Clinical Profile and Prognostication of Traumatic Diffuse Axonal Injury

Vaidyanathan R.[1], Noor Rubina Ahamadi[2], Aravind R.M.[3], Shivanand V.[4], Chandrashekar G.R.[5]

[1, 2,] Department of Anaesthesiology and Critical Care, Cauvery Heart and Multi-Speciality Hospital, Mysore, Karnataka, India. [3, 5] Department of General Surgery, Cauvery Heart and Multi-Speciality Hospital, Mysore, Karnataka, India. [4]Department of Neurosurgery, Cauvery Heart and Multi-Speciality Hospital, Mysore, Karnataka, India.

ABSTRACT

BACKGROUND

Diffuse Axonal Injury (DAI) is one of the most common causes of post-traumatic coma, disability and a persistent neuro-vegetative state. We wanted to study the clinical profile, prognostic factors and long-term outcome of patients admitted with traumatic diffuse axonal injury in our ICU.

METHODS

74 patients who were admitted to the ICU with diffuse axonal injury following brain trauma between Jan 2010 to Dec 2019 were included in the study. Baseline clinical assessment, GCS scoring, basic investigations including serology, complete blood count, and biochemistry, CT Brain along with x - ray of cervical spine, chest x - ray, x - ray pelvis and ultrasound abdomen was done for all patients. MRI brain was done for all patients with clinical suspicion of diffuse axonal injury within 36 hours of injury. All those patients with MRI proven diffuse axonal injury were included in the study. Patients who had significant parenchymal lesions in the brain in the form of contusions or haemorrhage in brain or those patients who underwent craniotomy were excluded from the study. All the patients were managed in ICU as per standard protocol of brain trauma foundation (BTF) guidelines.

RESULTS

Out of 74 patients, 65 required ventilatory support. There was no in-hospital mortality. The average length of ICU stay is 14.7 days which is directly related to the initial GCS score on admission and MRI grading of diffuse axonal injury. The lower GCS score and severe diffuse axonal injuries as shown by higher MRI grades were associated with longer duration of ICU stays. Presence of ventilator associated pneumonia (VAP) is a significant factor in determining the ICU stay and was seen in 35 % of the patients in our study. Major deficits as assessed by Glasgow outcome evaluation scale (GOC - E) at the end of one month post discharge was seen in 6 patients (8.1 %). However, at the end of 6 months, no significant motor deficits were seen in any of the patients. 2 patients died during the intervening 5 month follow up period due to unrelated causes. One patient was lost for follow up after one month.

CONCLUSIONS

The overall outcome in traumatic diffuse axonal injury is favourable with 0 % mortality as against a higher rate reported in available literature ranging from 30 – 70 %.[1] Disability rate at the end of 6 months was also nil in our study compared to varied distribution of 20 – 40 % reported in the literature. Infections remain one of the biggest challenges in managing these cases. A ventilator associated pneumonia (VAP) incidence of 35 % was seen in our series.

KEYWORDS

Diffuse Axonal Injury, Traumatic Brain Injury, GCS, MRI

Corresponding Author:
Dr. Vaidyanathan R,
Consultant Anaesthesiologist and Intensivist, Department of Anaesthesiology and Critical Care, Cauvery Heart and Multi-Speciality Hospital, Bannur Road, Near Teresian Circle, Mysore - 28, Karnataka, India.
E-mail: vaidyadr78@gmail.com

DOI: 10.18410/jebmh/2020/456

How to Cite This Article:
Vaidyanathan R, Ahamadi NR, Aravind RM, et al. Clinical profile and prognostication of traumatic diffuse axonal injury. J Evid Based Med Healthc 2020; 7(39), 2199-2203. DOI: 10.18410/jebmh/2020/456

Submission 07-06-2020,
Peer Review 20-06-2020,
Acceptance 12-07-2020,
Published 28-09-2020.

