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## RESEARCH ARTICLE

# AUTOPSY FINDINGS IN DIFFUSE AXONAL INJURY STATISTICAL REVIEW

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**ABSTRACT**

**Context:** Diffuse Axonal Injury is an important pathological substrate of Traumatic Brain Injury. Knowing the clinical, radiological and post-mortem features of diffuse axonal injury can significantly increase our understanding of this entity in particular and traumatic brain injury as a whole and may help us in treating as well as predicting the outcome of patients with diffuse axonal injury.
**Aim:** To analyze the clinical, radiological and gross & histological autopsy features of Diffuse Axonal Injury in severe head injury patients.
**Settings and Design:** Prospective Cross-sectional Study
**Methods and Materials:** 32 patients admitted to the neurosurgical ward of the Institute of Neurosurgery, Madras Medical College & RGGGH, between the period of October 2012 to March 2015, with Severe Head injury (GCS<8) and CT scan brain suggestive of Diffuse Axonal Injury were included in the study. Demographic data was collected and radiologic features were analyzed. Patients who died during the course of treatment were included in the study and autopsy was done. Of the 90 patients who had DAI, 32 patients expired and were subjected to autopsy and findings were analyzed.
**Results:** It was observed that SAH was the commonest gross autopsy finding (62.5%). Hypoxic Changes with cellular swelling were the common findings in microscopic examination. Microscopic Lesions in Thalamus were the most statistically significant post-mortem finding.
**Conclusions:** Thus in our study we found that in most cases CT Brain findings did not correlate with severity of head injury. The study shows that edema in the brain stem and corpus callosum were the predisposing causes of death.



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## INTRODUCTION

The adage that the dead teach the living cannot be truer than in severe head injury. Hence this study was taken up which analyze the neurological deficits and death as the result of diffuse closed head trauma sustained from high-speed automobile accidents which are difficult and confusing to comprehend. The long-term consequences from such diffuse inner cerebral trauma are still poorly defined (James *et al*., 2012; Sanjith, 2011; Smith *et al*., 2013). The diffuse degeneration of cerebral white matter is associated with sagittal and lateral acceleration with centro-axial trauma and has a different pathogenesis from outer focal head trauma, typified by subdural hematomas and coup injuries (Sahuquillo *et al*., 1989; John R.Parker *et al*., 1990). Unlike outer cerebral injury, over 50 percent of victims with diffuse axonal injury die within two weeks (Sanjith, 2011; Smith *et al*., 2013). These individuals characteristically have no lucid interval and remain unconscious, vegetative, or severely disabled until death. Compared to head trauma victims without diffuse axonal injury, there is a lower incidence of skull fractures, subdural hemorrhages, or other intracranial mass effect as well as outer brain contusions (James *et al*., 2012; Sanjith, 2011) Primary brainstem injuries often demonstrated at autopsy are seen in the reported cases (James *et al*., 2012; Sahuquillo *et al*., 1989; John R.Parker *et al*., 1990). Diffuse axonal injury is produced by various angles of acceleration with prolonged acceleration/ deceleration-usually accompanying traffic accidents.Lesssevere diffuse axonal injury causes concussion. Hence this study aims to analyze in detail the clinical, radiological and gross & histological autopsy features of Diffuse Axonal Injury in severe head injury patients.

### Aims & objectives of the study

To analyze the clinical, radiological and gross & histological autopsy features of Diffuse Axonal Injury in severe head injury patients.

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## MATERIALS AND METHODS

### Subjects

All patients admitted to the neurosurgical ward of the Institute of Neurosurgery, Madras Medical College & RGGGH with Severe Head injury (GCS<8) and CT scan brain suggestive of Diffuse Axonal Injury were be included in the study.

### Exclusion criteria

1. Patients who had severe parenchymal injuries.
2. Patients who had extra-axial and intra-axial hematomas.
3. Patients who had multiple injuries (solid organs and long bone fractures).
4. Patients who were not willing to take part in the study.

### METHODOLOGY

The patients who are admitted to the neurosurgical ward with Severe Head Injury (GCS<8) and a CT scan brain suggestive of diffuse axonal injury were included in the study. The demographic data was collected and the radiologic features were analyzed. The patients who died during the course of treatment were included in the study and the autopsy was done to study the features of diffuse injury in the brain. In our institution, in the study period, average about 50 patients per day get admitted in Trauma Ward Following Injury from RTA, fall, assault and industrial accidents etc. Of which on an average, 12 had head injury. Of this 12, we found that 2 patients had Severe Head Injury (GCS<8) & Diffuse Axonal Injury. Of this, one patient had moderate to severe DAI. In our study 90 patients had DAI, of whom 32 patients expired and were subjected to autopsy and findings were analyzed.

