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Original Research Article

Analysis and outcomes of diffuse axonal injury in tertiary care centre

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ABSTRACT

Aims & Objective: To report the clinical features, radiological features and outcomes of patients with diffuse axonal injury in a tertiary care centre.
Materials and Methods: Fifty five patients with history of trauma with low GCS and radiological evidence of DAI were studied from August 2016 to December 2018. It consisted 46 (84%) males and 9 (16%) females. Majority of the patients were in age group of 16-25. Most common modality of injury was RTA. Seven (12.7%) patients had grade 1 DAI, 36 (65.5%) patients had grade 2 DAI and 12 (21.8%) patients had grade 3 DAI. Follow up was done after 3 months of injury. Patients outcome was analysed using the Glasgow Outcome Scale.
Result: Patients with GCS 3-8 had GOS 1-3. Patients with GCS of 9-12 had GOS of 3-4 and Patients with GCS of 13-15 had GOS of 4-5. Most patients in our study had grade 2 DAI and GOS 4.
Discussion: Diffuse axonal injury is devastating types of traumatic brain injury. The acceleration-deceleration mechanism is responsible for DAI. It is most commonly analyzed based on the outcomes of GOS Scale.
Conclusion: Most of the patients in this study had grade 2 DAI. Good recovery was seen in grade 1 and 2 DAI and high mortality in grade 3 DAI.

1. Introduction

The adage that the dead teach the living cannot be truer than in severe head injury. Most of the severely head injured patients, even with the best of treatments end up with high morbidity and mortality.

Traumatic brain injury refers to widespread pattern of injury throughout the brain caused by traumatic disruption of nerve cells, with particular type of injury to the axons.[1]

There are four principal types of traumatic brain injury: diffuse vascular injury, diffuse axonal injury, hypoxic-ischemic encephalopathy and diffuse brain swelling.[2]

Clinically, diffuse axonal injury is characterized by generalized injury to the axons leading to immediate unconsciousness and coma longer than 6 hours of duration. It is most commonly seen in road traffic accidents or fatalities and occasionally in assaults or fall.[3,4]

It has been proved that the diffuse injury to the axons can also occur in a variety of other non-traumatic pathological conditions such as cerebral hypoxia, hypoglycemia.[5]

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 neuro-vegetative state.[6]

It causes cognitive, physical and behavioural changes that compromise social re-integration, return to productivity, and quality of life of patients and their families.[7,8]

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These changes persist beyond the acute phase of treatment and also continue for a long period after the traumatic event. Because the brain tissue is functionally impaired and not destroyed, so the brain may gradually regain normal function as the clinical condition stabilizes and neural connections are re-modelled due to plasticity.[9]

Axonal injury is frequently a result of traumatic brain injury which may cause other focal damage in the brain like contusions, lacerations or haemorrhage.

Depending on the severity of trauma, the axonal injury can be focal, multi-focal or diffuse.

In focal and multi-focal axonal injury the damaged axons are seen in one or few locations in the supratentorial parts of the brain, mainly in the corpus callosum and internal capsule, but not in the infratentorial brain regions.

DAI is usually associated with rapid angular (rotational) acceleration and deceleration of the brain.[10] Inflammatory responses following neural injury have been suggested as an important mechanism in DAI.

Direct mechanical forces do not completely tear axons and they result in axonal retraction balls but stimulate and induce progressive changes that impede axonal transport, which subsequently results in the local swelling of the axon prior to detachment from its downstream segment.[11]

The incidence of DAI is higher during autopsy than would be obvious on radiographic examination.[12] DAI represents approximately one- half of all intra-axial traumatic lesions.[13] No racial or sex predilection exists. DAI can occur at any age.

DAI may occur in utero, if a pregnant woman is subjected to sufficient force.[14]

Understanding the variables associated with recovery after TBI, is needed for the development of individualized therapy, the evaluation of care provided by the family and doctors and the development of systematic care focused on patient rehabilitation.

It is also important for recognizing the efficacy and use of new techniques and treatments, as these should result in better patient outcome, recovery and survival.[15]

Axonal injury has been characterized histologically using silver stains, horse-radish peroxidase uptake and, most commonly in recent years with neurofilament or amyloid beta precursor protein.

Electroencephalography has been used for evaluation of the clinical assessment of consciousness to support the diagnosis and prognosis. Electrical activity of brain tissue may have good prognostic value after brain injury.

