ORIGINAL ARTICLE

PATTERNS OF DIFFUSE AXONAL INJURY IN TRAUMATIC HEAD INJURY PATIENTS- A CT SCAN BASED STUDY FROM LIAQUAT NATIONAL HOSPITAL, KARACHI

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ABSTRACT

OBJECTIVE: The aim of this study was to record the incidence of patterns of diffuse axonal injury in traumatic head injury patients, that presented to a tertiary care hospital over a period of 06 months. **METHODS:** A retrospective, cross-sectional study was performed on data collected from computerized records and CT scan images of cases of traumatic head injury patients. The data was collected over a period of 06 months; from 01st July 2016 to 31st December 2016. The study center was the Department of Radiology, at Liaquat National Hospital, Karachi. **RESULTS:** A total of 123 patients presented to Liaquat National Hospital, Department of Radiology with the history of traumatic head injury over a period of 06 months. Only 23 out of these 123 patients (18.6%) who were clinically suspected of having diffuse axonal injury showed its different patterns confirmed on CT scan. 18 patients (78.2%) had contusions at gray white matter interface, 07 patients (30.4%) had contusions in corpus callosum, 04 patients (17.3%) had contusions in brain stem, 14 patients (60.8%) had contusions in cerebellum, 15 patients (65.2%) had skull fractures, 05 patients (21.7%) had intraventricular bleed while only 02 patients (8.6%) had global cerebral ischemia. The rest of 100 patients showed skull fractures, intra and extra axial bleeds with parenchymal contusions. **CONCLUSION:** The incidence of diffuse axonal injury is rare and is very low, but not uncommon in patients of traumatic head injury and cannot be disregarded. Timely diagnosis and management will be useful to lower morbidity and mortality.

Key words: Diffuse axonal injury, CT scan

Introduction

Traumatic brain injury (TBI) is a major cause of death in the population between 15 and 40 years of age in the industrialized nations. The incidence of TBI is estimated to be 200/100.000 in habitants in closed head traumas and 12/100.000 inhabitants in penetrating head traumas.[1] Diffuse axonal injury (DAI) can be found in 72% of patients with moderate or severe head injury and is a major reason for morbidity and neurological disorders in the chronic phase of TBI.[2,3,4]

In practice we define diffuse axonal injury as post-traumatic loss of consciousness which lasts for more than 6 hours in cases where no mass lesions were seen on routine imaging to explain the comatose state of the patient and more or less is a diagnosis of exclusion. However the term diffuse is probably a misnomer as the microscopic axonal pathology is more of a multifocal pattern of injury in the deep and subcortical white matter, more in the midline involving structures as the corpus callosum, splenium and the brainstem.[5,6]

Diffuse axonal injury (DAI) is a frequent result of traumatic acceleration/deceleration or rotational injuries

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and a frequent cause of persistent vegetative state in patients. In fact, DAI represents approximately one half of all intra-axial traumatic lesions.[7] This lesion is the most significant cause of morbidity in patients with traumatic brain injuries, which most commonly result from high-speed motor vehicle accidents. Any patient with a closed head injury who experiences extensive loss of consciousness and neurological deficits warrants neuroimaging.[8] Diffuse axonal injury typically consists of several focal white-matter lesions measuring 1-15 mm in a characteristic distribution.[9] The occurrence, localization and severity of shearing injuries is mainly determined by two factors: The direction and magnitude of the rotational acceleration or deceleration forces, and the difference in density and rigidity between two adjacent tissues, e.g., cerebral gray and white matter.[10,11]

Three grades of DAI, which correlate with neurological impairment, are differentiated by histopathological findings: In Grade 1 histological evidence of DAI is found in the white matter of the cerebral hemispheres; in Grade 2 additional focal lesions in the corpus callosum can be detected, and in Grade 3 further brain stem lesions are present.[12] Traumatic microbleeds (TMBs) in the white matter are considered as radiological marker for DAI.[13]