## OBSERVATIONS AND RESULTS

The overall results of this study are as shown below.

### Age

The Minimum Age of the patient was 18 and the Maximum Age of the patient was 85 in this study. The Mean was 43years.

### Loss of consciousness

All the patients in our study were associated with LOC.

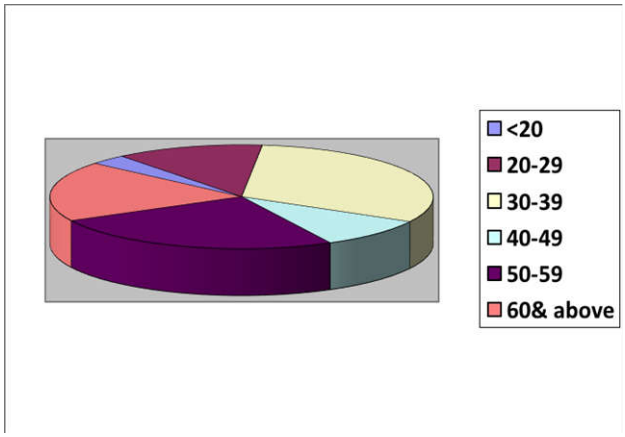



**Fig. 1.a. Demographic data of study sample- age**

**Table 1. Demographic data of study sample- age**

| Age | No |
|---|---|
| <20 | 1 |
| 20-29 | 4 |
| 30-39 | 10 |
| 40-49 | 3 |
| 50-59 | 8 |
| 60& above | 6 |
| | 32 |

**Table 2. Demographic data of study sample-sex**

| | Frequency | Percent |
|---|---|---|
| Male | 24 | 75.0 |
| Female | 8 | 25.0 |
| Total | 32 | 100.0 |

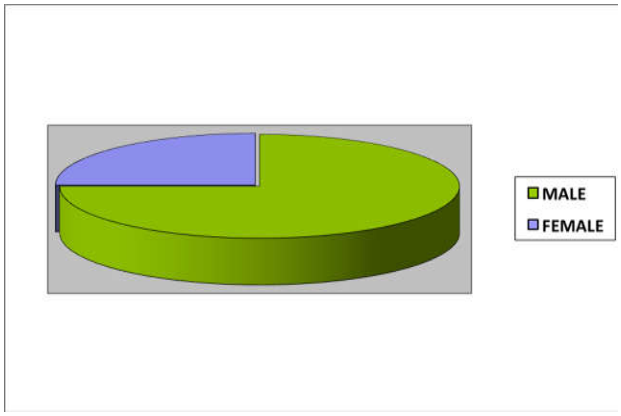



**Fig.1.b. Demographic data of study sample-sex**

### Seizures

In our study 17 out of 32 patients had seizure, of them 10 patients had seizure on the day of injury.

**Table 3. Prevalence of seizures in study population**

| | Frequency | Percent |
|---|---|---|
| Seizure | 17 | 53.1 |
| Without seizure | 15 | 46.9 |
| Total | 32 | 100.0 |

### Vomiting

In this study 14 patients had vomiting.

**Table 4. Prevalence of vomiting in study population**

| | Frequency | Percent |
|---|---|---|
| Present | 14 | 43.8 |
| Absent | 18 | 56.3 |
| Total | 32 | 100.0 |

### ENT bleed

In this study 10 patients had ENT bleed.

**Table 5. Prevalence of ENT bleed in study population**

| | Frequency | Percent |
|---|---|---|
| Present | 10 | 31.3 |
| Absent | 22 | 68.8 |
| Total | 32 | 100.0 |

## Glasgow Coma Scale (GCS)

All the patients in our study were unconscious, the average GCS was less than 6. There were 8 patients in GCS 3, 9 patients in GCS 4, 10 patients in GCS 5, 5 Patients with GCS 6.

