Original Research Paper

Volume - 14 | Issue - 11 | November - 2024 | PRINT ISSN No. 2249 - 555X | DOI : 10.36106/ijar

Radio-Diagnosis

STUDY OF MRI FINDINGS OF DIFFUSE AXONAL INJURY PATIENTS AND THEIR RELATION WITH CLINICAL NEUROLOGICAL OUTCOME

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ABSTRACT **Objectives:** Diffuse Axonal Injury (DAI) is among the most common type of traumatic brain injury, and it causes persistent vegetative state and unconsciousness after traumatic head injury. With MRI evolving as the modality of choice for evaluating the diffuse axonal injury, this study aims to identify the anatomical distributions of the lesion using various MRI sequences, categorize them, and follow up the patients for clinical outcome using the Glasgow outcome scale (GOS). **Material And Methods:** On 36 head trauma patients came to emergency department prospective observational study were done in 1 year duration. There clinical assessment done with GCS at admission and GOS at 3 months. MRI of such patients were obtained using FLAIR, DWI AND SWI sequences and DAI grade using Adam's grading were evaluated for different MRI sequences .Patient's prognosis was correlated with GCS at admission, DAI grade and total number of lesion/locations. Statistical analysis was done using SPSS Statistical software, ANOVA one way test, post hoc test (Turkey test) and Chi square test. **Result:** Study done on 36 male patients ranging from 18-50 year of age. The most common mode of head injury found to be road traffic accident -83% followed by fall-17% .Out of 36 patients, 21 patients (56%) had GCS <=8, 15 patients (44%) had GCS between 9 and 12. At 3 month follow up, out of a total of 36 patients, 2 patients (5.5%) expired (GOS-1) , 4 patients (11.1%) remained in persistent vegetative state (GOS-2), 13 patients (36.1%) and 12 patients (33.3%) were found to be severely (GOS-3) and moderately (GOS-4) disabled respectively and 5 patients (13.3%) showed good recovery (GOS-5). Mean GOS was 3.08± 1.03. Newer imaging -SWI able to detects lesion better (diagnosis of DAI) as compared to other older sequences like FLAIR and DWI. But no statistically significant found between total number of lesion/locations to the outcome and also newer imaging do not change the grade of DAI patients. **Conclusion :** Although advanced imaging in head injury, SWI helps diagnose the burden of lesions in DAI more efficiently than other imaging sequences, it is the grade of injury and GCS of patients at admission that predicts the outcome more efficiently.

KEYWORDS :

INTRODUCTION

Diffuse Axonal Injury (DAI) is among the most common type of traumatic brain injury, and it causes persistent vegetative state and unconsciousness after traumatic head injury. DAI is considered an important factor in determining morbidity and mortality in victims of traumatic brain injury. [1, 2]

Diffuse axonal injury is caused by widespread axonal and small vessels tearing by shearing forces that occur due to acceleration-deceleration effects of the mechanical input to the head caused due to shaking of the brain within the skull. [1]

It is most commonly seen in road traffic fatalities, occasionally in falls from a considerable height and due to assault. Though the terms DAI and traumatic axonal injury have been used interchangeably, it has been proved that the diffuse injury to the axons can also occur in other non traumatic pathological conditions such as hypoglycaemia, cerebral hypoxia, etc. So the more specific term traumatic axonal injury (TAI) has replaced diffuse axonal injury to specifically highlight axonal damage due to trauma. [4]

Computed tomography (CT) is the initial investigation of choice for any type of traumatic head injury, although Magnetic Resonance Imaging (MRI) is considered an investigation of choice for DAI. With MRI evolving as the modality of choice for evaluating the diffuse axonal injury, this study aims to identify the anatomical distributions of the lesion using various MRI sequences, categorize them, and follow up the patients for clinical outcome using the Glasgow outcome scale (GOS).

AIM AND OBJECTIVES

Aim:

Study of Magnetic resonance imaging findings of diffuse axonal injury patients and their relation with clinical neurological outcome.

OBJECTIVES:

1. Quantify the anatomical distribution of brain lesions associated with diffuse axonal injury using different MRI sequences.
2. Apply the Adams grading system using the MRI sequence.
3. Evaluation of prognosis after three months of injury.

