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Magnitude and Patterns of Post-Traumatic Epilepsy among Epilepsy Patients on Follow-Up at Tikur Anbessa Specialized Hospital and Zewiditu Memorial Hospital, Addis Ababa, Ethiopia: A Cross-Sectional Study

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ABSTRACT

Background: Post-traumatic epilepsy is characterized by development of at least one seizure after the first week following a traumatic brain injury (TBI). In Ethiopia, there is a lack of data regarding the prevalence of post-traumatic epilepsy among epileptic patients.

Objective: This study aimed to assess the prevalence of post-traumatic epilepsy among epilepsy patients on follow-up at Tikur Anbessa Specialized Hospital (TASH) and Zewidtu Memorial Hospital (ZMH).

Methods and materials: An institution-based cross-sectional study design was implemented among patients with epilepsy attending the neurology clinic of TASH and ZMH. Data was collected from patients and medical records using a structured questionnaire and data abstraction format respectively. Descriptive analysis was conducted to summarize the socio-demographic and clinical characteristics of participants.

Results: In this study, 280 patients with epilepsy participated from Tikur Anbesa Specialized Hospital and Zewidtu Memorial Hospital with a response rate of 85%. Among participants, 21 (7.5%) were diagnosed with post-traumatic epilepsy. The mean age of these patients was 41.5 years, with a male-to-female ratio of 1.6:1. Road traffic accidents were the primary cause of brain trauma (61.9%) and subdural hematoma (19.04%) and intraparenchymal hemorrhage (19.04%) were the commonest imaging finding. In the majority of cases (91.5%), seizures began within a period of three years following a traumatic event. Generalized tonic-clonic seizures (57.1%) were the most common seizure type and generalized epileptiform discharges (35%) were the most common EEG finding.

Conclusions: Post-traumatic epilepsy contributes significantly to the number of patients with epilepsy presenting to our neurology services, predominantly affecting the young active population, with road traffic accidents being the common mechanism.

KEYWORDS: Generalized tonic-clonic seizures, Neurology clinic, Post-traumatic epilepsy, Seizure prevalence, Road traffic accidents, Traumatic brain injury.

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INTRODUCTION

Background

Traumatic brain injury (TBI) is defined as any trauma to the scalp, skull, or brain. It is a leading cause of emergency visits contributing to both morbidity and mortality, leading to a diminished quality of life and severe outcomes for numerous survivors, particularly among younger children and the elderly [1]. Seizures are recognized as a frequent consequence following traumatic brain injury, persisting for extended periods, even years after the initial injury, across all age demographics [1-3]. The exact percentage of traumatic brain injury (TBI) patients who develop post-traumatic epilepsy (PTE) remains uncertain. However, estimates suggest that TBI serves as an underlying cause in approximately up to 20% of symptomatic epilepsies within the general population.[4]

Post-traumatic epilepsy (PTE) refers to the occurrence of recurring seizures that are not provoked, occurring more than one week after a traumatic brain injury (TBI) [1, 5, 6]. Various published reports indicate a wide range of incidence rates for post-traumatic epilepsy (PTE), spanning from 1.8% to 53% [3, 7]. The prevalence is higher among those with penetrating TBI than non-penetrating trauma [6, 8]. In approximately half of post-traumatic epilepsy (PTE) cases, seizures initiate within the first year following the traumatic event, and in 80% of cases, seizures manifest within the initial 2 years [9, 10] .

Epilepsy poses a significant public health concern in Ethiopia, with an estimated prevalence of 64 per 100,000 inhabitants. Furthermore, the pooled prevalence of traumatic brain injury (TBI) in Ethiopia was found to be 20%, which surpasses the rates reported globally and on the continent [4, 11]. Traumatic brain injury (TBI) predominantly affects young and active individuals, exhibiting a higher prevalence compared to continental and global statistics [12, 13]. Despite the significant number of epilepsy patients and the high incidence of traumatic brain injury (TBI), data concerning the prevalence of post-traumatic epilepsy and their clinical and socio-demographic profiles are scarce in Ethiopia. To the best of the author's knowledge, there have been no institution-based studies conducted in Ethiopia to determine the prevalence of post-traumatic epilepsy. Thus, this study aims to assess prevalence of post-traumatic epilepsy among epilepsy patients on follow-up at Tikur Anbessa Specialized Hospital (TASH) and Zewditu Memorial Hospital (ZMH).