Non contrast computed tomography scan of a trauma patient demonstrates multiple petechial hemorrhages characteristically located at the gray-white matter interface consistent with diffuse axonal injury. Classically, DAI has been considered a primary type injury, with damage occurring at the time of the accident. Of patients with DAI, 80% demonstrate multiple areas of injury on computed tomography (CT) scans. Magnetic resonance imaging (MRI) is the preferred examination for DAI (particularly with gradient-echo sequences), although CT scanning may demonstrate findings suggestive of DAI and is more practical and widely available.[14,15,16]

MR imaging is more sensitive than CT in the identification of shearing injuries because MR enables detection of non-hemorrhagic as well as hemorrhagic lesions.[10,11] However, MRI is contraindicated in patients with implanted pacemakers or certain types of metallic prostheses, as well as in patients who have metallic foreign bodies, such as bullet fragments, in their head or neck or near important vascular structures. In addition, MRI is difficult to perform on patients who have claustrophobia and on ventilator-dependent patients.

CT is standardly the first imaging test performed in the emergency department setting for evaluation of head trauma. The goal of emergency imaging is to depict lesions that need emergent neurosurgical treatment or in other ways alter therapy. In many institutions, MRI is reserved for showing lesions that could explain clinical symptoms and signs that are not explained by prior CT or to help better define abnormalities seen on CT.

Materials and Methods

A retrospective, cross-sectional study was performed on data collected from patients with a history of traumatic head injury. The study center was the Department of Radiology, at Liaquat National Hospital, Karachi. The data was collected for a period of 06 months; from 01st July 2016 to 31st December 2016. As this was a retrospective study, only computer records were accessed. No formal consent was required from the patients, nor was there any contact with them. Full confidentiality of patients was maintained by using CT numbers as the reference. Patients who were clinically suspected of diffuse axonal injury that underwent CT scanning for a definitive diagnosis were included. All examinations were performed on an MDCT scanner (Toshiba Activion 16 slice CT scanner). Plain CT scans (collimation. 4 x 2.5 mm; recons-