BACKGROUND

Diffuse Axonal Injury (DAI) is one of the most common and devastating forms of traumatic brain injury and is a major cause of unconsciousness and persistent vegetative state after head trauma. DAI is considered the most important factor in determining morbidity and mortality in victims of TBI and is the most common cause of posttraumatic coma, disability and a persistent neuro vegetative state.[1,2]

Diffuse axonal injury is caused from widespread tearing of axons and small vessels by shearing forces and is defined as prolonged post - traumatic coma over 6 hours following injury without any demonstrable mass lesion and after excluding all other causes of brain swelling or ischemic brain lesions. Diffuse axonal injury is caused by acceleration-deceleration effects of the mechanical input to the head upon shaking of the brain within the skull.[1]

Diffuse axonal injury causes cognitive, physical and behavioural changes that compromise social reintegration return to productivity and quality of life of the patients and their families. These changes persist beyond the acute phase of treatment and continue for a long period after the traumatic event. Because the brain tissue is functionally impaired but not destroyed, the brain may gradually regain normal function as the clinical condition stabilizes and neural connections are remodelled.[1]

Traumatic brain injury in general including DAI is classified as mild, moderate and severe based on the Glasgow coma scale (GCS).Traumatic brain injury patients with GCS of 13 to 15 are classified as mild injuries which comprises majority of the patients. Patients with GCS of 9 to 12 are considered to have moderate traumatic brain injury, while patients with GCS below eight are classified as having a severe traumatic brain injury. Further GCS of less than 5 are usually grouped under patients with very severe forms of injury.[3]

Conventionally magnetic resonance imaging (MRI) brain has been used to grade the severity of diffuse axonal injury. Based on the findings of MRI brain it can be graded into 3 grades. This is also known as the Adam's classification of diffuse axonal injury.[4] Grade I constitute a mild form of injury while grade III is severe form of injury involving brain stem.

- Grade I: Involves grey - white matter interfaces. This commonly involves parasagittal regions of frontal lobes, periventricular and temporal lobes. Less commonly, parietal and occipital lobes, internal and external capsules may be involved.
- Grade II: Involves corpus callosum in addition to stage I locations most commonly involving the posterior body and splenium but does advance anteriorly with increasing severity of injury.
- Grade III : Involves brainstem in addition to stage I and II locations most commonly involving rostral midbrain, superior cerebellar peduncles, medial lemnisci and corticospinal tracts.[4]

Similarly, the outcome of patients following diffuse axonal injury is usually assessed with the help of Glasgow Outcome Scale Extended (GOS - E) scale.[5, 6]

In this study an attempt is made to analyze the clinical profile of diffuse axonal injury and also to assess the prognostic factors on the long term outcome of diffuse axonal injury based on the clinical features, Glasgow coma scale (GCS) scoring and severity based on MRI grading.

METHODS

In this prospective observational study, 74 patients who were admitted to the ICU with diffuse axonal injury following brain trauma between Jan 2010 to Dec 2019 were included in the study. Baseline clinical assessment, Glasgow coma scale (GCS) scoring, basic investigations including serology, complete blood count, biochemistry, CT brain along with x - rays of cervical spine, chest x - ray, x - ray pelvis and ultrasound abdomen were done for all the patients. MRI brain was done for all patients with clinical suspicion of diffuse axonal injury within 36 hours of injury. All those patients with MRI proven diffuse axonal injury were included in the study. Patients who had significant parenchymal lesions in the brain in the form of contusions or haemorrhage or those patients who underwent craniotomy were excluded from the study. Patients with significant blunt injuries of chest, abdomen and fracture of pelvis were also excluded from the study. However patients who had isolated bone fractures like fractures of humerus, tibia, femur or ankle and isolated limb soft tissue injuries were included in the study. All the patients were managed in ICU with standard protocol for treatment of traumatic brain injury as per the brain trauma foundation (BTF) guidelines. Factors affecting length of hospital stay and ICU stay were assessed based on clinical features, age, GCS score and MRI grading of the injury All the patients were followed up after discharge, up to one month and after 6 months of discharge for any possible persisting neurological deficits and were assessed objectively using Glasgow outcome scale extended (GOS - E) scale.

All the statistical methods were done using SPSS 21.0 version for windows. $p < 0.05$ was considered statistically significant. Summary statistics was done by means of proportions for categorical/binary variables and mean along with standard deviation for continuous variables. Inferential statistics was done by using, Pearson correlation, one way ANOVA, and independent t test.

RESULTS

Age (in Yrs.)	No. of Patients	Percentage %
< 18	1	1.35
18 - 25	14	18.9
25 - 35	28	37.8
35 - 45	20	27.02
45 - 55	7	9.45
> 55	4	5.4
Total	**74**	**100**

Table 1. Age Wise Distribution of Patients

Majority of the patients admitted with diffuse axonal injury belonged to the younger age group of 25 - 35 years followed by 35 - 45 years age group. One child of 13 years

was the youngest and the oldest in the series was a 75 year old male patient.

