

Original Article

## Incidence of Epilepsy and Drug Dependence after Post Traumatic Contusions Managed Conservatively

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### ABSTRACT

**Objectives:** To determine the true incidence of epilepsy and drug dependence after post-traumatic contusions managed conservatively.

**Material and Methods:** A prospective observational study was carried out in, Punjab Institute of Neurosciences, Lahore. A total of 97 patients, from 15-65 years, who were diagnosed with cerebral contusions and being managed conservatively were enrolled from July 2019 to December 2019. They were followed-up for 12 – 18 months.

**Results:** A total of 23% patients developed early post-traumatic seizures (PTS) and 11% of patients developed late post-traumatic seizures with mild to moderate brain injury. 6% of patients with early PTS used antiepileptic drugs (AED) for at least three months during follow up and 7% with late PTS used AED. 8% of patients developed late PTS without any early PTS. The results of our study show that among 23% early PTS and 11% late PTS only 3 % actually required to use AED for at least 6 months. To prevent this, 3% of the population 44% were using AED supplementary.

**Conclusion:** In our study, the incidence of early and late PTS is comparable to the other studies. The non-judicious use of the anti-epileptic drug is common in our country which leads to an increase in the risk of drug resistance and cost-intensive for poor patients in developing countries as prophylactic and excessive use of anti-epileptics does not affect the PTE.

**Keywords:** Post Traumatic Epilepsy (PTE), Anti-Epileptic Drugs (AEDs), Post Traumatic Contusions (PTC), Post Traumatic Seizures (PTS).

**Abbreviations:** PTE: Post Traumatic Epilepsy. AEDs: Anti-Epileptic Drugs. PTC: Post Traumatic Contusions, PTS: Post Traumatic Seizures). TBI: Traumatic Brain Injury. CT: Computed Tomography.

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## INTRODUCTION

Traumatic brain injury is an injury to the brain, skull, or scalp by blunt or penetrating trauma. Traumatic brain injury (TBI) can be mild, moderate, or severe according to the severity of the injury. In UK 1 in 300 people will suffer from Traumatic brain injury (TBI) each year.<sup>1</sup> In Pakistan, nearly a third of patients had a TBI, and of them, about 10% had moderate to severe TBI.<sup>2</sup> Symptoms depend on the type of TBI and the area which is affected by injury but most commonly presented as vomiting, headache, altered sensorium, dizziness, and fits. Non-enhanced contrast Computed Tomography (CT) brain is the diagnostic tool. The most common complications are seizures, infections, poor coordination, behavioral changes, prolonged or permanent loss of consciousness<sup>3</sup>

Cerebral contusions, the bruise of brain parenchyma, is 20 – 30%<sup>4</sup> of severe head injuries in adults and 55% in pediatric patients occurring by acceleration/deceleration injuries or by direct trauma.<sup>5</sup> They appear as mixed density lesions on CT as heterogeneous areas of necrosis, hemorrhage, and infarction. They can be managed surgically (11%)<sup>6</sup> or non-surgically by close observation. Cerebral contusions can expand with time so strict monitoring is required. Post-traumatic seizures (PTS) or Post-traumatic epilepsy (PTE) can occur after TBI in up to 20% of the general population higher in penetrating head injuries than closed head injuries.<sup>7</sup> Brain contusions are an independent risk factor to increase the incidence of PTE.<sup>8</sup> It occurs mostly in young adults and children. PTS is a risk factor for PTE. PTE can be early with the incidence of 25-30% in severe head injury or late with incidence 10 – 13% within 2 years of head trauma<sup>9</sup>

Seizure prophylaxis with anti-epileptic drugs (AEDs) is a common practice in the Neurosurgery department. Different AED are used for this purpose but they do not alter the incidence of PTE or PTS except in high-risk patients. Prophylactically AEDs are used for 7 days, even if

there is no episode of seizure and for 6 – 12 months if there are early or late PTS.<sup>9</sup>

As no local data available and international guidelines not being followed every patient admitted with TBI is getting antiepileptic regardless of history of seizure and labeled as PTE. If there is no PTS then prophylactic AED has no impact in reducing the incidence of PTE. But in our society, there is no proper follow-up visits of the patients to hospitals so the majority of patients took AED for a longer time and this makes them prone to develop PTE. So we want to conduct a study to determine the true incidence of epilepsy and drug dependence in our patients with post-traumatic contusions.

