
Grade 3	12	18.75
Total	64	100

[Table/Fig-2]: MRI grading of DAI patient.

The most common type of head injury was a cerebral concussion (30.97%) n=215, followed by cerebral contusion (28.38%) n=197. The most common site for contusion was the parieto-temporal-occipital lobe (85.93%) [Table/Fig-3].

Region	Number (n)	Percentage (%)
Frontal lobe	48	75%
Parietal-temporo-occipital lobe	55	85.93%
Cerebellum	22	34.37%
Corpus callosum	30	46%
Brain stem	12	18.75%
Basal ganglia	8	12%
Thalamus	9	14.06%

[Table/Fig-3]: Distribution of contusion on MRI.

A total of 40% of patients were expired, 3.75% showed a vegetative state, 10% shows severe disability, and 7.5% shows moderate disability and good recovery was seen in 38.75% of patients [Table/Fig-4]. Regarding functional outcome, poor outcome was observed in 26.67% (n=4) of grade II DAI and 75% (n=9) of patients of grade III DAI [Table/Fig-5].

GOS	Number (n)	Percentage (%)
Death	32	40.00
Vegetative state	3	03.75
Severe disability	8	10.00
Moderate disability	6	7.50
Good recovery	31	38.75
Total	80	100

[Table/Fig-4]: Functional outcome of patients with DAI after six months.
*Lost in follow-up=14

MRI Grading	Poor outcome	Good outcome
Grade 1	0	23
Grade 2	04	11
Grade 3	09	03
Total	13	37

[Table/Fig-5]: MRI grading with functional outcome at six months of follow-up.

In the grade 3 MRI category, there were a total of 12 patients; out of them, two patients were expired, three patients had a vegetative state, four patients had a severe disability, two patients had a moderate disability, and only one patient had a good recovery, it showed significant association (p-value=0.001) [Table/Fig-6].

MRI grade	GOS	Number (n)	Total	p-value
Grade 1	MD	2	23	0.465
	GR	21		
Grade 2	SD	4	15	0.465
	MD	2		
	GR	9		
Grade 3	Death	2	12	0.001
	VS	3		
	SD	4		
	MD	2		
	GR	1		

[Table/Fig-6]: Association of MRI grading with the functional outcome at six months of follow-up.
VS: Vegetative state; SD: Severe disability; MD: Moderate disability; GR: Good recovery.
Chi-square test was used

DISCUSSION

According to Mesfin FB et al., and Vieira RDCA et al., the true incidence of DAI is unknown [14,15]. However, it is estimated that roughly 10% of all TBI admitted to the hospital will have some degree of DAI. Salko Z et al., did a study DAI- Incidence and Outcome' from 2012 to 2014 and published in 2015 and found that in 2012, there were 181 cases of head trauma and out of them 19 cases were diagnosed with DAI [16]. In 2013, there were 199 patients with head trauma and out of them 32 were diagnosed with DAI. In 2014, there were 228 cases of head trauma and out of them l2 were diagnosed with DAI. Finally, they concluded that in three year period, they admitted 608 patients with head trauma. 60 patients were diagnosed with DAI so, finally concluded that the incidence of DAI was around 10% in head injury patients. In the present study incidence of DAI was 13.45% which was almost similar to above mentioned studies. In present study, mean age of patients with DAI was 33.97 years. Elick VMM et al., from Netherlands conducted a study and concluded that the mean age of patient with DAI was 35.3 years [17]. Vieira RDCA et al., conducted a study in pretoria and they found mean age of 32 years in their series [15]. Sahuquillo J et al., conducted a study in which they had noted a lower mean age of 26 years [18]. Lee H et al., in the Korea did a study and noted a higher mean age of 40.78 years [19]. This finding occurred because India has more than 50% of its population below the age of 25 and more than 65% below the age of 35 and secondly various human factors associated with younger age group like over speeding, overtaking, not wearing helmet, driving under the influence of alcohol and sudden road crossing without observation.