When performed from 15 days to 4 years after injury, EEG may provide an objective and quantitative measure of the severity of brain injury. It can detect early seizure activity, and provide information about sleep patterns during polysomnography.[16]

Sleep disturbances are common after DAI, and may cause insomnia, hypersomnia, and altered sleep-wake cycles.[17]

Annually, 262 per 100,000 inhabitants are admitted for TBI in Europe and it accounts for one third of all injury associated deaths in the United States.[18] TBI has profound socioeconomic impact.[19]

2. Materials and Methods

The study was conducted in the department of neurosurgery, Sri Ramachandra institute of higher education and research, Porur, Chennai.

2.1. Study design

Longitudinal observational study.

2.2. Sample

Material for this study was obtained from the patients admitted to Sri Ramachandra institute of higher education and research, Porur from September 2016 to December 2018. The study was conducted in a group of 55 cases admitted in the Department of Neurosurgery with a diagnosis of diffuse axonal injury who satisfied the inclusion and exclusion criteria. All symptoms and signs at the time of presentation and during the course in the hospital, which were recorded in the proforma. All the cases were diagnosed to have diffuse axonal injury on coumputed tomography scans and MRI brain. Their outcome and follow up statuses were noted. In the end the clinical presentation, course in the hospital and the outcome were analysed.

2.3. Inclusion criteria

1. Patients with severe TBI present with altered sensorium.
2. Multiple areas of injury on CT scans.
3. Any patient who demonstrates clinical symptoms disproportionate to his or her CT scan findings.
4. Instantaneous loss of consciousness and patients remaining in a persistent vegetative state,
5. Radiological evidence of diffuse axonal injury.

2.4. On the basis of CT Brain

1. One or more small intraparenchymal haemorrhages less than 2 cm in diameter, located in the cerebral hemispheres
2. Intraventricular haemorrhage
3. Haemorrhage in the corpus callosum
4. Small focal areas of haemorrhage less than 2 cm in diameter, adjacent to the third ventricle
5. Brainstem haemorrhage.

2.5. Adams classification

Grade I- Widespread axonal damage in white matter of cerebral hemispheres

Grade II- White matter damage extending to the cor- pus callosum with tissue tear hemorrhages

Grade III- Pathology of grade I-II and in addition, tis- sue tear hemorrhages in the brainstem

2.6. Exclusion criteria

1. Patients with abdominal injury
2. Chest injury
3. Long bones injury.

2.7. At the time of presentation

Once the patients were brought to the emergency department with the history of head trauma, patients underwent triage by the department of emergency medicine and received primary aid and resuscitation.

After the primary survey, cervical spine was stabilized with collar and patients with compromised airway and breathing or with GCS 8 or less were intubated and ventilated. Active fluid resuscitation was performed if circulation was at compromise.

Patients suspected to be at high risk for post traumatic seizures were loaded with intravenous fosphenytoin as per body weight. Tetnus toxoid was given to all patients. Patients with open wound, antibiotic was given. Once the patient was stabilized CT scan brain was done.

2.8. Neurological evaluation

Detailed history, stressing upon loss of consciousness, vomiting, seizures and ENT bleed was taken. Detailed neurological assessment was done according to GCS. Pupils were checked. Cardiovascular, respiratory, abdominal system were examined.

After all the assessment, patient was seen by orthopaedic, OMFS, Genrel surgery department and treatment was given accordingly.

2.9. Further management

According to the GCS patient is shifted to ICU or ward. Requirement of ICU admission depended on the severity of head injury and GCS. In ICU, patients were monitered by neurosurgeon and neuroanesthetist. Serial assessment of patients in ICU was done and some patients who showed neurological deterioration were intubated

2.10. Follow up

Follow up was done in out-patient department and by telephonic conversation at 3 months after discharge. Neurological status and glasgow outcome scale was used to grade the patient's outcomes.

3. Results

Patients with GCS 3-8 had GOS 1-5. Patients with GCS of 9-12 had GOS of 3-5 and Patients with GCS of 13-15 had GOS of 4-5. Most patients in our study had grade 2 DAI and GOS 4.

Table 1: Profile of the patients enrolled (n-55)

S.No.	Profile	Statistics
1.	Age(years)	
	Min. - Max.	17 - 83
	Mean ± SD	38.4 ± 16.6
2.	Gender	
	Male: Female	46 : 9
3.	Hospital stay(days)	
	Min. - Max.	1 - 64
	Mean ± SD	19.2 ± 14.9
4.	GCS at admission	
	Min. - Max.	3 - 15
	Mean ± SD	8.7 ± 4.0
5.	Intubation	
	Yes : No	29 : 26
6.	MRI done	
	Yes : No	20 : 35
7.	Morbidity	
	Yes : No	11 : 32
8.	Mortality	
	Yes : No	8 : 47