## MATERIAL AND METHODS

### Study Design and Setting

This was a prospective observational study of 97 patients diagnosed with cerebral contusions conducted in Punjab Institute of Neurosciences, Lahore in a 6-month period from July 2019 to Dec 2019 after approval from the ethical committee.

### Inclusion Criteria

All patients with age 15 – 65 years were included in the study who were admitted in causality department of neurosurgery and followed up for one year.

### Exclusion Criteria

We excluded patients out of age range, those requiring surgery at any stage during admission, high risk patients, patients who were known epileptics, patients with prior history of head trauma, pregnant patients, and patients with a previous history of neurosurgical procedures.

### Data Collection

Patients' medical records were examined in which their age, gender, mode of injury whether falling

from height or road traffic accident, their initial Glasgow Coma Score, lesion on CT, time of first seizure, initiation of AED, duration of AED taken, follow-up noted after 12 months. All data was recorded on a proforma by the researchers. Twelve patients were lost to follow up and 15 expired.

### Data Analysis

All data were entered and analyzed using SPSS Version 24. Mean ± S.D used for quantitative data like age. Frequency (%) was used for Categorical data like gender and PTE. p-value of < 0.05 was considered significant. Data was stratified for age, gender, and GCS (Glasgow Coma Scale).

## RESULTS

### Age Range

Age range was 15 – 65 years. Mean age was 40 years in our study. See Table 1 for details.

Age (in Years)	No. of Patients
15 – 30	29
31 – 45	27
46 – 65	41

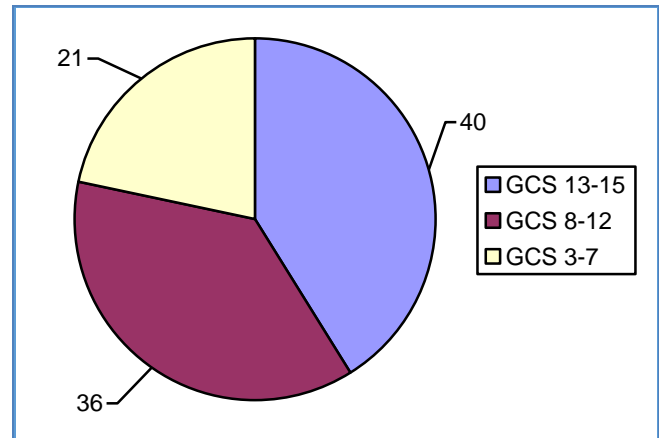
### Gender Distribution

We included 97 patients, out of which 74 were male and 23 were female patients.

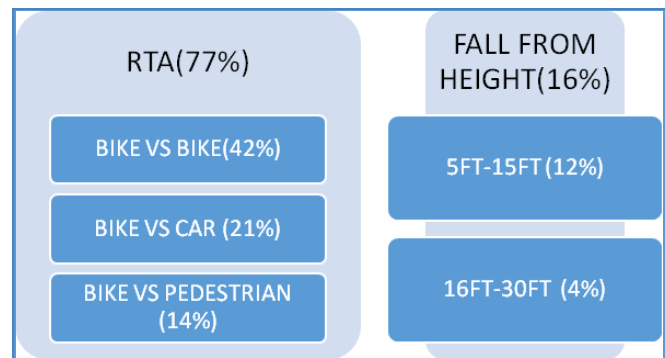
### Clinical Presentation

40% presented with mild TBI, 36% with moderate TBI and 21% with severe TBI (Figure 1). Overall, Road Traffic Accident is the most common etiology and then followed by fall from height. Among RTA, bike versus bike was the most common mechanism of injury (Figure 2). Most of our patients presented with loss of consciousness and vomiting. On CT brain, the most common