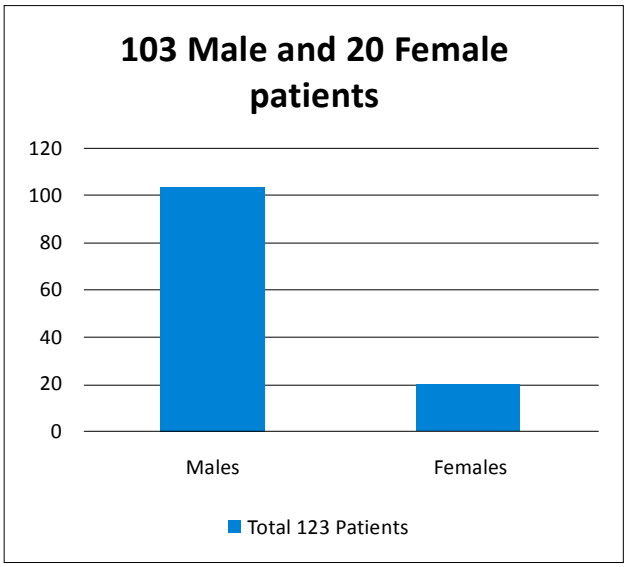


Figure 1a: Gender distribution

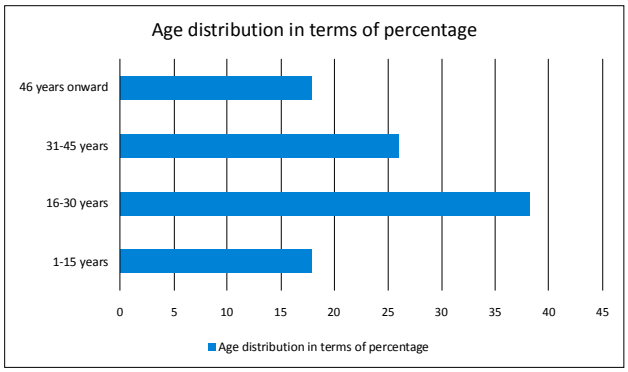


Figure 1b: Age distribution

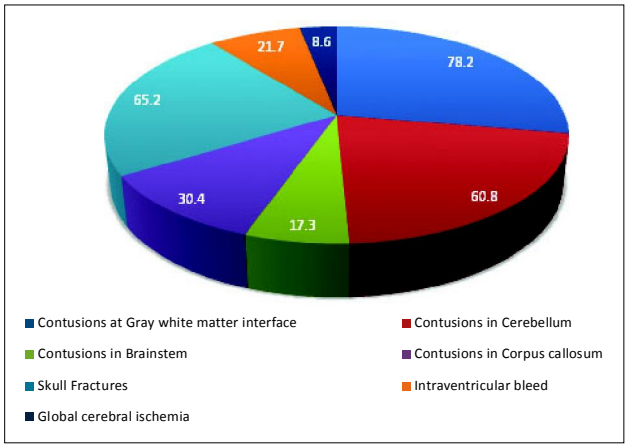


Figure 1c: Diagrammatic illustration of different patterns of DAI with other findings in terms of percentage

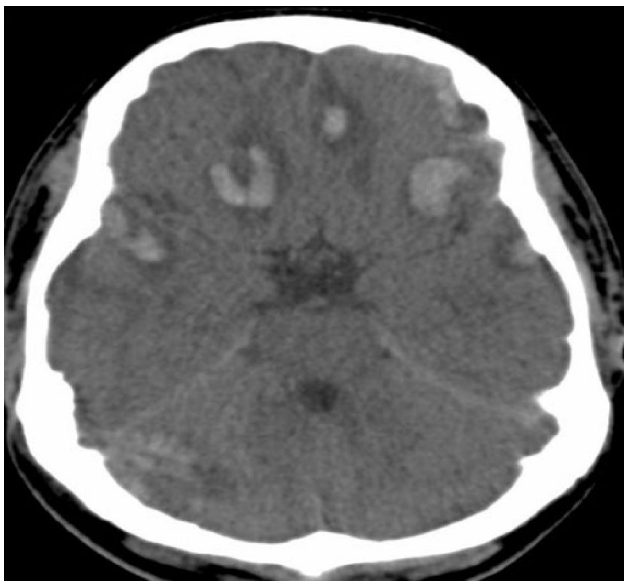
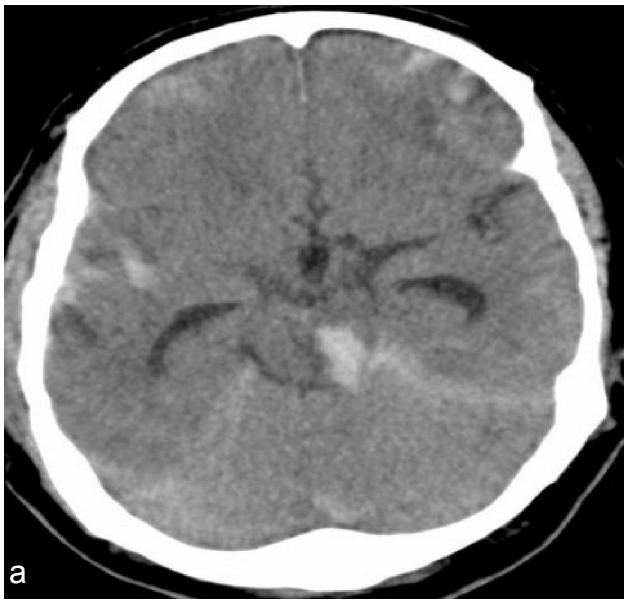


Figure 2: CT scan Axial Brain Image: Multiple hemorrhagic contusions are seen at gray white matter interface of bilateral frontal and temporal regions with perifocal edema and mild effacement of cortical sulci. Contusion hematoma is also seen in cerebellum on right side.

truction section thickness, 4 mm; reconstruction intervals, 4 mm) were obtained. CT scans were retrospectively reviewed on PACS workstations and a constellation of findings were recorded; including skull fractures, intra and extra axial bleeds (extradural, subdural, subarachnoid hemorrhages), contusions at gray white matter interface, contusions in corpus callosum, brain stem and cerebellum, intraventricular bleed and global cerebral ischemia (Fig. 2, 3a & b, 4a & b and 5a &b).



