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Diffuse axonal injury: Epidemiology, associated risk factors and outcome: An institutional study from teritairy care centre in central India

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Abstract
Aim: The aim of this study was to describe the outcome of patients with primary diagnosis of DAI and to identify clinical and sociodemographic factors associated with mortality and functional capacity 6 months after the injury.
Materials and Methods: A total of 100 adult patients admitted in the department of neurosurgery between September 2019 and March 2021 with mild, moderate and severe traumatic brain injury (GCS ≤ 12) diagnosed to have DAI on CT and MRI, were included in this study. Patients were tracked for up to 6 months following discharge and their outcomes were graded as satisfactory or unsatisfactory using the Glasgow Outcome Scale Extended (GOS-E).
Results: Most of the patients with Grade 1 DAI had satisfactory outcome at end of 6 months and most of Grade 3 Dai patients expired within 6 months post injury.
Conclusion: The results of our study show that the outcome of DAI patients is determined by the severity of traumatic brain injury and the grade of DAI and is unaffected by patients age, gender, or TBI modality.

Keywords: diffuse axonal injury, glasgow outcome scale extended (Gos-E), neurovegetative state, quality of life

Introduction

Diffuse axonal damage (DAI) is one of the most prevalent complications of traumatic brain injury (TBI), which occurs in around 40–50% of all TBI patients. It is one of the most common cause of coma, disability, and a prolonged neurovegetative state [1, 2]. The occurrence of DAI depends on the mechanism of injury. It is more common in higher energy trauma, especially road traffic accidents [1-3], fall from height and assault on head. In Diffuse axonal injury (DAI), there is microscopic damage to the axons in the brain neural tracts, corpus callosum, and rostral brainstem. After initial head trauma, there will be acceleration- deceleration changes and rotational forces within the brain matter causing an extensive damage to axons and vasculature in the white matter. This axonal degeneration leads to persistent neurodegeneration and brain network disconnection [4, 5].

In DAI, computed tomography (CT) scan characteristics are typically limited to diffuse white matter microhemorrhages and brain edema [2]. DAI is usually suspected on the clinical grounds and CT can suggest the diagnosis, but the modality of choice is magnetic resonance imaging (MRI). MRI can detect even tiny quantities of blood products and has a better sensitivity for identifying DAI [6]. The treatment in DAI is focused on maintaining the intracranial pressure (ICP), supportive management, prevention of secondary brain injuries, and multidisciplinary rehabilitation.

DAI causes significant changes in cognition and physical and social conduct in patients, jeopardizing social reintegration, productivity, and quality of life [7,8]. Due to the fact that In many cases the brain tissue is functionally comprimised but not anatomically destroyed, there is a good chance that as the clinical situation stabilizes and neuronal connections will be restored overtime due to plasticity and the brain will progressively restore normal function [10]. Patients with radiographically apparent hemorrhages will have bad prognosis, which is assumed to be related to the total lesions discovered [14]. Understanding the variables associated with recovery

after TBI is needed for the development of individualized therapy and the development of systematic care focused on patient rehabilitation. Thus, the aim of this study is to describe the outcome of patients with diagnosis of DAI and to identify clinical and sociodemographic factors associated with mortality, morbidity and functional capacity 6 months after the injury.

Materials and Methods

A total of 100 adult patients treated in the department of neurosurgery between September 2019 and March 2021 with mild, moderate and severe traumatic brain injury (GCS ≤ 12) who are diagnosed to have DAI on CT and MRI, were included in this prospective study after obtaining Institutional ethical committee approval. Patients with intracranial hematoma on CT scan (requiring surgical intervention), past history of brain surgery or any other CNS pathology were all ruled out of the study. All patients were admitted in our department's neurointensive unit, where they were closely monitored for vital signs, neurological status, intake/output monitoring, serum electrolytes, and other parameters. All of the patients received oxygen support (titrated based on arterial blood gases), intravascular fluids based on weight, dehydration therapy, antiepileptic medications and other supportive medication. Nasogastric tube insertion was done and feeding was started after 24 hours of the injury. All the patients were managed conservatively and were not monitored for ICP.