METHOD AND MATERIALS

Study setting and study design

The study took place in Tikur Anbessa Specialized Hospital (TASH) and Zewditu Memorial Hospital (ZMH) located in Addis Ababa, the capital city of Ethiopia, which are among the largest referral hospitals in the country. The neurology department established in TASH treats around 1200 epileptic patients annually. ZMH is one of the hospitals treating a large number of epileptic patients with around 520 patients seen at the epilepsy clinics annually. The epilepsy clinics in both hospitals are staffed with general practitioners, residents, nurses, and senior neurologists. An institution-based cross-sectional study design was conducted from August 12, 2023 to February 28, 2024.

Source population and study population

All patients who are on follow-up at neurology clinics for epilepsy at ZMH and TASH, Addis Ababa, were the source population. The study population is all adults with epilepsy follow-up attending clinic visits during the data collection period at ZMH and TASH and fulfilled the inclusion criteria.

Eligibility criteria

All adults with epilepsy aged ≥18 years who are on follow-up were included in this study. All adults with epilepsy who were very sick, unable to communicate, or with incomplete medical records were excluded from the study.

Sample Size Determination

The sample size was computed using a single population proportion formula with assumed proportion of posttraumatic epilepsy among epilepsy patients at 50%, 5% margin of error, and a confidence level of 95%. After finite population correction for N=1620 and 5% nonresponse rate was considered, a final sample size of 327 was reached.

Sampling procedure and Technique

The number of study participants was allocated proportionately among the hospitals based on the total number of patients with epilepsy being treated at each hospital. A total of 222 participants were allocated to TASH and 105 patients to ZMH. A simple

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random sampling method using a lottery method after preparing a sampling frame was employed to select the study subjects. Patients were interviewed after they refilled their medication. The patient's medical record number was listed accordingly and signed to avoid patient selection more than once if repeated visits occurred during the study period.

Data Collection procedure

Data were collected from patients and medical records by neurology resident physicians after training and practical demonstrations on interview techniques and measurement procedures were given. Data collectors were also trained about participants' rights and confidentiality. The primary investigator supervised the data collection. Data completeness and consistency were checked at the end of each data collection day. All questions were prepared in English and translated into Amharic and back-translated to English to check its consistency. A pre-test of the data collection tool was conducted on 5% of the sample size at Yekatit 12 Hospital Medical College, to identify potential gaps that could have occurred once the data collection started

Data management and Analysis

Data entry and coding were done using Epidata version 3.1 and exported to SPSS version 27 for analysis. Categorical variables were summarized using frequencies with percentages, while continuous variables were presented as mean with a standard deviation (SD) after checking normality of distribution.

Operational Definitions

Post-traumatic epilepsy: recurrent and unprovoked seizures that occur at least a week after TBI and up to 20 years after the initial trauma [6]. The effect of TBI on seizures was considered inconclusive for those who had first-time seizure onset more than 20 years after TBI.

Traumatic brain injury: any alteration of the brain or skull related to a blow to the head and associated with one or more of the following characteristics: changes in levels of consciousness, Memory disturbances, confusion associated with deficits in orientation, and Neurological signs, such as brain injury observable on neuroimaging, new onset or worsening of seizure disorder, visual field deficits, and hemiparesis.[14]

Ethical consideration

Ethical approval was obtained from Addis Ababa University, School of medicine institutional review board and ethical clearance committee of City Government of Addis Ababa Health Bureau. A formal letter from the university and the health bureau addressed to the participating hospitals was taken and submitted. Informed written consent was obtained from the participants after thoroughly discussing the idea behind the study, and study participant rights. Participants were also assured that the confidentiality of the information they provided would be maintained and names of the study subject will not be included in the data.