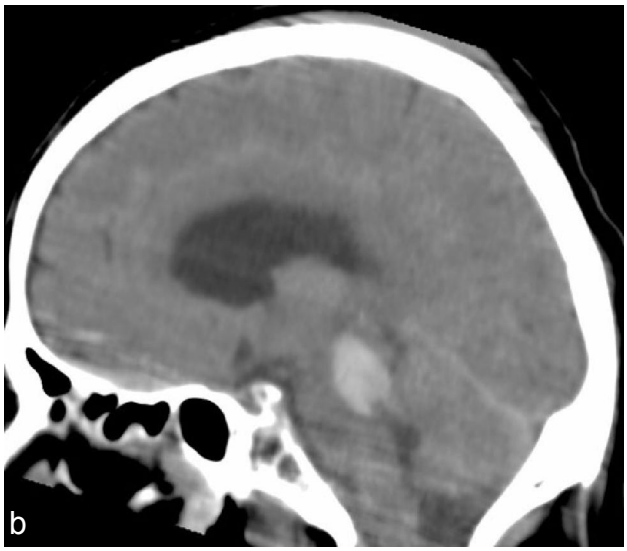
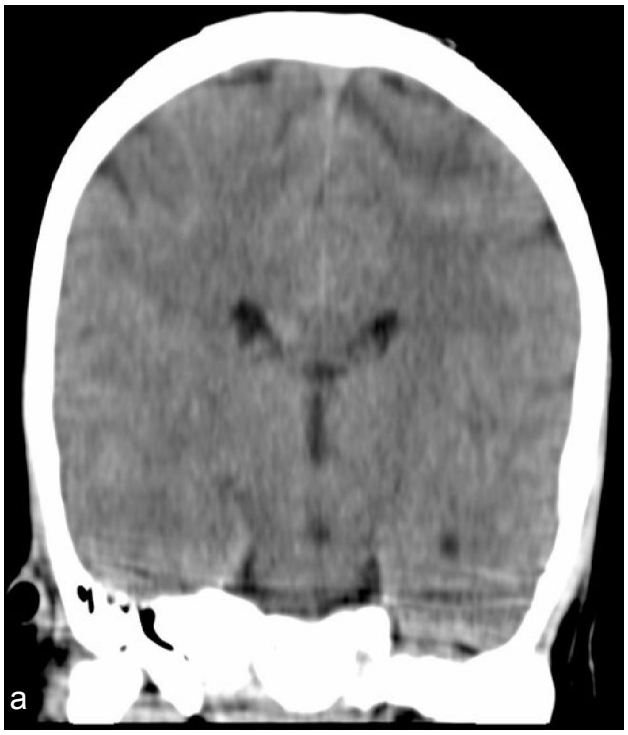


Figure 3a & b: CT scan Axial & Sagittal Brain Image: A contusion hematoma is seen in pons on left side with extension into midbrain superiorly and left cerebellar peduncle inferiorly. There is subarachnoid hemorrhage with blood in cortical sulci, tentorium and interhemispheric fissure



