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Original Article

Outcome of diffuse axonal injury in moderate and severe traumatic brain injury

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ABSTRACT

Background: Diffuse axonal injury (DAI) is a common presentation in neurotrauma. Prognosis is variable but can be dependent on the initial presentation of the patient. In our study, we evaluated the outcome of diffuse axonal injury.

Methods: This study was conducted at a tertiary care center from September 2018 to December 2019 and included 133 adult patients with moderate or severe head injury (GCS ≤ 12) diagnosed to have the DAI on the basis of MRI. At 3 months, the result was assessed using the Extended Glasgow Outcome Scale (GOS-E).

Results: There were a total of 97 (72.9%) males and 36 (27.1%) females with an average age of 32.4 ± 10 years with a mean GCS of 9 at admission. The most common mode of head trauma was road traffic accidents (RTAs) in 51.9% of patients followed by fall from height in 27.1%. Most patients were admitted with moderate traumatic brain injury (64.7%) and suffered Grade I diffuse axonal injury (41.4%). The average hospital stay was 9 days but majority of patients stayed in hospital for ≤ 11 days. At 3 months, mortality rate was 25.6% and satisfactory outcome observed in 48.1% of patients. The highest mortality was observed in the Grade III DAI.

Conclusion: We conclude that the severity of the traumatic head injury and the grade of the DAI impact the outcome. Survivors require long-term hospitalization and rehabilitation to improve their chances of recovery.

Keywords: Diffuse axonal injury, Glasgow outcome scale extended, Magnetic resonance imaging, Traumatic brain injury

INTRODUCTION

Diffuse axonal damage (DAI) is one of the most prevalent complications of traumatic brain injury (TBI), which occurs in 40–50% of all TBI patients and a major cause of these patients going into a coma.[20,22] It was originally described in 1956 as small cerebral lesions with a diameter of <15 mm, located in areas of gray and white matter junction and midline structures that are susceptible to shear forces.[2] After initial head trauma, there are acceleration-deceleration changes and rotational forces within the brain matter that cause an extensive damage to axons and vasculature in the white matter. This axonal degeneration is not just limited to the initial phases of TBI; it can also lead to persistent neurodegeneration and brain network disconnection.[11,13,19]

In DAI, computed tomography (CT) scan characteristics are typically limited to white matter microhemorrhages and traumatic brain edema.[2] DAI is generally suspected on the clinical grounds and CT can suggest the diagnosis, but the modality of choice is magnetic resonance imaging (MRI). It can detect even tiny quantities of blood products and has a better sensitivity for identifying DAI.[15] The treatment in DAI is focused on maintaining the intracranial pressure (ICP), prevention of secondary brain injuries, and multidisciplinary rehabilitation.

Thus, DAI causes significant changes in cognition and physical and social conduct in patients, jeopardizing social reintegration, productivity, and quality of life.[8,10,18] Due to the fact that the brain tissue is compromised in function but not destroyed, there is a good chance that as the clinical situation stabilizes and neuronal connections are reconstructed overtime due to plasticity, the brain will progressively restore normal function.[4,18] Patients with radiographically apparent hemorrhages have a bad prognosis, which is assumed to be related to the total lesions discovered.[14]

MATERIALS AND METHODS

A total of 133 adult patients admitted in the department of neurosurgery between September 2018 and December 2019 with moderate and severe traumatic brain injury (GCS ≤ 12) diagnosed to have DAI on MRI, were included in this prospective study after obtaining Institutional Review Board (IRB) approval. Patients with a significant intracranial hematoma on CT scan (requiring surgical intervention), a history of brain surgery, or an extracranial injury were all ruled out of the study. All patients were admitted in our department's neurotrauma unit, where they were closely monitored for vital signs, neurochecks, intake/output monitoring, serum electrolytes, and any complications. All of the patients received oxygen (titrated based on arterial blood gases), intravascular fluids based on weight, and antiepileptic medications (only for patients with seizure episode). A nasogastric tube was inserted and feeding began within 24 hours of the injury. All the patients were managed conservatively and no patient was monitored for ICP in our studied population due to resource constraints.

The severity of DAI was determined using Adams e*t al.* proposed grading system (Grades I–III), which is based on the detection of axonal injury in the cerebral hemispheres, with a preference for 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 to move.

Patients were tracked for up to 3 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. $P \leq 0.05$ was labeled significant.