RESULT

A total of 280 patients participated in the study with a response rate of 85%. After evaluation, 21(7.5%) of the participants were labeled to have post-traumatic Epilepsy. Among those diagnosed with PTE, more than half were male patients (61.9%) with a male-to-female ratio of 1.6:1 and the mean age of the patients with PTE was 41.5±11.2 years. The highest number of cases was recorded in the age group 29-39 years.

Furthermore, none of the patients with PTE had a family history of epilepsy, developmental delay, or childhood febrile seizures before sustaining the injury.

Table 1- General characteristics of target population

Variables		Frequency(n=21)	Percentage (%)
Gender			
	Male	13	61.9
	Female	8	38.1
Age groups			
	18-28	2	9.5
	29-39	10	47.6

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	40-50	4	19
	51-61	4	19
	>62	1	4.8
Occupation			
	Civil servant/Employee	8	38.1
	Driver	1	4.8
	Daily Laborer	3	14.3
	House wife	3	14.3
	Student	1	4.8
	Farmer	1	4.8
	Unemployed	4	19.9
Other factors			
Family history of epilepsy		1	4.8
Childhood febrile seizure		0	0
Alcohol consumption		2	9.5

The mechanisms of injury varied among those with post-traumatic epilepsy, with road traffic accidents accounting for 61.9%, domestic accidents for 33.3%, and assaults being the least common at 4.8%. Among those who sustained TBI, 17 (81%) had an initial loss of consciousness, 4 had motor deficits, and 2 had early seizures. In terms of neuroimaging findings, 14 out of the 21 patients had abnormal findings. Among them, 4 patients had subdural hematoma and parenchymal hemorrhage, while the rest had depressed skull fractures and chronic sequelae of traumatic brain injury such as encephalomalacia (**Table 2**).
Electroencephalogram (EEG) was performed for 17 patients, with focal and generalized epileptiform discharges found in 35% of the cases. Normal wake EEG was observed in 23% of the patients.

Table -2 Characteristics of traumatic brain injury resulting in the development of post-traumatic epilepsy, TASH and ZMH, Ethiopia, 2024

Variables		Frequency n=21	Percentage
Mechanism of injury			
	Road traffic accident	13	61.9
	Domestic accident	7	33.3
	Assaults	1	4.8
Neurologic deficit after the injury			
	Initial loss of consciousness	15	71.4
	Motor deficits with Initial loss of consciousness	4	19.04
	Early seizure	2	9.5
Imaging findings			
	Subdural hematoma	4	19.04
	Intra-parenchymal haemorrhage	4	19.04
	Depressed skull fracture	3	15.7
	Encephalomalacia	3	15.7
	Not done	7	57.8

Fifty-seven percent of the patients had generalized epilepsy, with focal epilepsy accounting for 43%. Regarding seizure frequency before the initiation of anti-epileptic drugs, our findings revealed a broad spectrum, with weekly seizures being the most common occurrence (41.1% of patients), followed by daily seizures (17.9%) and monthly seizures (19.3%).

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The timing of seizure onset post-injury was most commonly within 1 to 3 months for 52.4% of the cases, with only 9.5% of the patients experiencing onset after 3 years (**Figure 1**). The type of head trauma did not significantly predict or affect the time of onset of seizures (p=0.54).