**Table 6. Admission GCS of study population**

| GCS | Frequency | Percent |
|---|---|---|
| 3 | 8 | 25.0 |
| 4 | 9 | 28.1 |
| 5 | 10 | 31.3 |
| 6 | 5 | 15.6 |
| Total | 32 | 100.0 |

In this study patients with GCS less than 5 died.(84.4 %)

**Table 7. Eye opening score in study population**

| Score | Frequency | Percent |
|---|---|---|
| 1 | 29 | 90.6 |
| 2 | 3 | 9.4 |
| Total | 32 | 100.0 |

**Table 8. Verbal response score in study population**

| | Frequency | Percent |
|---|---|---|
| ET | 32 | 100.0 |

**Table 9. Motor response score in study population**

| | Frequency | Percent |
|---|---|---|
| 1 | 8 | 25.0 |
| 2 | 9 | 28.1 |
| 3 | 13 | 40.6 |
| 4 | 2 | 6.3 |
| Total | 32 | 100.0 |

**Table 10. Pupil size at the time of admission**

| Pupil Size | Frequency | Percent |
|---|---|---|
| 3.0 | 18 | 56.3 |
| 3.5 | 4 | 12.5 |
| 4.0 | 10 | 31.3 |
| Total | 32 | 100.0 |

**Table 11. Pupillary reflex at the time of admission**

| Pupillary Reflex | Frequency | Percent |
|---|---|---|
| Present | 7 | 21.9 |
| Absent | 25 | 78.1 |
| Total | 32 | 100.0 |

**Table 12. Dem at the time of admission**

| DEM | Frequency | Percent |
|---|---|---|
| Present | 7 | 21.9 |
| Absent | 25 | 78.1 |
| Total | 32 | 100.0 |

**Table 13. Clinical grading of DAI in study population**

| Clinical Grading | Frequency | Percent |
|---|---|---|
| 1 | 3 | 9.4 |
| 2 | 12 | 37.5 |
| 3 | 17 | 53.1 |
| Total | 32 | 100.0 |

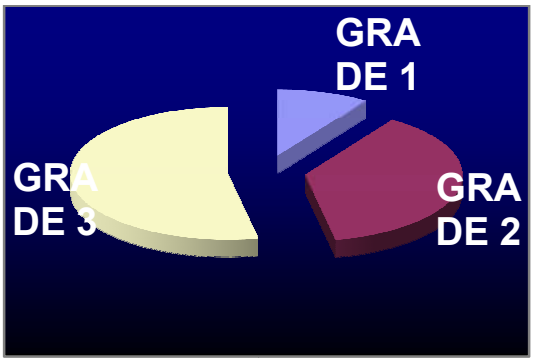
## Clinical Grade

More number of Patients with clinical grading "GRADE – 3" died, 17 out of 32 (53.1%)

**Fig. 2. Clinical grading of diffuse axonal injury**

| DAI grade | Description |
|---|---|
| mild | coma > 6-24 hrs, followed by mild-to-moderate memory impairment, mild-to-moderate disabilities |
| moder-ate | coma > 24 hrs, followed by confu-sion & long-lasting amnesia. Mild-to-severe memory, behavior-al and cognitive deficits |
| severe | coma lasting months with flexor and extensor posturing. Cogni-tive, memory, speech, sensorimo-tor and personality deficits. Dysautonomia may occur |

**Fig.3. Distribution of clinical grading of DAI in study population**




## CT brain grading

In this study, CT brain was normal in 10 patients out of 32. In 6 patients (18.8%) lesions were found in thalamus. In Wadate *et al* study CT brain was normal in 16% of patients. Our study it was 31.25%.

**Table 14. Location of lesion in CT brain**

| | |
|---|---|
| Lesions in Thalamus | 6 |
| Lesions in Midbrain | 4 |
| Lesions in Pons | 4 |
| Lesions in Medulla | 5 |
| Lesions in Corpus Callosum | 3 |
| No Lesions in CT Brain | 10 |