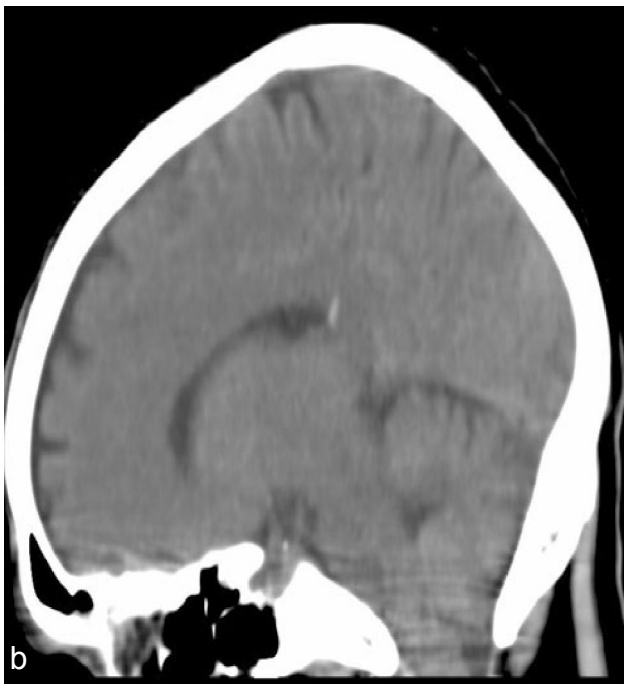
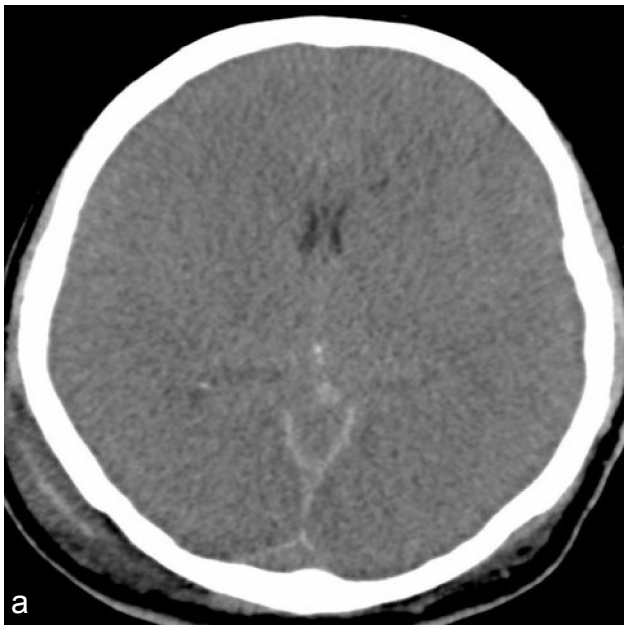


Figure 4a & b: CT scan Coronal & Sagittal Brain Image: Small linear hemorrhagic contusion is noted in the region of corpus callosum in midline posteriorly with blood in cortical sulci.



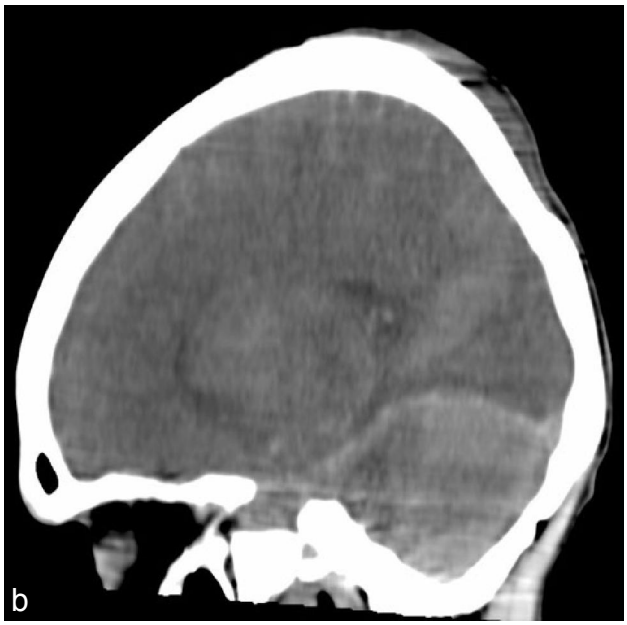


Figure 5 a & b: CT scan Axial & Sagittal Brain Image: Diffuse hypodensity is seen involving the cerebral hemispheres bilaterally with loss of gray white matter differentiation (Reversal sign). There is apparent high attenuation of cerebellum and brainstem relative to cerebral hemispheres (White cerebellum sign). Findings represent Global cerebral ischemia

Results

A total of 123 patients presented to Liaquat National Hospital, Department of Radiology with the history of traumatic head injury over a period of 06 months.