MATERIALS AND METHODS

STUDY POPULATION

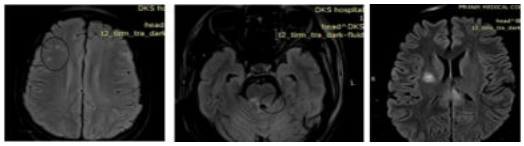
We had included all the patients, who came to emergency department in our hospital between January 2020 –December 2020 with traumatic head injury due to any mode and having Glasgow coma scale score (GCS) of 12 or below 12, irrespective of their age and sex.

We excluded all those patients who were presented to the hospital late (after 72 hours) after the injury, or the patients having associated other injuries like subdural hematoma, extradural or intracerebral haemorrhages requiring emergency operative procedure, diagnosed case of seizure disorder or any intracranial pathology like brain tumour, tuberculoma etc, previous history of surgical procedure for any intracranial pathology and the patients who were having contraindication for MRI because of metallic implants or pacemakers. Ultimately we had included 36 patients in our study and followed up the patient for 3 months for assessment of their outcomes.

METHODOLOGY

After obtaining consent from relatives of the patients, evaluation of the patient's clinical status was done using GCS scale after 24 hours to avoid confliction effect due to hyper acute injury. Patient's level of consciousness during acute setting may not reflect the GCS score of the patient in true sense, then they then were subjected to a CT scan as early as possible and subsequently taken for MRI after stabilizing the patient within 72 hours. Results of the MRI findings were noted and arranged in tabulated form. Patient outcome noted after three months of injury, using Glasgow outcome scale (GOS).Outcome association correlated with GCS at admission, the number of brain lesions, no of the location of the lesions, and grading of diffuse axonal injury(Adam's grading).

Adams grading of diffuse axonal injury
According to the anatomic distribution of injury:
Grade I involves gray-white matter interfaces
Grade II involves corpus callosum in addition to Stage I locations
Grade III involves brainstem in addition to Stage I and II locations.



Grade I Grade II Grade III

IMAGE ASSESSMENT

Images of all the sequences were taken in axial sections and analyzed. The lesions (2–15 mm) were defined as circumscribed foci of signal-intensity abnormality, including hypointense, hyperintense, and mixed intensity lesions. Perilesional edema and the lesions at the base and surface associated with signal void due to calcification of blood vessels were excluded.

FLAIR images show hyperintensity to the lesion areas. DWIs were evaluated with the corresponding apparent diffusion coefficient (ADC) maps to differentiate between lesions with increased, decreased, or unchanged diffusion rates. Since susceptibility effects from blood products can interfere with reliable ADC measurements, hypointense (hemorrhagic) lesions depicted on DWI were not evaluated for their ADC change. SWI sequences are particularly useful in unfolding the paramagnetic effects of petechial hemorrhages and produce a hypointensity in areas of acute and early subacute hemorrhage. Lesions that were not visualized on previous sequences were detected by SWI.

For each sequence and for the combination of all sequences, the total number of lesions was determined separately. The sensitivity was assessed by comparing the ability to detect the distribution of the lesions at various locations and the total number of lesions.

The location was selected in five regions; corpus callosum, cortico-medullary junction, posterior fossa deep cerebral nuclei, and brain stem, and locations (n = 20) were included as follows: bilateral temporal lobe, bilateral frontal lobe, bilateral parietal lobe, bilateral occipital lobe, bilateral basal ganglia, bilateral thalamus, corpus callosum-body, splenium, bilateral cerebellar hemisphere, vermis, pons, midbrain, and medulla.

The prognostic role was assessed by comparing the final Glasgow outcome scale score to Glasgow coma score at admission, the total number, and the location of lesions detected by different sequences, as well as Grades of DAI as per different imaging sequences.

STATISTICAL ANALYSIS AND METHODS:

All the data were entered in an Excel sheet Microsoft Office Excel 2007 and analyzed statistically using SPSS Statistical Software and XL STAT. All the outcome variables were summarized in the form of mean ± standard deviation. The difference between the mean value of the groups was analyzed using the ANOVA one-way test and was further analyzed with a post hoc test, and all the qualitative data were compiled in the form of proportions. The Chi-square test was used for the analysis of the differences between proportions.

EQUIPMENT USED:

Siemens Magnetom Skyra 3 Tesla MRI machine.
Siemens Spectra 3 Tesla MRI machine.