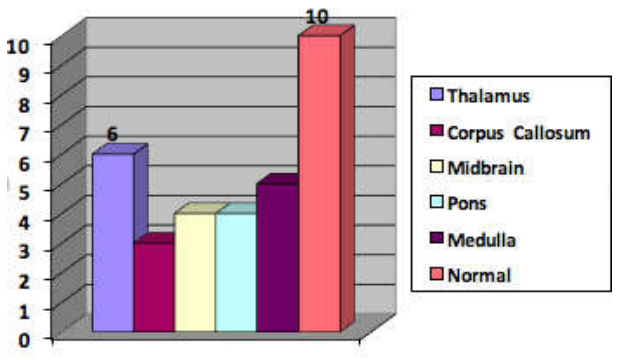



**Fig.4. Location of lesion in this study**

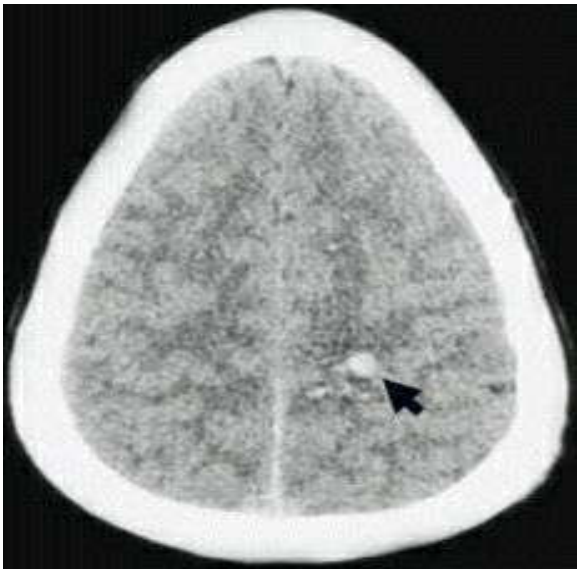


**Fig.5. Subcortical Lesion**

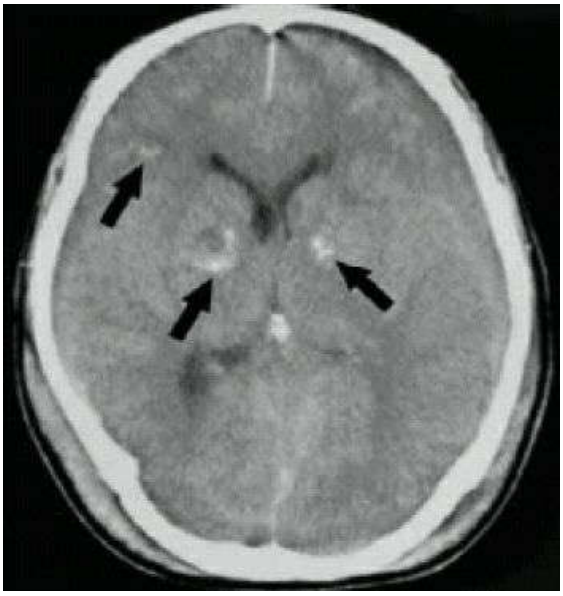


**Fig.6. Subcortical and thalamic lesions in CT**

In this study, though CT brain was normal in most of the cases, autopsy revealed lesions in various locations of the brain which become pathognomic.

## Gross Findings in Autopsy

SAH was the commonest finding - in 20 patients out of 32 (62.5%) which is correlating with Wadate *et al*. study.

**In Wadate *et al*. study it was 64%**

| | |
|---|---|
| 1. | SAH – 20 cases |
| 2. | Contused Brain |
| 3. | Contused Brain with Hemorrhagic Spots |
| 4. | Diffuse Punctate Haemorrhagic Spots |
| 5. | Left Frontal Thin SDH |
| 6. | Left Sylvian Region ICH |
| 7. | Left Ventricular IVH |
| 8. | Right Frontal ICH |
| 9. | Right Sylvian Region ICH |
| 10. | Right Temporal ICH |
| 11. | Right Thalamic ICH |
| 12. | Small Bifrontal Contusion |