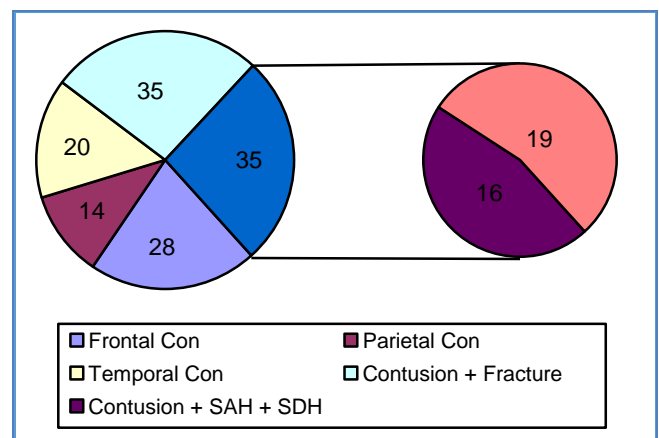
lesion was frontal contusion (25%) followed by parietal (14%) and then temporal contusions (17%) (Figure 3). 6% contusions were associated with fracture and 17% associated with a subdural



**Figure 1:** GCS (Glasgow Coma Scale) at the Presentation.



**Figure 2:** Etiology and Mechanism of Injury.



**Figure 3:** Lesion on CT.

hematoma and subarachnoid hemorrhage. More than 13% patients had frontotemporal or parietotemporal contusion. 15% had bilateral contusions.

**Outcome**

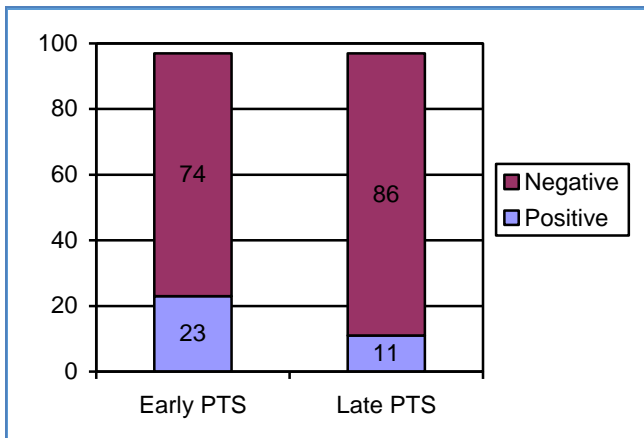
A total of 23% of patients developed early post-traumatic seizures (PTS) and 11% of patients developed late post-traumatic seizures with mild to moderate brain injury (Figure 4). 12% of patients developed early PTS within 24 hours of post-TBI while 11% developed within 2-7 days of injury. Late PTS developed after 7 days of injury. 6% of patients with early PTS used antiepileptic drugs (AED) for at least three months during follow up and 7% with late PTS used AED (Table 2). 8% of patients developed late PTS without any early PTS. The most frequently used AED was Epival 18% with PTS, next was levetiracetam 4% and then phenytoin 3%. 48% of patients received prophylactic AED for at least 7 days and 5% developed PTS despite the use of prophylactic AED.

**DISCUSSION**

Traumatic Brain injury is acquired form of injury and accounts for over fifty thousand deaths annually and 1.7 million emergency department (ED) visits over in the US.<sup>8</sup> Cerebral contusions are a form of primary brain injury, in which there is a focal region of hemorrhage and necrosis usually, involving the cerebral cortex and subcortical white matter. Cerebral contusions are fairly common, found in 8% of all TBI cases<sup>9</sup> and 13% to 35% of severe injuries.<sup>10</sup> The incidence of cerebral contusions is 9.7% in 6 months in our study. The mortality rates of patients with no cerebral contusions and cerebral contusions are 3.9%, 21.8%, respectively<sup>11</sup> and in our study, the incidence of mortality is 15%.