GCS On Admission	Number of Patients	Percentage
< 5	05	6.8 %
5 - 8	24	32.4 %
9 - 12	43	58.1 %
> 12	02	2.7 %
Total	**74**	**100.0 %**

Table 2. GCS on Admission

GCS	Duration of ICU Stay in Days		
	No. of Patients	Mean ICU Days	SD
< 5	5	26.00	1.41
5 - 8	24	18.17	5.70
9 - 12	43	11.98	6.07
> 12	2	5.00	. 00
Total	**74**	**14.74**	**7.15**

Table 3. ICU Stay and GCS Score

One Way ANOVA, p <0.0001

Correlations		
ICU Days	ICU DAYS	GCS
Pearson Correlation	1	-0.791
Sig. (2 - Tailed)		0.000
N	74	74

Table 4. Correlation of ICU Days with GCS

**Correlation is significant at the 0.01 level (2 - tailed)

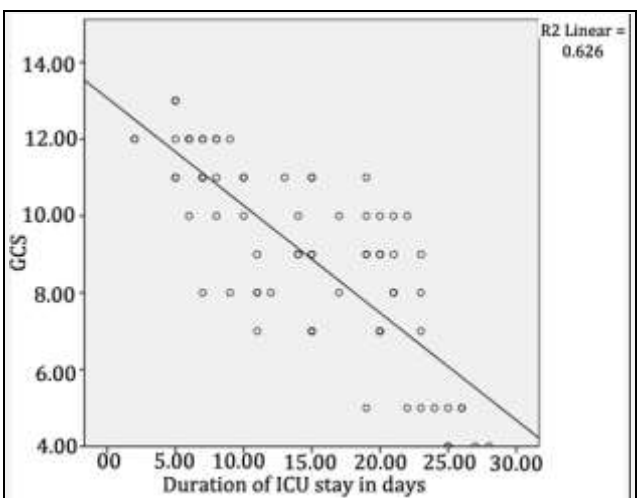

Figure 1. Correlation Coefficient Curve for GCS & No. of Days

The patients were grouped into 4 groups based on the initial GCS on admission with GCS < 5 constituting very severe head injury, GCS of 5 - 8 classified as severe head injury, GCS of 9 - 12 as moderate head injury and GCS >12 as mild head injury. Out of 74 patients, 58.1 % of them had moderate head injury (GCS = 9 - 12) with an average ICU stay of 11.98 days and a standard deviation of 6.07 from mean. This was followed by patients with severe head injury (GCS = 5 - 8) who constituted 32.4 % of the admitted cases and had an average ICU stay of 18.17 days with a standard deviation of 5.7 from mean. Patients with mild injuries with an initial GCS of greater than 12 constituted only 2.7 % of the cases and they occupied on an average 5 days in ICU. Patients with severe head injury of GCS less than 5 on admission had the longest duration of ICU stay with an average of 26 days and a standard deviation of 1.4 from mean.

On further analysis with Pearson correlation model, the correlation coefficient was - 0.791 and a p value <0.0001 indicating nearly 63 % (R^2 linear = 0.626) of change in the duration of ICU stay as determined by GCS, with lower GCS scores occupying higher ICU days as shown in the illustrative graph.

MRI Grading	Number of Patients	Percentage
Grade I	22	29.72
Grade II	39	52.70
Grade III	13	17.56
Total	**74**	**100.0%**

Table 5. MRI Grading

MRI Grading	Duration of ICU Stay in Days		
	Count	Mean	SD
Grade I	22	6.32	1.89
Grade II	39	16.46	4.47
Grade III	13	23.85	3.51
Total	**74**	**14.74**	**7.15**

Table 6. ICU Stay and MRI Grading

One Way ANOVA, p <0.0001

The severity of diffuse axonal injury was also graded as per their MRI findings into 3 grades as mentioned above. Out of the total 74 patients, 39 patients had grade II injury which comprised 52.7 %.They had an average ICU stay of 16.46 days with a standard deviation of 4.47 from mean. This was followed by patients with grade I DAI with 22 patients falling in this group and they had an average length of ICU stay of 6.32 days with a standard deviation of 1.89 from mean. Similar to low GCS, patients with severe head injury involving brain stem (Grade III) had the longest duration of ICU stay with an average ICU stay of 23.85 days with a standard deviation of 3.51 from mean. 13 patients (17.56 %) had grade III DAI. Statistical analysis with one way ANOVA and independent t test revealed a significant association of severity of DAI as assessed by MRI brain correlating strongly with the duration of ICU stay with a p value less than 0.0001.