Regarding the etiologies, road traffic accidents (RTA) is the major cause of injury in 86.2% of the cases, while fall from heights constitute only 13.8% (Tab. 1). Regarding gender distribution, the sample consisted of 103 males (83.7 %) and 20 females (16.2%) (Fig. 1a). Out of 123 patients, 22 (17.8%) had age range of 1-15 years, 47 (38.2%) had 16-30 years, 32 (26%) had 31-45 years and 22 (17.8%) had more than 46 years (Tab. 2) (Fig. 1b). The overall mean age of 23 study subjects was 29.35 ± 16.59 years. The age was further stratified in two groups according to gender. The detailed descriptive statistics of age and according to gender groups are presented in (Tab. 4).

Road Traffic accidents (RTA)	106 Patients	86.2%
History of fall	17 Patients	13.8%
TOTAL SUBJECTS	**123 Patients**	**100%**

Table 1: Mode of injury.

1-15 years	22 Patients	17.8%
16-30 years	47Patients	38.2%
31-45 years	32 Patients	26.0%
46 years onward	22 Patients	17.8%
TOTAL SUBJECTS	**123 Patients**	**100%**

Table 2: Age distribution

Contusions at gray white matter interface	18 Patients	78.2%
Contusions in corpus callosum	07Patients	30.4%
Contusions in brainstem	04 Patients	17.3%
Contusions in cerebellum	14 Patients	60.8%
Skull fractures	15 Patients	65.2%
Intraventricular bleed	05 Patients	21.7%
Global cerebral ischemia	02 Patients	8.6%

Table 3: Patterns of diffuse axonal injury (DAI) with other findings in our study of 23 out of 123 patients

Out of 23 study subjects, 20 were male and 3 were female. Only 23 out of these 123 patients (18.6%) who were clinically suspected of having diffuse axonal injury showed its different patterns confirmed on CT scan. 18 patients (78.2%) had contusions at gray white matter interface, 07 patients (30.4%) had contusions in corpus callosum, 04 patients (17.3%) had contusions in brain stem, 14 patients (60.8%) had contusions in cerebellum, 15 patients (65.2%) had skull fractures, 05 patients (21.7%) had intraventricular

	Mean ± S.D
Age	29.35±16.59
Mean age of Males	28.95±17.16
Mean age of Females	32 ±14.73
Gender	
Male	20(87%)
Female	3(13%)
Contusions at Gray white matter interface	
Yes	18(78.2%)
No	5(21.7%)
Contusions in corpus callosum	
Yes	7(30.4%)
No	16(69.6%)
Contusions in brain stem	
Yes	4(17.3%)
No	19(82.6%)
Contusions in cerebellum	
Yes	14(60.8%)
No	19(39.1%)
Skull fractures	
Yes	15(65.2%)
No	8(34.8%)
Intra ventricular Bleed	
Yes	5(21.7%)
No	18(78.3%)
Global cerebral ischemia	
Yes	2(8.6%)
No	21(91.3%)

Table 4

bleed while only 02 patients (8.6%) had global cerebral ischemia (Tab. 3) (Fig. 1c). The rest of 100 patients showed skull fractures, intra and extra axial bleeds with parenchymal contusions. The detailed frequency distribution is presented in (Tab. 4).

Descriptive statistics were calculated using SPSS version 21. Stratification was done and post stratification Chi square test was applied to observe the effect of modifiers on outcome. P-value ≤ 0.05 was considered as significant. Stratification with respect to contusions at gray white matter interface, contusions in corpus callous, contusions in brain stem, contusions in cerebellum, skull fractures, intra ventricular bleed,

global cerebral ischemia was done to observe effect of these modifiers on age groups and gender. P-value ≤ 0.05 was considered as significant. The results showed that there was insignificant association of age groups with contusions at gray white matter interface (p=0.618), contusions in corpus callous (p=0.007), contusions in brain stem (p=0.28), contusions in cerebellum (p=0.669), skull fractures (p=0.685), intra ventricular bleed (p=1.00), global cerebral ischemia (p=0.178). The detailed results of association with age group are presented on (Tab. 5).