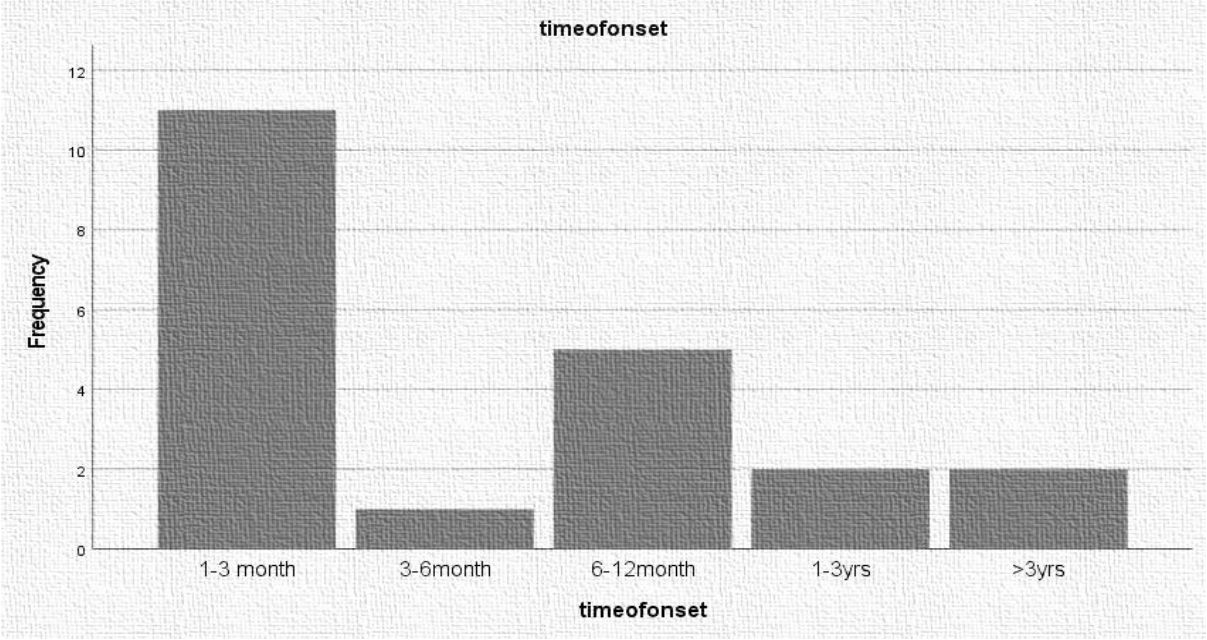

Figure 1- Time of seizure onset after injury among patients with post-traumatic epilepsy patients at TASH and ZMH, Ethiopia, 2024.

Generalized tonic–clonic seizures (GTCS) were the prevalent seizure type 12 (57.1%) with rest accounted by focal seizure (7:33.3%) and focal to bilaterally tonic clonic seizure (2:9.5%). (**Table 3)**

Table 3: Seizure type and pattern among patients with post-traumatic epilepsy patients at TASH and ZMH, Ethiopia, 2024.

Variables		Frequency(n=21)	Percent
Seizure type			
	GTC	12	57.1
	Focal with or without impaired awareness	7	33.3
	Focal to bilateral tonic-clonic	2	9.5
Seizure frequency before ASM			
	Daily	7	33.3
	Twice weekly	3	14.3
	Weekly	9	42.9
	Monthly	2	9.5

Regarding treatment, mono-therapy was the predominant strategy, employed in 76.2% of patients, with phenytoin being the most commonly prescribed drug followed by carbamazepine. Bi-therapy was utilized in 23.8% of cases, with phenytoin combined with phenobarbital being the most common combination. A slight majority of patients (57.1%) did not experience seizures in the last year after initiation of ASD.

DISCUSSION

The study aimed to investigate the magnitude of post-traumatic epilepsy among epileptic patients on follow up at TASH and ZMH. In this study, it was found that 21(7.5%) of the patients with epilepsy who were on follow-up in the selected hospitals had post-

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traumatic epilepsy. This figure is consistent with a study conducted in Cameroon that reported 8.1% prevalence of PTE [15] but lower than reported in a study done in Nigeria (19.6%) and South Africa [16, 17]. The study's showed that young adults and males constituted the group affected more by PTE. This is in line with researches done in Nigeria, Cameroon, and China [15, 16, 18]. This findings could be related to the observation that male young adults engage in higher levels of physical activity and participate in more hazardous pursuits, thereby increasing their susceptibility to traumatic brain injury (TBI).

In this study, over half of the cases of traumatic brain injury (TBI) were attributed to road traffic accidents (RTAs). This finding is consistent with previous research conducted in various countries, where RTAs were also identified as the primary cause of TBI [16, 18, 19]. The length of epileptogenesis, or the time until the first seizure, varies from patient to patient. Within a year after their TBI, over 80% of patients in this study experienced their first seizure, and over 90% did so within two years. These outcomes are marginally greater than those found in prior research, which found that 80% of individuals had their first seizure during the first two years after the TBI [15, 16, 18].