RESULTS

Our study included 133 patients who were diagnosed as DAI on MRI. According to gender distribution, males were 97 (72.9%) while female patients were 36 (27.1%) and the average age of patients was 32.41 ± 10.02 years. The more prevalent causes of injury were road accident in 69 (51.9%) patients and fall in 36 (27.1%). A moderate injury was seen in 86 (64.7%) patients in our study while 47 (35.3%) patients had severe TBI. Out of 133 patients, most were found to have a Grade I injury, seen in 55 (41.4%) as shown in [Table 1] while Grade II and Grade III DAI was seen in 48 (36.1%) and 30 (22.5%) patients, respectively. In mild TBI, the average number of lesions was 11.6; in severe TBI, the average number of lesions was 13.4. A total of 26 patients had related intracranial abnormalities on MRI, although these were rated (by two neurosurgeons) as mild and had no effect on the patient's ultimate prognosis. The average hospital stay was 9 days (2–17 days) but majority of the patients, 78 (58.6%) remained hospitalized for 11 days or less. The most common complication was chest infection 10 (7.5%) which caused longer hospital stay or delayed weaning off ventilator. Eleven (8.2%) patients ultimately needed any kind of surgical intervention. Seven (5.2%) patients with severe TBI needed tracheostomy to wean off from the ventilator support while 4 (3.0%) patients were surgically managed for hydrocephalus (which was not present on the first CT scan) where three were treated with ventriculoperitoneal shunt and one with external ventricular drain. Satisfactory outcome was seen in 64 (48.1%) and unsatisfactory outcome in 69 (51.9%) patients [Table 2]. Among patients with satisfactory outcome, 73.4% showed complete recovery with no injury-related problems and 26.6% retained some injury-related problems but resumed normal activities. In our study, 34 (25.6%) patients expired. Of these deaths, 24 were male patients while 10 females and about 59% of patients were between 18 and 30 years age [Table 3]. Patients with a history of fall from height showed mortality of 33.3% while RTAs had 20%. Grade III DAI was associated with the highest mortality rate (44.1%), while

Table 1: Distribution of DAI grades among patients.

Grade of DAI	Number of patients	Percentage
Grade I DAI	55	41.4
Grade II DAI	48	36.1
Grade III DAI	30	22.5

Table 2: Outcome in DAI.

Outcome	GOS-E grade	*n* (%)
Death	Grade 1	34 (25.6)
Unsatisfactory	Grade 2	10 (7.5)
	Grade 3	6 (4.5)
	Grade 4	3 (2.2)
	Grade 5	7 (5.2)
	Grade 6	9 (6.7)
Satisfactory	Grade 7	17 (12.7)
	Grade 8	47 (35.3)

Grades I and II DAI was associated with death rates of 23.5% and 32.3%, respectively.

DISCUSSION

The aim of our study was to bring focus on the diffuse axonal injury, to evaluate the outcome of DAI based on its grade, and to identify significant predictors of prognosis. The bulk of our patients (72.9%) was men, similar to Vieira *et al.* who found that 89.7% of their patients were men and Ahuja *et al.* (94.4% male).[3,7] No association between gender distribution and outcome of DAI was seen in our study. The majority of patients in our study were young, with 45.1% being between the ages of 18 and 30 years. Similar statistics were seen in two other studies, 43.6%[7] and 48.59%[3] where the young population was more affected. Adverse outcome in our patients was not found to be dependent on the age of the patients ($P > 0.05$) but mortality was higher in the young population as compared to old. In our analysis, the most prevalent cause of DAI and mortality was a road traffic accident (51.9%). Vieira *et al.* found RTA to be the leading cause of DAI in 83.8% of their patients, and Abu Hamdeh *et al.* found RTA in 60% of his patients.[1,7] DAI is more prevalent with RTA because the head is subjected to rotational accelerations, the brain lags behind, resulting in shearing and straining of the parenchyma. This process leads to axotomy, Wallerian degeneration and cytoskeleton damage causing membrane leakage, osmotic imbalance and disturbed axonal transport.[9]

Our patients were classified according to severity of TBI, 64.7% had moderate while 35.3% had severe injury. When outcome of DAI was assessed according to severity of TBI, we found a significant relationship between the two ($P < 0.05$) as given in [Table 4]. Severe head injury patients showed higher mortality rates while moderate injury had more satisfactory outcomes. Abu Hamdeh *et al.* demonstrated that the 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 I (41.4%), while Grade III DAI had the worst prognosis, with the highest fatality rate (44.1%) of all grades. The severity of DAI and the outcome have a substantial relationship, with the more severe DAI, the worse the outcome ($P < 0.05$) as given in [Table 5].

Table 3: Characteristics among survivors and nonsurvivors in DAI.