## Autopsy images

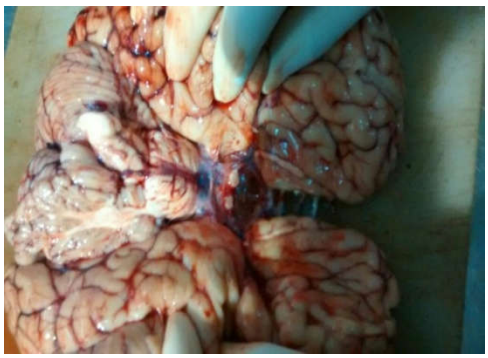


**Fig.7. Brain Stem Contusion**

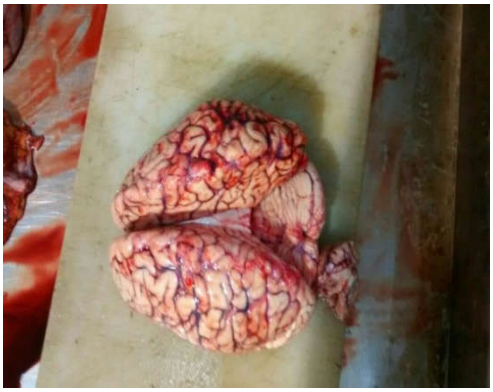


**Fig.8. Gross Specimen With SAH**

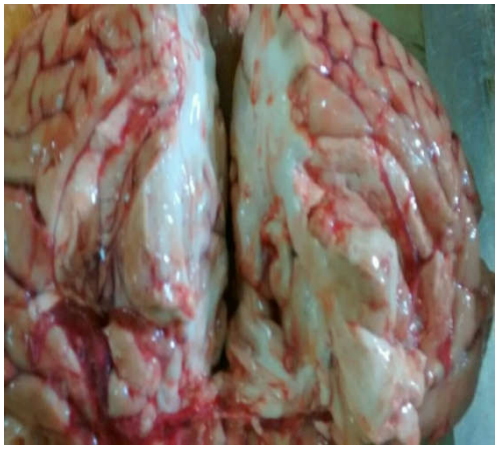


**Fig.9. Midbrain Petechial bleed**

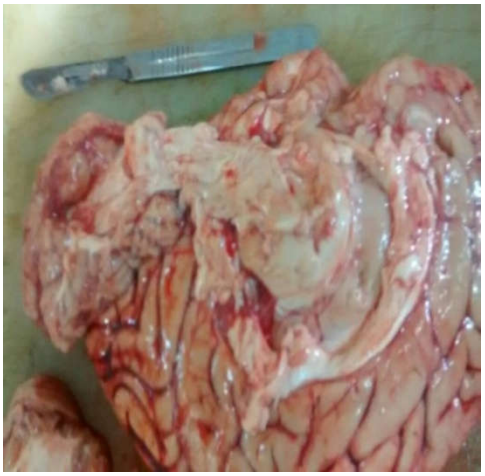


**Fig. 10. Brain Stem Cisternal Bleed**

**Table 15. Gross finding on autopsy**

| | Frequency | Percent | Valid Percent | Cumulative Percent |
|---|---|---|---|---|
| Contused Brain | 1 | 3.1 | 3.1 | 3.1 |
| Contused Brain with Hemorrhagic Spots | 1 | 3.1 | 3.1 | 6.3 |
| Diffuse Punctate Haemorrhagic Spots | 1 | 3.1 | 3.1 | 9.4 |
| Left Frontal Thin SDH | 1 | 3.1 | 3.1 | 12.5 |
| Left Sylvian Bleed | 1 | 3.1 | 3.1 | 15.6 |
| Left Ventricular IVH | 1 | 3.1 | 3.1 | 18.8 |
| Right Frontal ICH | 1 | 3.1 | 3.1 | 21.9 |
| Right Sylvian bleed | 1 | 3.1 | 3.1 | 25.0 |
| Right Temporal ICH | 1 | 3.1 | 3.1 | 28.1 |
| Right Thalamic ICH | 1 | 3.1 | 3.1 | 31.3 |
| Small Bifrontal Contusion | 2 | 6.3 | 6.3 | 37.5 |
| SAH | 20 | 62.5 | 62.5 | 100.0 |
| Total | 32 | 100.0 | 100.0 | |

## Microscopic findings in autopsy

On microscopic examination Hypoxic Changes with cellular swelling, Microhemorrages, White Matter Degeneration, Axonal swelling were found (James *et al*., 2012; Sanjith, 2011; John R.Parker *et al*., 1990). Among them Hypoxic Changes with cellular swelling were the commonest finding. In Parker *et al* study (John R.Parker *et al*., 1990) autopsy microscopic findings were mostly diffuse degeneration of cerebral white matter, but in our study Hypoxic Changes with cellular swelling were the common findings