OBSERVATION/RESULTS

1.DISTRIBUTION OF MODE OF TRAUMA

Mode of injury	Number of the patients	Percent
Road traffic accident	30	83.34
Fall from height	06	16.67
Total	36	100.0

We included 36 patients in our study. The majority are having road traffic accidents as a cause of traumatic brain injury.

2. DISTRIBUTION ACCORDING TO GENDER

Gender	Number of patients
Male	36 (100%)
Female	00 (0%)
Total	36 (100%)

All the patients that we found for our study were male.

3. DISTRIBUTION OF GLASGOW COMA SCALE SCORE OF THE PATIENT AT ADMISSION.

GCS at admission	Number of patients	Percentage
<8	21	58.34
8-12	15	41.66
TOTAL	36	100

We included 36 patients in our study, out of which 21 patients (58.34%) had GCS <8 (41.66%) at the time of admission, and 15 patients had GCS between 8-12.

Mean GCS -7.38 ±2.63.

4. GLASGOW OUTCOME SCALE SCORE AT THREE MONTHS

GOS AT 3 MONTHS(SCORE)	Number of patients	Percentage
Death(1)	02	5.56
Persistent vegetative state(2)	04	11.11
Severe disability(3)	13	36.11
Moderate disability(4)	12	33.34
Good recovery(5)	05	13.88
Total	36	100

Mean GOS at three months 3.08± 1.03

We included 36 patients in our study, out of which 02 died(5.5%) after three months follow up, 04 patients were in the persistent vegetative state (11.12%),13 patients were severely disabled (36.11%),12 patients were moderately disabled (33.34%), and 05 patients (13.88)were having good recovery at three months follow up.

5. DISTRIBUTION OF LESIONS IN DAI PATIENTS

LESION DISTRICT	SWI		DWI		FLAIR	
	NUMBER	%	NUMBER	%	NUMBER	%
CEREBRAL HEMISPHERE(CH)	543	68.5	173	64.3	131	67.4
CORPUS CALLOSUM(CC)	160	20.1	55	20.4	36	18.7
DEEP BRAIN NUCLEI(DBN)	39	4.9	20	7.4	10	5.2
BRAIN STEM(BS)	36	4.6	14	5.2	09	4.8
CEREBELLUM(CB)	15	1.9	07	2.7	07	3.9
TOTAL	793	100	269	100	193	100

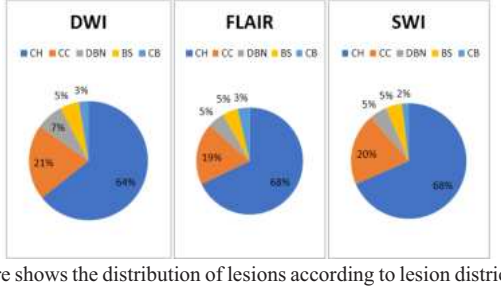


Figure shows the distribution of lesions according to lesion districts in various sequences.

6. RELATIVE SENSITIVITY OF VARIOUS IMAGING SEQUENCES IN DETECTING THE NUMBER AND LOCATIONS OF LESIONS

Imaging (n=30)	Total no. of the lesions	mean no. of lesions ± SD	Total locations of the lesion	Mean no. of locations ±SD
FLAIR	193	5.38±3.22	108	3.0±2.0
DWI	269	7.52± 4.49	136	3.77±2.37
SWI	793	21.86±9.55	182	5.0±3.18

In our study, we have taken 36 patients in which a total of 793 lesions were spotted in SWI sequence with a mean of 21.86±9.55 lesions.269 lesions in DWI sequence with a mean of 7.52± 4.49 lesions and 193 lesions in FLAIR sequence with a mean of 5.38±3.22.The cerebral hemisphere was found to have the highest number of lesions in all sequences on assessing the various images individually and together. It is mainly the frontal and parietal regions that are injured more than the temporal and occipital regions. This is followed by the corpus callosum. After this, deep cerebral nuclei, brainstem (mainly midbrain), and cerebellum were affected.