Post-traumatic epilepsy is an important and poorly understood sequel of TBI. PTE is a recurrent, unprovoked post-traumatic seizure disorder resulting from injury to the brain usually after 7 days of head injury.<sup>12</sup> It is an acquired form of epilepsy. It can be due to excitotoxicity of glutamate release, free radicals release, excessive inflammation, or in people with ApoE-E4 allele leading to disruption of blood-brain barrier.<sup>14</sup> The most commonly affected lobes are frontal and temporal but in our study the affected lobes are frontal (25%) followed by parietal and then temporal.<sup>15</sup>

In a civilian study, the incidence rate for early PTS ranges between 4 and 25%, whereas the incidence rate for late PTS ranges between 9 and 42%.<sup>13</sup> Severe TBI risk of PTE is 7.1% at 1 year and 11.5% at 5 years and after moderate TBI it is 0.7% at 1 year and 1.6% at 5 years of injury. In our study, the incidence of early and late PTS is comparable to other studies but at 1 year the incidence is 2% in moderate and mild TBI which was much less than in other studies. In our study, about 48% of patients received prophylactic AED which was enrolled for observation without any indication but only 3% developed PTE. This non-judicious use of the anti-epileptic drug is



**Figure 4:** Early and Late PTS (Post Traumatic Seizures).

PTS	AED Used
Early PTS	6%
Late PTS	7%

common in our country which leads to an increased risk of drug resistance and cost-intensive for poor patients in developing countries as prophylactic and excessive use of anti-epileptics does not affect the PTE. And this extraneous use of AED is more in the periphery about 70% due to poor follow-up visits in outpatient departments. The results of our study show that among 23% early PTS and 11% late PTS only 3% actually required to use AED for at least 6 months. To prevent this 3% of the population 44% were using AED supplementary.

In most of the neurotrauma centers, AEDs are initiated prophylactically without any regard for the established guidelines. Most of these patients are discharged on AEDs. Once AEDs have been initiated, most health care providers are reluctant to discontinue the drugs due to lack of detailed knowledge, personal preferences, fear of poor follow-up to monitor withdrawal, and lack of multidisciplinary management. Prophylactic use of Phenytoin prevents early PTS (14.2% – 3.6%)<sup>3</sup> and reduces the incidence of late PTS. Next to it is levetiracetam and carbamazepine. Phenytoin and levetiracetam have similar efficacy. In this study, the most common drug used was Epival next levetiracetam and phenytoin which was also against the international study protocol. Taking AEDs is not just taking a pill, rather it is a lifestyle modifying process that requires extensive patient education, long term use, and financial cost, repeated lab investigations for monitoring, drug interactions, face social stigmata, strict follow-up, and strict compliance.

## CONCLUSION

AEDs should be prescribed according to documented indications for initiation and should be discontinued immediately when discontinuation criteria are fulfilled. There should be national guidelines for AEDs prescription consistent with our resources and social structure. These national guidelines should be implemented

nationwide for uniformly optimal patient management.

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### Additional Information

**Disclosures:** Authors report no conflict of interest.

**Ethical Review Board Approval:** The study was conformed to the ethical review board requirements.

**Human Subjects:** Consent was obtained by all patients/participants in this study.

**Conflicts of Interest:**

In compliance with the ICMJE uniform disclosure form, all authors declare the following:

**Financial Relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work.

**Other Relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

### AUTHORS CONTRIBUTIONS

Sr.#	Author's Full Name	Intellectual/Contribution to Paper in Terms of
1.	Faiq Sheikh	Study design and methodology.
2.	Rabia Saleem	Paper writing, referencing, and data calculations.
3.	Jamal Nasir	Data collection and calculations.
4.	Noman Saleem	Analysis of data and interpretation of results.
5.	Ahmed Sultan and Abuzar Rauf	Literature review and manuscript writing.
6.	Muhammad Anwar Chaudhary	Analysis of data and quality insurer.