	Age		
	≤30 13(56.5%)	>30 10(43.5%)	P-value
Contusions at Gray white matter interface			
Yes	11(84.6)	7(70)	
No	2(15.4)	3(30)	0.618**
Contusions in corpuscallosum			
Yes	7(53.8)	0(0)	
No	6(46.2)	10(100)	0.007**
Contusions in brain stem			
Yes	1(7.7)	3(30)	
No	12(92.3)	7(70)	0.281**
Contusions in cerebellum			
Yes	7(53.8)	7(70)	
No	6(46.2)	3(30)	0.669**
Skull fractures			
Yes	9(69.2)	4(40)	
No	4(30.8)	6(60)	0.685**
Intra ventricular Bleed			
Yes	3(23.1)	2(20)	
No	10(76.9)	8(80)	1.00**
Global cerebral ischemia			
Yes	0(0)	2(20)	
No	13(100)	8(80)	0.178**

Chi-Square test is applied,
*P-value ≤ 0.05 consider as significant
**Insignificant at >0.05

Table 5

The results showed that there was also insignificant association of gender with age (p=0.560),contusions at gray white matter interface (p=0.539), contusions in corpus callous (p=0.526), contusions in brain stem (p=0.453), contusions in cerebellum (p=0.253), skull fractures (p=0.094), intra ventricular bleed (p=1.00), global cerebral ischemia (p=1.00). The detailed results of association with gender are presented on (Tab. 6).

	Gender		
	Male 20(87%)	Female 3(13%)	P-value
Age			
≤30	12(60)	1(33.3)	
>30	8(40)	2(66.7)	0.56**
Contusions at Gray white matter interface			
Yes	16(80)	2(66.7)	
No	4(20)	1(33.3)	0.539**
Contusions in corpuscallosum			
Yes	7(35)	0(0)	
No	13(65)	3(100)	0.526**
Contusions in brain stem			
Yes	3(15)	1(33.3)	
No	17(85)	2(66.7)	
Contusions in cerebellum			0.453**
Yes	11(55)	3(100)	
No	9(45)	0(0)	0.253**
Skull fractures			
Yes	12(60)	3(100)	
No	8(40)	0(0)	0.094**
Intra ventricular Bleed			
Yes	5(25)	0(0)	
No	15(75)	3(100)	1.00**
Global cerebral ischemia			
Yes	2(10)	0(0)	
No	18(90)	3(100)	1.00**

Chi-Square test is applied,
*P-value ≤ 0.05 consider as significant
**Insignificant at >0.05

Table 6

Discussion

Brain trauma produces diverse spectrum of injuries in which diffuse axonal injury is a well-recognized major contributing factor to long-term disability. DAI results from accelerative-decelerative forces associated with high-energy head trauma, which give rise to shearing forces that act at regions of the brain with different densities and compliances. Gray matter-white matter junctions and the region adjacent to the falx are the most susceptible location for this type of damage. DAI that is more common and associated with microbleeding is called hemorrhagic DAI. DAI without microbleeding or with isolated microbleeding has also been reported.[17]

Intraparenchymal bleeding, including white matter microbleeding, is also a major feature of TBI. There

are two manifestations of DAI. The first one is small petechial hemorrhages throughout the brain that result from the rupture of small blood vessels. The second is linear hemorrhages at subcortical white matter regions, particularly in the posterior frontal and parietal lobes.[18]

These small petechial hemorrhages scattered throughout the white matter, particularly in parasagittal white matter, are typically called diffuse vascular injury (DVI). All cases of DVI show severe DAI and fall in a spectrum of similar pathological conditions. Thus, appreciating the properties of DVI, as understood through microbleeding petechial hemorrhages, helps give diagnostic insight into potential DAI.[19]

The pathophysiology of DAI includes disruption of the axolemmal membrane as a result of trauma followed by disruption of electrochemical homeostasis with passage of multiple ions along their concentration gradient. Loss of oxidative phosphorylation and production of ATP as a result of intra mitochondrial calcium overload also is a contributing factor to the pathology. The orderly activation of proteases like caspases and calpains are also disrupted, contributing to disruption of subaxolemmal membrane and neuronal cytoskele-ton.[20,21]