The severity of DAI was determined using Adams *et al*. proposed grading system (Grades I–III), which is based on the detection of axonal injury in the cerebral hemispheres. Axonal injury in the gray-white junction (Grade I), the corpus callosum (Grade II), and the dorsolateral, rostral brainstem (Grade III) [2]. The MRI was performed with the assistance of the institutional radiology department between 3 to 7 days after admission, depending on the patient's clinical stability.

Patients were tracked for up to 6 months following discharge and their outcomes were graded as satisfactory or unsatisfactory using the Glasgow Outcome Scale Extended (GOS-E). The GOS-E score of 1 was taken as death, scores 7 and 8 as satisfactory outcome while scores from 2 to 6 were taken as unsatisfactory outcome.

Observation and Results

Table 1: Age and sex wise distribution of the studied cases

Age Group	Male (with%)	Female (with%)	Total (%)
20-29	21(29.1%)	8(28.5%)	29 (29%)
30-39	18(25%)	6(21.4%)	24(24%)
40-49	12(16.6%)	6(21.4%)	18(18%)
50-59	11(15.2%)	5(17.8%)	16(16%)
60±	10(13.8%)	3(10.7%)	13(13%)
Total	72(72%)	28(28%)	100

Table 1 shows about the distribution of the studied cases according to age and sex. Male cases were predominantly higher than those of female subjects. Among the male majority of the cases(29.1%) were seen in 20 to 29 years age group while among female category majority of the cases (28.5%) were observed in 20-29 year age range.

Table 2: Mechanism of injury of the studied cases

Type of injury	Number of cases	Percentage
Road Traffic Accident	73	73%
Fall From Height	18	18%
Assault	7	7%
Other	2	2%

Table 2 shows mechanism of injury among studied cases. Majority of cases (73%) are a consequence of road traffic accident, followed by (18%) fall from height, (7%) of cases are due to assault. only 2% of cases are due to causes other than the above mentioned.

Table 3: Severity of head injury

Severity of traumatic brain injury	Number of cases	Percentage
Mild	4	4%
Moderate	68	68%
Severe	28	28%

Table 3 shows majority (68%) of cases are having moderate brain injury on admission while 28% of cases are suffering from severe brain injury. only 4% of cases in this study are having mild brain injury at time of admission.

Table 4: Grading of diffuse axonal injury

Grade of DAI	Number of cases	Percentage
Grade -1	26	26%
Grade -2	47	47%
Grade -3	27	27%

Table 4 shows majority (47%) of cases are having Grade 2 DAI followed by 27% having grade 3 DAI and 26% of cases are having Grade 1 DAI.

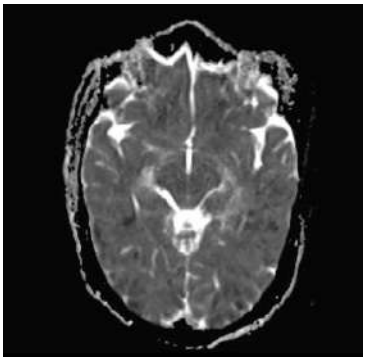

Fig 1: Mri showing Grade 3 DAI

Table 5: Number of days of hospitalization

Number of days	Number of cases	Percentage
< 10 days	42	42%
10-21 days	38	38%
>21 days	20	20%

Table 5 shows majority of patients 42% needed less than 10 days of hospital stay. 38% of patients stayed in hospital for 10-21 days, 20% of patients stayed for > 21 days.

Table 6: Outcome of Dai After 6 Months

Outcome	GOS-E Grade	Number of cases	Percentage
Dead	Grade- 1	22	22%
UN Satisfactory	Grade -2	10	10%
	Grade-3	6	6%
	Grade-4	4	4%
	Grade-5	5	5%
	Grade-6	5	5%
Satisfactory	Grade-7	28	28%
	Grade-8	20	20%

Of the 100 patients included in our study 22% patients expired. 48% of patients had satisfactory outcome at end of 6 months of which 23% of patients had grade 1 DAI 23% of patients had grade 2 DAI and 2% of patients had grade 3 DAI. 30% of patients had unsatisfactory outcome of which 3% of patients had grade 1 DAI, 22% of patients had grade 2 DAI and 5% of patients had grade 3 DAI.