Characters	*n* (%)	Survivors, *n* (%)	Nonsurvivors, *n* (%)	*P* value
Age				
18 or above to 30 years	60 (45.1)	40 (40.4)	20 (58.8)	0.118
Above 30 to 50 years	40 (30.1)	34 (34.3)	6 (17.6)	
Above 20 years	33 (24.8)	25 (25.2)	8 (23.5)	
Gender				
Male	97 (72.9)	73 (73.7)	24 (70.5)	0.721
Female	36 (27.1)	26 (26.2)	10 (29.4)	
Mechanism				
RTA	69 (51.9)	55 (55.5)	14 (41.1)	0.346
Fall	36 (27.1)	24 (24.2)	12 (35.2)	
Assault	11 (8.3)	9 (9.1)	2 (5.8)	
Others	17 (12.8)	11 (11.1)	6 (17.6)	
Severity of TBI				
Moderate	86 (64.7)	68 (68.6)	18 (52.9)	0.075
Severe	47 (35.3)	31 (31.3)	16 (47.)	
Grade of DAI				
Grade I	55 (41.4)	47 (47.4)	8 (23.5)	0.01
Grade II	48 (36.1)	37 (37.3)	11 (32.3)	
Grade III	30 (22.6)	15 (15.1)	15 (44.1)	
No. of lesions				
<10	36 (27.1)	27 (27.2)	9 (26.4)	
11–24	53 (39.8)	38 (38.3)	15 (44.1)	0.818
≥25	44 (33.0)	34 (34.3)	10 (29.4)	
Duration of stay				
≤10 days	78 (58.6)	58 (58.5)	20 (58.8)	0.573
10 days	55 (41.4)	41 (41.4)	14 (41.1)	

Management of pure DAI is nonsurgical with an aim to keep 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 crucial criteria to consider when predicting the outcome. We found that duration of hospital stay did not change the outcome of DAI in our study but longer stays were associated with lesser number of patients falling into category of satisfactory outcome. The majority of the patients (58.6%) were only in the hospital for 11 days or less. Although the length of a hospital stay has no bearing on prognosis, it does represent the requirement for long-term nursing care and rehabilitation.

The existence and quantity of DAI hemorrhagic lesions revealed by MRI have been linked to outcome, although the predictive relevance of cerebral location is not thoroughly investigated.[5,6,12,24] In our study, number of hemorrhagic lesions on MRI did not show any prognostic value in terms

Table 4: Outcome of DAI compared with severity of TBI.

Severity of TBI	Outcome		Total	*P*-value
	Satisfactory	Unsatisfactory		
Moderate	47	39	86	0.041
Severe	17	30	47	
Total	64	69	133	

Table 5: Outcome of DAI compared with grades of DAI.

Grade of DAI	Outcome		Total	*P*-value
	Satisfactory	Unsatisfactory		
Grade I	32	23	55	0.020
Grade II	24	24	48	
Grade III	8	22	30	
Total	64	69	133	

of survivability ($P > 0.05$) as given in [Table 3]. A study that examined the progression of traumatic axonal damage in 58 individuals with moderate or severe TBI using magnetic resonance imaging (MRI) found that the bigger the count of lesions identified early after trauma, the worse the functional impairment at 12 months.[12] The size and number of lesions revealed by MRI carried out in the first 48 h of hospitalization were substantially connected with the neurological impairment reported at the time of discharge, according to a research of 26 DAI patients.[17] In a study of 50 patients, the average time to regain consciousness was 1–2 weeks for Grade I DAI patients, 3–4 weeks for Grade II patients, and 3–4 months for Grade III patients.[23]

The GOS-E was used to assess patients' clinical outcomes 3 months after sustaining a head injury in our research group. In literature, mortality after DAI is found to be variable from 30.8%[7] to 62%[21] while in our study, it was 25.6%. 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 48.1% of our patients had a satisfactory outcome on the GOS-E, whereas 26.3% failed to improve on 3-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 change the management and outcome of these DAI patients. Our study was limited to 3 months follow-up so the role of prolonged rehabilitation and long-term outcome beyond 3 months was not studied. The severity of the TBI with which the patient was first hospitalized, as well as the severity 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 findings of our study show that the outcome of DAI is determined by the severity of the traumatic brain injury and grade of DAI and is unaffected by age, gender, or TBI modality. In general, individuals with diffuse axonal injury who have a very low GCS at admission and grade III DAI have the worst outcome and the greatest mortality. A longer hospital care and rehabilitation will aid in the improvement of clinical and functional outcomes in survivors.

Authors' contributions

Dr. Farrukh Javeed conceived and designed the study, did data collection and manuscript writing. Dr. Ali Afzal did statistical analysis and editing of manuscript. Dr. Asad Abbas did data collection and manuscript writing. Dr. Lal Rehman did review and final approval of manuscript.

All authors read and approved the final version of the manuscript.

Declaration of patient consent

Institutional Review Board (IRB) permission obtained for the study.

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Conflicts of interest

There are no conflicts of interest.

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