(VAP) Infection	Duration of ICU Stay in Days		
	No. of Patients	Mean	SD
Absent	51	11.04	5.17
Present	23	22.96	2.60

Table 7. Incidence of VAP

p<0.0001, independent t test

Out of 74 patients, 65 required ventilatory support. Out of these patients 35 % of them had developed ventilator associated pneumonia (VAP). Independent t test analysis showed the presence of infection to be significantly associated with the duration of ICU stay with a p value less than 0.005. There was no in hospital mortality.

Patients were assessed objectively at the end of one month and at the end of 6 months after discharge with a Glasgow outcome scale – extended (GOS - E) scoring sheet. Patients were assessed for possible deficits and their recovery in a scale of 1 - 8,1 being worst outcome or death, 2 is persistent vegetative state, 3 & 4 are severe disabilities – upper and lower grade, 5 & 6 are moderate disabilities - upper & lower grade, 7 & 8 are good recoveries with lower and upper recoveries respectively.

At the end of one month post discharge, 1 patient had severe disability of upper grade, 1 patient had moderate disability of upper grade, 4 patients had moderate disabilities of upper grade and another 2 patients had good recovery

but of a lower grade. All the remaining 61 patients had a good recovery of grade 1 with no deficits related to the brain injury that could affect their daily life and were capable of resuming their pre-injury level of social and leisure activities without any reduced work capacity. At the end of 6 months, 2 patients died during the intervening 5 months follow up period due to unrelated causes. One patient died due to pulmonary embolism and the other due to sepsis because of severe chest infection. One patient was lost for follow up after one month when he didn't had any deficit. All the remaining 6 patients who had measurable deficits with a GOS-E score between 2 to 6 at the end of 1 month post discharge recovered fully at the end of 6 months with no remnants of brain injury and regaining their full social and leisure activities along with their vocation with no decreased work capacity as well. All their GOS-E scores were 8 at the end of 6 months.

DISCUSSION

Diffuse axonal injury has traditionally been termed as a devastating disease with a poor outcome and is a major cause of unconsciousness and persistent vegetative state after severe head trauma. In some series, over 90 % of patients with severe DAI never regained consciousness.[7] Those who do wake up often remain significantly impaired.[8,9] Length of duration of hospital or ICU stay has been consistently shown to be associated with dependence or low GOS - E scores, a scale which is widely used to assess any residual neurological deficits which will affect normal day to day activities or the quality of life following traumatic brain injury.[1,5,6] In our study we were able to demonstrate that the initial GCS on admission and MRI grading were significantly associated with an increased duration of ICU stay and hospital stay. The lower GCS scores and severe diffuse axonal injuries with a higher MRI grades were significantly associated with a longer duration of ICU stay.

Similarly severity of DAI, initial GCS score, presence of infection and duration of hospital stay were seen to be associated with poor outcome even after 6 months in many of the earlier reported studies.[1,8,9] We have been able to report a superior outcome at the end of 6 months with none of the patients being dependent or left with severe disability. However, the presence of infection (VAP), low GCS and severity of DAI were significantly associated with a longer duration of ICU stay.

Literature consistently describes a moderate to poor outcome following diffuse axonal injury especially those lesions affecting corpus callosum (grade II) and brain stem (grade III) with a frequency of disability ranging from 40.0 – 87.5 % and dependency ranging from 20.0 – 41.3 % for patients with DAI as evaluated by GOS-E at 6 months after injury.[4,10-16] However, in our study a vast majority of patients had a good outcome with more than 90 % recovering fully with none of the survivors being dependant or having any disabilities at the end of 6 months after discharge.

Severe DAI stood out as a risk factor for mortality in many earlier works with mortality at 6 months being reported to be as high as 30%,[1] however in our study outcome was highly favourable with a mortality at 6 months of only 2.9 %.

CONCLUSIONS

Though management of diffuse axonal injury and long-term care is challenging with significant mortality and long-term morbidity, we found a highly favourable result in our study with a mortality of just under 3 %. In a 6 month follow up period, the outcome in the survivors was also very satisfactory with no dependence or disability as assessed by GOS - E scale and majority of them could get back to their earlier vocation, though more than 84 % fell in the mild or moderate injury group and around 16 % of patients had severe diffuse axonal injury. GCS on admission, severity of DAI and presence of infection seemed to be strongly associated with the duration of ICU stay.

Financial or Other Competing Interests: None.

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