Table 2: Age distribution of patients with diffuse axonal injury (n-55)

Age(years)	Number	Percentage (%)
1 - 20	6	10.9
21 - 40	26	47.3
41 - 60	17	30.9
61 - 80	5	9.1
>80	1	1.8

Table 3: Gender distribution of patients enrolled (n-55)

Gender	Number	Percentage (%)
Male	46	83.6
Female	9	16.4

Table 4: Distribution of patients according to mode of injury (n-55)

Mode of injury	Number	Percentage (%)
Road Traffic Accident(RTA)	41	74.5
Fall	8	14.5
Others	6	11.0

Table 5: Distribution of patients according to stay in hospital (n-55)

Hospital stay (days)	Number	Percentage (%)
1 - 7	9	16.4
8 - 14	16	29.1
15 - 21	8	14.5
22 - 28	5	9.1
> 28	13	23.6
NA	4	7.3

Table 6: Distribution of patients according to symptoms (n-55)

Presenting symptoms	Number	Percentage (%)
Loss of consciousness	55	100.0
Headache	51	92.7
Vomiting	38	69.1
ENT bleeding	20	36.4
Seizures	6	10.9

Table 7: Distribution of Glasgow Coma Scale among patients at admission (n-55)

Glasgow Coma Scale	Number	Percentage (%)
3 - 8	30	54.5
9 - 12	11	20.0
13 - 15	14	25.5

Table 8: Distribution of patients according to intubation requirement (n-55)

Intubation required	Number	Percentage (%)
Yes	29	52.7
No	26	47.3

Table 9: Mortality status of patients (n-55)

Mortality	Number	Percentage (%)
Yes	8	14.5
No	47	85.5

Table 10: Follow-up Status of patients enrolled in the study (n-55)

Follow-up status	Number	Percentage (%)
Died	8	14.5
LAMA	4	7.3
Followed-up	43	78.2

Table 11: Distribution of Glasgow Coma Scale among patients at Follow-up (n-43)

Glasgow Coma Scale	Number	Percentage (%)
3 - 8	3	7.0
9 - 12	7	16.3
13 - 15	33	76.7

Table 12: Distribution of patients according to morbidity reported (n-43)

Morbidity	Number	Percentage (%)
Yes	11	25.6
No	32	74.4

Table 13: Results of Glasgow outcome scale among patients enrolled (n-55)

Glasgow outcome scale Grade	Number	Percentage (%)
NA	4	7.3
Graded	51	92.7
5	10	19.6
4	18	35.3
3	12	23.5
2	3	5.9
1	8	15.7

Table 14: Distribution of patients according to grade of DAI (n-55)

DAI Grade	Number	Percentage (%)
1	7	12.7
2	36	65.5
3	12	21.8

Table 15: MRI status of patients enrolled (n-55)

MRI done	Number	Percentage (%)
Yes	20	36.4
No	35	63.6

Table 16: Glasgow coma score (GCS) at admission among patients underwent MRI and their Glasgow outcome score (GOS) (n-20)

Glasgow outcome score(GOS)	Glasgow coma scale(GCS)			
	3 - 8	9 - 12	> 12	Total
1	0	0	0	0
2	0	0	0	0
3	1	0	0	1
4	2	3	8	13
5	0	0	6	6
Total	3	3	14	20

Table 17: Tracheostomy status of patients enrolled (n-55)

Tracheostomy done	Number	Percentage (%)
NA	4	7.3
Yes	15	27.3
No	36	65.5

Table 18: DAI grade of patients according to their Glasgow coma scale (GCS) (n-55)

DAI grade	N	Glasgow coma scale						X^2	df	p-value
		3 - 8 (n-30)		9 - 12 (n-11)		13 - 15 (n-14)				
		N	%	N	%	N	%			
1	7	0	0.0	3	42.9	4	57.1			
2	36	18	50.0	8	22.2	10	27.8	19.412#	4	0.0001*
3	12	12	100.0	0	0.0	0	0.0			

- Fisher's exact test
* Significant at p< 0.05

Table 19: Glasgow outcome scale (GOS) of patients according to their Glasgow coma scale (GCS) (n-51)

GOS grade	N	Glasgow coma scale						X^2	df	p-value
		3 - 8 (n-28)		9 - 12 (n-9)		13 - 15 (n-14)				
		N	%	N	%	N	%			
1	8	8	100.0	0	0.0	0	0.0			
2	3	3	100.0	0	0.0	0	0.0			
3	12	11	91.7	1	8.3	0	0.0	28.142#	8	0.0001*
4	18	5	27.8	5	27.8	8	44.4			
5	10	1	10.0	3	30.0	6	60.0			

- Fisher's exact test
* Significant at p< 0.05

4. Discussion

This longitudinal, observational study was conducted in 55 patients of Diffuse Axonal Injury in the department of neurosurgery, Sri Ramachandra institute of higher education and research, porur, Chennai from September 2016 to December 2018.