In the present study, male:female ratio was 4.33:1, which was comparable to other studies. Izzy S et al., found that male:female ratio was 2.85:1 which was significantly higher [20]. Humble SS et al., (2018) concluded that, male:female ratio was 2.45:1 [21]. Vieira RDCA et al., reported that male to female ratio was 8.75:1 [15]. The reason behind this finding was that, the society is male dominated and the male population use to go to work on motor vehicles due to which incidence of an accident is much higher.

DAI Grading on MRI

Humble SS et al., found grade I DAI patients were 44.64%, grade 2 were 31.54% and grade 3 were 23.80% [21]. Moen et al., (2014) concluded that grade 1 DAI was found in 44.64% of patients, grade 2 DAI in 31.54% of patients and grade 3 found in 23.80% of patients [22]. Lee HJ et al., did a study by which they concluded that, grade I DAI patients were 44.64%, grade 2 DAI patients were 31.54% whereas, grade 3 patients were 23.8% [19]. Paterakis K et al., concluded that, grade1 DAI patients were 20.83%, grade 2 DAI 45.83% and grade 3 DAI patients were 33.33% [23]. The present study showed grade 1 DAI patients were 50%, grade 2 DAI patients were 31.25% and grade 3 DAI were18.75%.

In present study, patients falling in grade I or grade II DAI category were higher (in terms of percentage) than above mentioned studies, reason behind such finding is mostly due to the protocol of brain MRI in the department in which patients with severe TBI were not shifted for MRI and SWI sequences were not done in most of patients due to financial burden. Studies mentioned in previous research showed that there were more patients in the grade II or III group, indicating that differences in the sequencing of MRI methods may have influenced these results [24-27]. Other studies have suggested that Diffusion Tensor Imaging (DTI) could be a more sensitive method for evaluating DAI lesions compared to conventional MRI. Additionally, SWI has been shown to have a higher detection rate of haemorrhagic lesions than conventional MRI. However, MRI can be challenging to perform on DAI patients due to accompanying injuries and unstable vital signs. Therefore, the decision to perform an MRI should be carefully considered based on the patient's clinical condition. It's worth noting that MRI SWI was not available at the Institute, where the study was conducted.

Association of MRI Grading with Functional Outcome

Lagares A et al., conducted a study and concluded that patients with poor outcome in grade I DAI were 22% in grade II DAI were 44% and in grade III DAI were 82% [26]. In the present study patients with poor outcome in grade I DAI 0% in grade II DAI were 26.67% and in grade III DAI were 75%.

The outcome after six months was better in present study as compared to Lagares A et al., reason behind this finding is that in present study death, vegetative state, severe disability were included in poor outcome and moderate disability and good recovery were included in good outcome [26]. Whereas, in Lagares A et al., death, vegetative state, severe disability and lower moderate disability were included in poor outcome and upper moderate disability and good recovery were included in good outcome [26]. Vieira RDCA et al., conducted a study which showed functional outcome in form of GOS with 48% of good recovery, 12% moderate disability, 6.67% severe disability, 1.33% vegetative state and 32% had expired [15]. This is comparable with present study that shows 38.75% of good recovery, 7.50% moderate disability. A 10% severe disability, 3.75% vegetative state and 40% had expired. Petkus V et al., conducted a study which showed functional outcome in form of GOS with 10.71% of good recovery and 35.71% moderate disability and 25% severe disability, patients with vegetative state were 3.57% and death in 25% patients [27]. Higher rate of mortality in the present study might be due to lack of primary health care facility and less trained paramedical staff that shifted the patients from accident site to hospital.

Limitation(s)

Due to the unavailability of the SWI sequence and differences in timing and sequencing of MRI examinations, there may be variations in the results of the study. While the MRI examinations were performed based on the patient's condition, some patients suspected of having DAI did not undergo MRI due to their clinical condition.

CONCLUSION(S)

The DAI is one of the main mechanisms involved in TBI, often requiring long term hospitalisation. Patients with MRI grade I and 2 tend to have better outcomes. Conducting MRI examinations in DAI patients can aid in predicting a patient's prognosis and establishing a treatment direction using a systematic protocol.

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