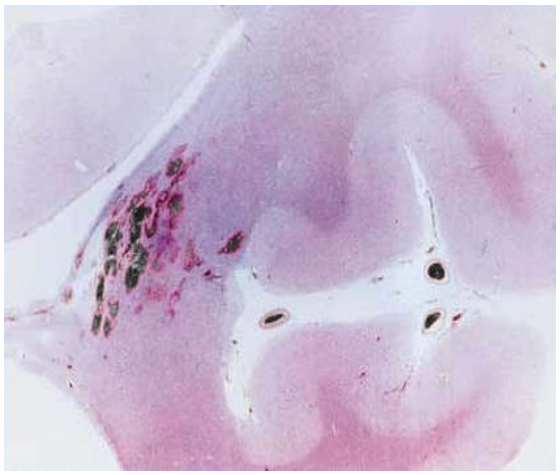


**Fig.11. Low power Hematoxylin eosin stain demonstrating DAI & Petechial Hemorrhage**

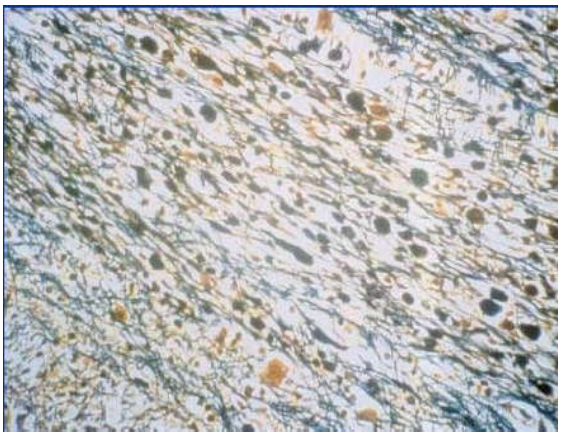


**Fig.12. Silver stain indicating Axonal terminal bulbs**

**Table 16. Microscopic Findings in Autopsy: Lesions in Thalamus**

| Microscopic Findings | Frequency | Percent | Valid Percent | Cumulative Percent |
|---|---|---|---|---|
| Hypoxic Changes | 22 | 68.8 | 68.8 | 68.8 |
| Microhemorrages | 10 | 31.3 | 31.3 | 100.0 |
| Total | 32 | 100.0 | 100.0 | |

**Table 17. Microscopic Findings in Autopsy : Lesions in Corpus Callosum**

| | Frequency | Percent | Valid Percent | Cumulative Percent |
|---|---|---|---|---|
| Hypoxic Changes | 16 | 50.0 | 50.0 | 50.0 |
| Microhemorrages | 14 | 43.8 | 43.8 | 93.8 |
| White Matter Degeneration | 2 | 6.3 | 6.3 | 100.0 |
| Total | 32 | 100.0 | 100.0 | |

**Table 18. Microscopic Findings in Autopsy:Lesions in Midbrain**

| | Frequency | Percent | Valid Percent | Cumulative Percent |
|---|---|---|---|---|
| Hypoxic Changes | 19 | 59.4 | 59.4 | 59.4 |
| Microhemorrages | 9 | 28.1 | 28.1 | 87.5 |
| White Matter Degeneration | 4 | 12.5 | 12.5 | 100.0 |
| Total | 32 | 100.0 | 100.0 | |

**Table 19. Microscopic Findings in Autopsy : Lesions in Pons**

| | Frequency | Percent | Valid Percent | Cumulative Percent |
|---|---|---|---|---|
| Hypoxic Changes | 21 | 65.6 | 65.6 | 65.6 |
| Microhemorrages | 6 | 18.8 | 18.8 | 84.4 |
| White Matter Degeneration | 4 | 12.5 | 12.5 | 96.9 |
| Axonal Retraction Balls | 1 | 3.1 | 3.1 | 100.0 |
| Total | 32 | 100.0 | 100.0 | |

**Table 20. Microscopic Findings in Autopsy : Lesions in Medulla**

| | Frequency | Percent | Valid Percent | Cumulative Percent |
|---|---|---|---|---|
| Hypoxic Changes | 22 | 68.8 | 68.8 | 68.8 |
| Microhemorrages | 5 | 15.6 | 15.6 | 84.4 |
| White Matter Degeneration | 4 | 12.5 | 12.5 | 96.9 |
| Axonal Retraction Balls | 1 | 3.1 | 3.1 | 100.0 |
| Total | 32 | 100.0 | 100.0 | |