The clinical features, radiological features and outcomes of patients with diffuse axonal injury were noted and compared with observations made by other authors in their studies.

All the cases presenting to emergency department with history of head injury were subjected to CT Brain, out of which 55 patients were included in the study.

1. Diffuse Axonal Injury refers to widespread pattern of injury throughout the brain caused by traumatic disruption of nerve cells, with particular injury to the axons.
2. It is most commonly seen in road traffic accidents and occasionally in assaults or fall.
3. There can be multiple areas of injury on CT scans.
4. Any patient who demonstrates clinical symptoms disproportionate to his or her CT scan findings is also categorised as diffuse axonal injury
5. The consequences of DAI can be cognitive, physical, and behavioural changes that compromise social behaviour, return to work, and quality of life of patients and their families.
6. It is graded by CT Brain and MRI Brain.

4.1. On the basis of CT brain

1. One or more small intraparenchymal haemorrhages less than 2 cm in diameter, located in the cerebral hemispheres
2. Intraventricular haemorrhage
3. Haemorrhage in the corpus callosum
4. Small focal areas of haemorrhage less than 2 cm in diameter, adjacent to the third ventricle
5. Brainstem haemorrhage.

4.2. Adams classification on the basis of MRI Brain

Grade I**-** Widespread axonal damage in white matter of cerebral hemispheres

Grade II- White matter damage extending to the corpus callosum with tissue tear haemorrhages

Grade III- Pathology of grade I-II and in addition, tis- sue tear haemorrhages in the brainstem

1. Outcome of patients with diffuse axonal injury is analysed by Glasgow outcome scale.

5. Conclusion

1. Out of 55 cases 46 were male and 9 were females.
2. Majority of patients were in the age group of 21-40 years and mean age was 38.41 yrs. Youngest patient was 17years and oldest was 83 years old.
3. Most common mode of injury was Road traffic accident, in 41 patients (74.5%), fall in 8 patients (14.5%) and other mode of injury like work place injury etc in 6 patients (10.9%).
4. Duration of Loss of consciousness was more than 6 hours in majority of patients.
5. Most common presenting complaint seen in all patients in our study was headache and vomiting.
6. In this study group 30 pts had GCS 3-8, 11 pts had GCS of 9-12 and 14 pts had GCS of 13-15.
7. Out of 55 patients 29(52.7%) were intubated and 15(27.2%) patients underwent tracheostomy.
8. All patients (55) underwent CT but only 20 patients underwent MRI. Other 35 patients didn't undergo MRI due to logistic reason.
9. As no classification of DAI is available on CT scan finding, grading of DAI for patients who had undergone CT scan is done based on MRI grading system of DAI.
10. Seven patients (12.7%) had grade 1 DAI, 36 patients (65.5%) had grade 2 DAI and 12 patients (21.8%) had grade 3 DAI.
11. Patients with diffuse axonal injury grade II and III had maximum days of hospital stay as compared to grade I.
12. Minimum hospital stay was 1 day and maximum was 64 days.
13. Inotropes were started on 13 patients in which 11 patients were under GCS 3-8 and 2 patients under GCS 9-12.
14. Maximum follow up was one and half years.
15. Outcome of the patients were noted according to Glasgow outcome scale.
16. Out of 55 patients 8 patients expired.
17. Eight (15.7%) patients had GOS 1, 3 (5.9%) patients had GOS 2, 12 (23.5%) patients had GOS 3, 18 (35.3%) patients had GOS 4 and 10 (19.6%) patients had GOS 5.
18. Most of the patients in this study had grade 2 DAI. Good recovery was seen in grade 1 and 2 DAI and high morbidity and mortality in grade 3 DAI
19. Patients with GCS of 3-8 had GOS 1-5. Patients with GCS of 9-12 had GOS of 3-5 and Patients with GCS of 13-15 had GOS of 4-5. Most patients in our study had grade 2 DAI and GOS 4.
20. The available world literature has observed cognitive, physical, and behavioral changes, outcome in patints with diffuse axonal which have been mentioned earlier. In our study similar observations were made with in concerance with reference to studies. The major difference being the mortality rate which again proves

that RTA and head injuries cause loss of life and burden to state and family.

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7. Conflict of Interest

The authors declare no relevant conflicts of interest.

8. Source of Funding

None.

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