To test the relative sensitivity of various MRI sequences, we applied the HOC test that shows SWI can detect a significantly higher number of lesions at the highest number of locations compared to other MRI sequences with a P < 0.005. (significant)

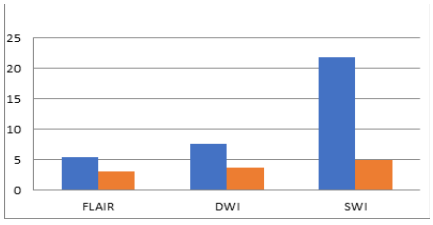
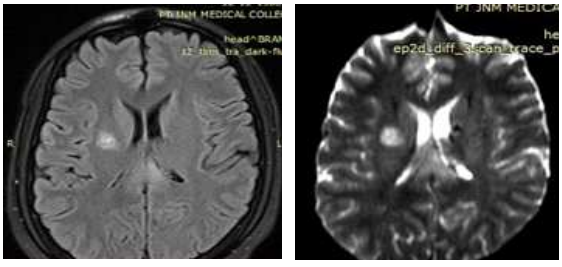
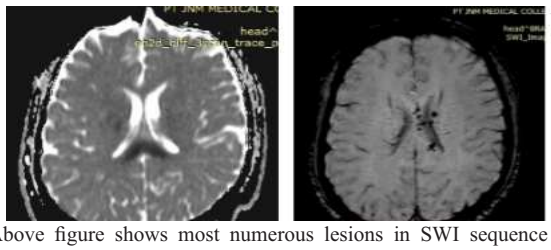


Fig shows the mean number of lesions/number of locations detected by various MRI sequences (Blue- number of the lesion, orange – number of locations).

A.FLAIR B.DIFFUSION



C. CORRESPONDING ADC D.SWI



Above figure shows most numerous lesions in SWI sequence as compared to FLAIR and DWI sequence.

7. ASSOCIATION OF THE OUTCOME OF PATIENTS WITH GCS AT ADMISSION.

Serial.no	GCS at admission	No of patients	Outcome (mean±SD)
1	<8	21	2.71±0.76
2	8-12	15	4.33± 0.47
3	>12	00	-
Total		36	

Among thirty-six patients, those having GCS ≤8 (21 patients) had an average GOS of 2.71± 0.76, and those having GCS between 9 and 12 (15 patients) had an average GOS score of 4.33± 047. On analyzing, a significant association (P = 0.003) was found between GCS and outcome at three months. Those patients with poorer GCS at admission had a final poorer outcome at three months.

8. ASSOCIATION BETWEEN THE OUTCOME AND THE NUMBER OF LESIONS DETECTED BY VARIOUS SEQUENCES.

Outcome	No of patients	No of lesions					
		SWI		DWI		FLAIR	
		Mean	SD	mean	SD	mean	SD
Death	2	32	4	14.5	0.5	11	0
Persistent vegetative State	4	23	11.42	7.5	4.5	5	2.73
Severe disability	13	27.15	8.08	9.76	4.31	7.15	3.25
Moderate disability	12	15.58	5.37	5.32	2.31	3.54	1.38
Good recovery	5	18.2	9.17	5.62	3.72	3.44	1.85
Total	36						

It seems that in every sequence, patients with a higher number of lesions had a poorer outcome. However, on analyzing the outcome to the number of lesions in each sequence, we found that there was no statistical association present between the numbers of the lesions to the outcome(P>0.005)(no statistically significant).

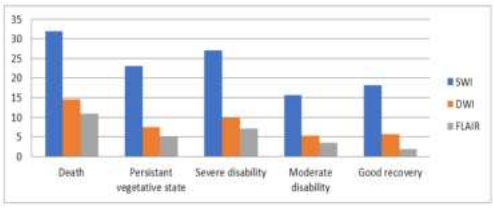


Fig shows the mean number of lesions associated with various outcome groups as per various MRI sequences.

9. ASSOCIATION BETWEEN PATIENTS' OUTCOME TO THE LOCATION OF LESIONS DETECTED BY VARIOUS SEQUENCES.

Outcome	No of patients	No of lesions					
		SWI		DWI		FLAIR	
		MEAN	SD	MEAN	SD	MEAN	SD
Death	2	10.5	5.5	8	3	6.5	2.5
Persistent vegetative State	4	6.00	3.67	4.25	2.77	3.25	2.27
Severe disability	13	5.84	2.06	4.46	1.78	3.15	1.29
Moderate disability	12	3.33	1.92	2.41	1.38	2.08	1.11
Good recovery	5	3.82	3.10	3.0	2.2	2.60	1.82
Total	36						

There was no statistically significant difference found between locations of lesion and outcome (P > 0.05)