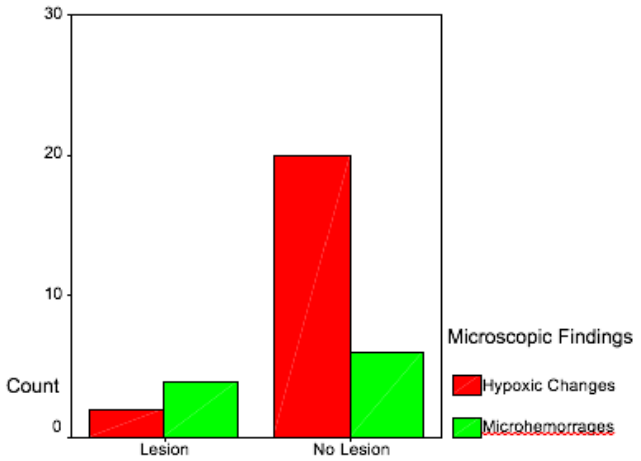



**Fig.13. CT: Lesions in Thalamus**

**Statistics**

**Table 21. CT : Lesions in Thalamus * Microscopic Findings in Autopsy -Lesions in Thalamus**

| | | | Microscopic Findings in Autopsy : Lesions in Thalamus | | Total | P value |
|---|---|---|---|---|---|---|
| | | | Hypoxic Changes | Microhemorrages | | |
| CT : Lesions in Thalamus | Lesion | Count | 2 | 4 | 6 | |
| | | % within CT : Lesions in Thalamus | 33.3% | 66.7% | 100.0% | |
| | | % within Microscopic Findings in Autopsy : Lesions in Thalamus | 9.1% | 40.0% | 18.8% | |
| | No Lesion | Count | 20 | 6 | 26 | |
| | | % within CT : Lesions in Thalamus | 76.9% | 23.1% | 100.0% | |
| | | % within Microscopic Findings in Autopsy : Lesions in Thalamus | 90.9% | 60.0% | 81.3% | |
| Total | | Count | 22 | 10 | 32 | |
| | | % within CT : Lesions in Thalamus | 68.8% | 31.3% | 100.0% | |
| | | % within Microscopic Findings in Autopsy : Lesions in Thalamus | 100.0% | 100.0% | 100.0% | 0.038* |

**Table 22. Chi-Square Tests**

| | Value | df | Asymp. Sig. (2-sided) | Exact Sig. (2-sided) | Exact Sig. (1-sided) |
|---|---|---|---|---|---|
| Pearson Chi-Square | 4.311(b) | 1 | .038 | | |
| Continuity Correction(a) | 2.521 | 1 | .112 | | |
| Likelihood Ratio | 4.021 | 1 | .045 | | |
| Fisher's Exact Test | | | | .060 | .060 |
| Linear-by-Linear Association | 4.177 | 1 | .041 | | |
| N of Valid Cases | 32 | | | | |

a Computed only for a 2x2 table
b 2 cells (50.0%) have expected count less than 5. The minimum expected count is 1.88.

By using **Chi-Square Test P value = 0.038 (P<0.05),** statistically significant. Microscopic Lesions in Thalamus was statistically significant compared with other CT brain lesions

## DISCUSSION

- Most common age group among 30-39 years
- All DAI patients were associated with LOC.
- Patients with GCS less than 5 mostly died. (84.4 %)
- More than 50% of the Patients with clinical grading 3 expired.
- In this study most patients with severe DAI did not had any skull fractures.
- CT brain was normal in one third of patients.
- SAH was the commonest gross autopsy finding (62.5%)
- Hypoxic Changes with cellular swelling were the common findings in microscopic examination and was statistically significant in parameters evaluated.
- All patients with normal CT brain, microscopically demonstrable lesions were common & statistically significant.
- Microscopic Lesions in Thalamus was more statistically significant.

**Conclusion**

- Thus in our study we found that in most cases CT Brain findings did not correlate with severity of head injury.
- In this study, CT brain was normal in 10 patients out of 32. In 6 patients (18.8%) lesions were found in thalamus
- By using Chi-Square Test P value = 0.038 (P<0.05), statistically significant. Microscopic Lesions in Thalamus was statistically significant compared with other CT brain lesions
- SAH was the commonest finding - in 20 patients out of 32 (62.5%)
- Postmortem conclude that edema (cellular swelling) in brain stem and corpus callosum were the predisposing causes of death probably due to hypoxia and free radical in most cases.
- This aspect needs further biochemical analytical study which the students propose to take up as a future research.

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