Table 7: Outcome at 6 months compared with grades of DAI

Grade of DAI	Outcome			Total
	satisfactory	Un satisfactory	Dead	
Grade 1	23	3	0	26
Grade 2	23	22	2	47
Grade 3	2	5	20	27
Total	48	30	22	100

Of the 100 patients included in our study 42% of patients needed air way management and ventilator support initially and 28% of patients needed tracheostomy ro wean off from ventilator support.

26% of patients needed inotrope support and 14% of patients were later operated by orthopedic team for long bone fractures. 6% of patients needed ICD insertion for pneumo and haemothorax,4% of patients needed Spine fixation for fracture vertebrae.

Discussion

The aim of our study was to evaluate the outcome of DAI based on its grade, and to identify significant predictors of prognosis. Majority of our patients (72%) were men, similar to Vieira *et al*. who found that 89.7% of their patients were men and Ahuja *et al*. (94.4% male). Most of patients in our study were young, with 29% being between the ages of 20 and 29 years. Similar statistics were seen in two other studies, 43.6% [7] and 48.59% [3] where the young population was more affected. In our study, the most prevalent cause of DAI and mortality was a road traffic accident (73%). Vieira *et al*. found Road traffic accident to be the leading cause of DAI in 83.8% of their patients, and Abu Hamdeh *et al*. found Road traffic accident in 60% of his patients [1, 7]. DAI is more prevalent with RTA because as the head is subjected to rotational accelerations, the brain lags behind, resulting in shearing and straining of the brain parenchyma. This process leads to axotomy, Wallerian degeneration and cytoskeleton damage of neural tissue causing membrane leakage, osmotic imbalance and disturbed axonal transport [9].

Our patients were classified according to severity of TBI,4% had mild, 68% had moderate while 28% had severe injury. Severe head injury patients showed higher mortality rates while mild and moderate injury had more satisfactory outcomes. Abu Hamdeh *et al*. demonstrated that initial GCS and motor score have predictive significance for the outcome of DAI patients ($P < 0.05$) [1]. In our study, the most common grade of DAI was Grade 2 (47%), while Grade III DAI had the worst prognosis, with the highest fatality rate (90.9%) of all grades. The severity of DAI and the outcome have a substantial relationship, with the more severe DAI, the worse the outcome. Management of only DAI is nonsurgical with an aim to maintain the intracranial pressure within or near to the normal limits and to prevent secondary complications. The patient's age, the severity of the TBI, and the DAI grading are all considered crucial criteria when predicting the outcome. The majority of the patients (42%) were only in the hospital for 10 days or less.

The GOS-E was used to assess patients' clinical outcomes 6 months after sustaining head injury in our research group. In literature, mortality after DAI is found to be variable from 30.8% [7] to 62% [16] while in our study, it was 22%. Similar mortality rates were obtained by Vieira *et al*. and Zahirovic *et al*. in their published trials, with death rates of 30.8% and 25.4%, respectively [7, 16]. We also discovered that 48% of our patients had a satisfactory outcome on the GOS-E, whereas 30% failed to improve on 6 month follow-up and remained in the group of unsatisfactory outcome.

There were few limitations in our study. It was a single-institution study and we had to exclude the associated intracranial hematomas patients which can significantly alter the management protocol and outcome of these DAI patients. Our study was limited to 6 months follow-up so the role of prolonged rehabilitation at home and long-term outcome beyond 6 months was not studied. The severity of the TBI with which the patient was first hospitalized, as well as the Grade of DAI, had a substantial impact on the result in our research group, with poor outcomes in low initial GCS and higher DAI grades.

Conclusion

The results of our study show that the outcome of DAI patients is determined by the severity of traumatic brain injury and the Grade of DAI and is not affected by patients age, sex or TBI modality. In general, patients with diffuse axonal injury who have a very low GCS at admission and grade III DAI have the worst outcome and greatest mortality and patients with good GCS at admission and Grade 1 DAI will have satisfactory outcome. A longer hospital care and rehabilitation at home will aid in the improvement of clinical and functional outcomes and productivity in survivors.

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