10. CORRELATION OF OUTCOME TO THE GRADE OF DIFFUSE AXONAL INJURY PATIENTS AS PER DIFFERENT IMAGING SEQUENCES.

Outcome (GOS SCORE)	No of patients	Adams grading					
		SWI		DWI		FLAIR	
		MEAN	SD	MEAN	SD	MEAN	SD
Death(1)	2	2.5	0.5	2.5	0.5	2.5	0.5
Persistent vegetative State(2)	4	2.5	0.5	2.5	0.5	2.5	0.5
Severe disability(3)	13	2.46	0.49	2.46	0.49	2.46	0.49
Moderate disability(4)	12	1.75	0.35	1.75	0.35	1.75	0.35
Good recovery(5)	5	1.20	0.4	1.20	0.40	1.20	0.40
Total	36						

When the association was tested between the outcome to the grade of DAI patients, based on various imaging sequences, it was shown that those patients who expired (GOS-1) during the follow-up period had an average grade of 2.5 according to all imaging sequences. Those patients (n = 4) with GOS 2 had a mean of 2.5 as per all sequences. Severely disabled (GOS-3) patients had an average grade of 2.46 on all sequences. Moderately disabled (GOS-4) patients had an average grade of 1.75 in all sequences. Patients who recovered well (GOS-5) had a 1.20 grade as per all sequences. However, no significant difference was observed in the outcome to the grade of DAI patients based on various imaging sequences (P > 0.005) noted on analysis.

DISCUSSION

In our study, a road traffic accident is the most common cause of head injury (83 %) of total cases, followed by fall from height (17%).

The lobes of the brain most likely to be injured are the parietal and temporal lobes.[5]

The corpus callosum, basal ganglia, thalamus, internal capsule are the areas where damage can occur more easily because of the difference in densities[16] between them and the rest of the brain.[15] In the present study, among all districts/regions that we categorized within the parenchyma of the brain, it is the cerebral hemisphere (543 lesions out of 793 in SWI sequence), which was affected most commonly, followed by the corpus callosum (160/793), deep cerebral nuclei (39/793), brainstem (36/793), and cerebellum (15/793) in descending order of number as well as location. Chung et al. in 2012 [6] also reported the lesions in case of head trauma almost the same frequency order as we see in our study. Rainer Scheid et al. in 2002 [7] reported the involvement of the corpus callosum in 21.2% population of their study, which is nearly as same as we found in our study (20.1%).

Several studies had done in the past that relates to the role of GCS in predicting the clinical outcome. Wilberger et al. [8] found a positive correlation between the GCS score at admission and the eventual outcome of patients (GOS) with DAI. Their study observed that in severe head injury cases, 42% of the patients died or were severely disabled or remained vegetative at discharge. Mild and moderate head injury did well in terms of outcome. In patients with brainstem or corpus callosum injury, the outcome is extremely poor. Horn et al. [9] suggested the best prognosticators for traumatic brain injury: patient's initial GCS score at admission, presence of abnormalities on CT scan, and pupillary responses. He inversely correlated the clinical outcome to GCS.

Our study also reflects the positive correlation of GCS at the patient's admission to the clinical outcome. Our patients (21/36) who had a severe head injury with a GCS score ≤8 had a poorer outcome. Two of the patients died (6%), and the rest of them were remained in a persistent vegetative state (GOS-2) or were severely disabled (GOS-3). Those patients (15/36) who had a moderate head injury (GCS-9–12) were moderately disabled (GOS-4) or having good recovery (GOS-5).

Due to its wide availability, low cost, rapidity [10] less examination time, compatibility with life-support devices such as ventilators, etc. and the convenience in planning for any surgical intervention, a non-contrast CT scan of the head is an initial investigation of choice FOR evaluation of seriously injured patients (Tchekmedyian et al., 2013). However, in Diffuse axonal injury patients, it can be grossly normal or show multiple scattered tiny hemorrhagic contusions within the brain's parenchyma. MRI is considered in these situations for further evaluation (Gentry et al., 1988b; Ogawa et al., 1992). [11]

Routine sequences like T1, T2, FLAIR, or DWI can miss the actual burden of pathology due to head trauma. A sequence (such as SWI) that increases the susceptibility artifact from the blood products must be done to recognize small petechial hemorrhages.

FLAIR imaging shows lesions as white matter hyperintensities. Carlos Marquez de la Plata et al. [12] performed a quantitative assessment of white matter lesions in Diffuse axonal injury patients in 2007 using MRI FLAIR images. However, these images are more sensitive to non-hemorrhagic lesions (NHLs) and are found far below the hemorrhagic lesions in diffuse axonal injury patients, so the diagnostic capability is unreliable. Our study observed that MRI FLAIR imaging could identify a 5.38 mean number of lesions (24%) and a 3.0 mean number of locations.