Before the advent of neuroimaging, the characteristics of diffuse axonal injury were defened by Adams et al and Gennarelli et al from a histopathological viewpoint. Their experimental studies suggested that centripetal extension of a shearing injury into the brain stem caused prolonged unconsciousness. Further more they emphasized the importance of injury to the corpus callosum and dorsolateral midbrain, and described diffuse axonal damage in the cerebral hemispheres. The coexistence of these two injuries was considered to represent the most severe histological grade in fatal human cases.[22,23,24]

On the basis of neuropathologic findings, some authors now consider DAI a misnomer because injury is frequently not diffuse but multifocal, and as such, the term traumatic axonal injury has been suggested to be more appropriate.[25] The degree of microscopic injury usually is considered to be greater than that seen on diagnostic imaging, and the clinical findings reflect this point. DAI is suggested in any patient who demonstrates clinical symptoms disproportionate to his or her CT scan findings. DAI results in instantaneous loss of consciousness, and most patients (>90%) remain in a persistent vegetative state, since brainstem function typically remains unaffected.

It has been shown in various studies that non contrast CT scan is highly accurate in diagnosing intracranial hemorrhage. By diagnosing the presence of intracranial hemorrhage, it is possible to provide in-time management to the patients. In a study performed by Racadio et al, it was found that 46% of patients had intracranial hemorrhage. In the crash trial which was the largest trial conducted among traumatic head injury, 56% of patients had some type of intracranial hemorrhage. Similarly, Ruiz et al found that traumatic intracranial hemorrhages were found in 23% of 160 head injury patients.

Our study was aimed in detecting the incidence of different patterns of diffuse axonal injury in clinically suspicious patients who suffered traumatic head injury and confirmed on CT scan. All these 23 patients out of 123 patients have different patterns of diffuse axonal injury. (Tab. 3). This statistic of a striking 18.6% cannot be ignored because it will effect the prognosis and outcome of the patient as early detection of diffuse axonal injury is very important. (Fig. 1c). The rest of 100 patients showed skull fractures with intra and extra axial bleeds, parenchymal contusions and generalized brain edema.

Our study showed that the hemispheric gray-white matter was considered the most common location for DAI (78.2%). This is probably due to peripheral location that increases the vulnerability for trauma and abrupt change in tissue density between the gray and white matter. We found cerebellar contusions in 60.8% followed by contusions in corpus callosum and brain stem i.e. 30.4% and 17.3% respectively. A possible explanation is that almost all patients included in this study had suffered RTA and the centripetal forces, generated by high-speed impact usually effects the deeper areas of the brain such as the corpus callosum and the brainstem. The resultant damage is axonal since the axons are torn or stretched such that axoplasmic transport and the electrical network become impaired.

Although our study leads to significant findings, it was not aimed towards determining the best intervention and management of the condition; nor was there any follow up with the patients to ascertain the sequelae of this affliction. Also, being a single institution experience, it is somewhat confined to a less

than diverse group of patients. A multi-center study would be even more thorough in determining the prevalence of diffuse axonal injury in patients suffering from trauma.

Conclusion

Even with closed head injury, the brain can suffer severe damage from DAI due to shearing forces. The sites of predilection are well documented and include the gray-white matter interfaces at the subcortical region, corpus callosum, brainstem, and cerebellum.The incidence of diffuse axonal injury is low, but not uncommon in patients who suffered from trauma and cannot be disregarded. Timely diagnosis and management will be useful to lower morbidity and mortality. Currently, most of the commonly used diagnostic standards are noninvasive methods, such as neuropsychological assessment, CT/MRI imaging, and biochemical markers. However, each individual method of diagnosing DAI has its own specificlimitations. In the future, after further investigation and assessment of the pathological mechanism underlying DAI, a multimechanism form of diagnosis may be available. Only 23 cases of DAI were detected in 123 head injured patients over a period of 06 months in our study representing its relative rarity, however a larger multicenter study would be more representative.

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