Following traumatic brain injury (TBI), neuroimaging techniques such as brain CT scans or MRIs enable the visualization of the nature and scope of brain damage. Following epileptogenesis, neuroimaging aids in excluding alternative causes and illustrating sequelae resulting from the TBI [20]. Within this study, imaging was performed on only two-thirds of the patients. Among those who underwent imaging, the most frequently observed lesions were subdural hematoma and parenchymal hemorrhage, with depressed skull fracture being the subsequent common finding. In contrast, a study in Nigeria reported depressed skull fracture as the most common cause followed by subdural hematoma [16], while another study in Cameroon reported hemorrhagic contusion followed by diffuse axonal injury [15].

EEG during epileptic seizures or follow-up was not collected from all participants; thus, we were not able to verify the seizure type based on EEG. However, among those who had EEG, abnormal findings were reported in thirteen out of seventeen patients (76% of cases), with focal and generalized epileptiform discharge being the most common finding.

Furthermore, more than half of the patients had generalized tonic–clonic seizures (GTCS), with other seizure like focal and focal to bilateral tonic clonic accounting for the rest of the seizure types. Comparable figures were reported by Ogunrin et al. with 51% [16] and Motahet al. in Cameroon with 47.6% having GTCS [15].

The selection of anti-seizure medications (ASMs) for post-traumatic epilepsy (PTE) is influenced by several factors, including the availability of specific drugs, the type of seizures experienced by the patient, their tolerance to medications, and potential drug interactions. The selection of anti-seizure drugs (ASMs) in an environment with low resources, like Ethiopia, is constrained. In this study, treatment predominantly involved mono-therapy in more than three-fourths of the cases, with phenytoin being the most commonly prescribed drug, followed by carbamazepine. In Cameroon, Motah et al. found similar findings, with 86% of the patients on mono-therapy. Sodium valproate was the most commonly prescribed anti-seizure medication (ASM), followed by carbamazepine [15].

The utilization of anti-seizure medications in this study demonstrated positive outcomes, with over half of the patients experiencing freedom from seizures within the last year. In a study done by Ogunrin et al. in Nigeria, it was discovered that 87% of patients achieved seizure freedom after three months of treatment with anti-seizure medications (ASMs) [16] and another study in Cameroon found that more than two-thirds had achieved seizure freedom [15].

When anti-seizure medications (ASMs) fail to provide significant reduction in seizures, other methods like Vagus nerve stimulation and epilepsy surgery may be able to better manage seizures [20, 21]. However, since none of the patients in this study satisfied the requirements for refractory seizures, no surgery was performed on any of the patients.

STRENGTH AND LIMITATION

This study is the first study, to the best of the author's knowledge, which examined the magnitude of post-traumatic epilepsy among epileptic patients in Ethiopia. However, the study was not without limitations. Firstly, the study used a cross-sectional study design, which limits inference on causality. Secondly, long-term EEG monitoring and neuroimaging during the acute phase of TBI were lacking for some subjects limiting the understanding disease presentations. Finally, Most of the participants in the study were from Addis Ababa and the surrounding areas; therefore, the results might not be representative of the general situation in Ethiopia. Thus, further studies are needed to fully clarify the clinical characteristics of PTE and factors associated with PTE.

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CONCLUSION AND RECOMMENDATION

The magnitude of PTE in our study was comparable with findings from other countries. Post-traumatic epilepsy primarily affected young adult males and the TBI was mainly attributed to road traffic accidents. On imaging, parenchymal lesions and subdural hematomas are the most often seen brain abnormalities. Generalized tonic-clonic seizures are the predominant seizure class reported by patients. Further research is needed to investigate the long-term outcomes, factors associated with the development and latency of post-traumatic epilepsy, and potential neuropsychological consequences of post-traumatic epilepsy, as well as to explore other clinical features associated with this condition.

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