Conventionally, DWI has been used to diagnose acute stroke because of its high sensitivity for acute ischemia within the brain parenchyma. However, DWI has a sensitivity for another cerebral disease also, including diffuse axonal injury. However, DWI is very sensitive only to non-hemorrhagic lesions and not that good at detecting hemorrhagic lesions. In our study, we observed that DWI detected a number of lesions with a mean of 7.47 and a number of locations with a mean of 3.63. Toshibumi Kinoshita et al. performed a study in 2006 comparing DWI and FLAIR imaging and concluded that the sensitivity of DWI to lesional detection in DAI lesions was almost similar to that of FLAIR. In our study, we observed that the detection rate of DWI was a little higher as compared to FLAIR imaging.

SWI is particularly helpful in evaluating DAI patients that are often associated with punctate hemorrhages in the deep subcortical white matter of brain parenchyma, which are not routinely seen on CT scans or conventional other MRI sequences. SWI uses the magnetic susceptibility differences between the tissues, causing phase differences between various regions containing paramagnetic deoxygenated blood products (deoxyhemoglobin, intracellular methemoglobin, and hemosiderin) and the surrounding tissue. Jun Liu et al. in 2014 observed the role of SWI in detecting lesions and found SWI to be better than other conventional MRI sequences in detecting the burden of pathology and also helpful in predicting outcome. In our study on SWI imaging, we were able to detect the highest number of lesions with 22.13 lesions per person. It can detect a rate of 6.03 lesions per person. Hence, we observed in our study that SWI is far better than other routine sequences for the detection of diffuse axonal injury lesions.

In our study, we tried to find a correlation between the clinical outcome to the number/location of the lesions. We counted the number/location of lesions shown by each sequence separately for each clinical outcome group, but none of the sequences, including SWI, could show any correlation to the clinical outcome. Although patients with a higher number of lesions seem to have a poorer outcome than those with a lesser number, we found there was no statistical significance between the number/location of lesions to the clinical outcome. Bansal et al. in 2018 [13] also counted the number/location shown by each sequence for each outcome group and found none of the MRI sequences showing any correlation with the outcome as we found in our study.

Carlos Marquez de la Plata et al., in 2007, performed a quantification study of white matter volume and correlated it to the outcome of patients. He said that volumetric assessment of DAI lesions in adult patients with traumatic brain injury during the acute phase of the illness is reliable and is reproducible, and it is associated with functional clinical outcomes. Still, there is no significant correlation between the clinical outcome and the number of hemorrhagic lesions in DAI patients noted. In a recent study, Jun Liu in 2014 shows the role of SWI in detecting lesions that were better than conventional MRI sequences and also more helpful in predicting the outcome.

A discrepancy has been reported between findings using various MRI sequences and final clinical outcomes. Studies have shown that although extensive white matter injury is more consistently associated with a poor prognosis, the presence of focal signal-intensity abnormalities indicating shearing injury was seen in patients with both poor and good clinical outcomes.

When we could not find any significant correlation to the clinical outcome, we categorized the DAI patients in different grades of DAI as per Adam's classification according to different MRI sequences. We could not find any significant difference in grade as depicted by FLAIR, DWI, and SWI. This means that the lesion deciding the grade of DAI in the patients can be picked up by conventional sequences with almost similar accuracy. Therefore, the grade of DAI patients will not vary much according to different MRI sequences. However, with increasing grades in any sequence, a patient's prognosis becomes poorer.

Our study shows that although the SWI is better than DWI and FLAIR sequences in diagnosing the DAI by picking up a higher number of lesions, the number/ location of lesions does not correlate with the outcome. It is the grade of DAI at admission that predicts the outcome better. In patients found to have sustained injury at deep locations of brain parenchyma like near basal cisterns and the brainstem had a comparatively poor prognosis than others. The involvement of the brainstem in TBI is a very important predictor of long-term clinical outcome. [14]

CONCLUSION

Although advanced imaging in head injury, SWI helps diagnose the burden of lesions in DAI more efficiently than other imaging sequences, it is the grade of injury and GCS of patients at admission that predicts the outcome more efficiently.

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