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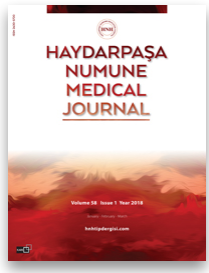


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ORIGINAL ARTICLE

# Status Epilepticus: A Tertiary Care Hospital Experience

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## Abstract

**Introduction:** Status epilepticus (SE) is characterized by the presence of prolonged seizures or the absence of returning to a normal level of consciousness between episodes, and it is one of the most important life-threatening neurological emergencies. This study examined the etiological features, EEG findings, and accompanying comorbid conditions of SE patients.

**Methods:** SE patients followed up in the neurology clinic between January 2014 and June 2020 were reviewed retrospectively. The demographic data, seizure type, EEG findings, anti-seizure medications, and comorbid conditions were evaluated.

**Results:** A total of 62 patients were included in the study. The study was continued with 45 patients (24 female, 21 male) as there were missing data in the files of 17 patients. The most common type of seizure at presentation was convulsive SE (CSE) (88.8%). It was observed that 38 of 45 patients had a known diagnosis of epilepsy (84%), and levetiracetam was the most preferred anti-seizure medication, followed by valproic acid. The most common comorbid condition was infections (35.5%). The mean hospitalization for SE was 11.7 days. The most common EEG pattern was paroxysmal slow waves (25.6%).

**Discussion and Conclusion:** SE is a neurological condition that can affect epilepsy patients of all ages and requires rapid intervention due to the high risk of mortality and morbidity. It is important to determine the etiology and maintain effective treatment of SE to prevent recurrent SE.

**Keywords:** Comorbidity; epilepsy; mortality; status epilepticus; treatment.

Epilepsy is one of the most common brain diseases, affecting approximately 70 million people worldwide [1]. Status epilepticus (SE) is defined as a continuous seizure lasting for at least 5 minutes or 2 or more consecutive seizures without returning to a normal level of consciousness [2]. The incidence of SE is 9.9-42/100,000, and the presence of prolonged seizures is a life-threatening neurological emergency [3,4]. To prevent neuronal network changes and neuronal death caused by SE, it is important to terminate the seizures safely and quickly and to restore the patient's consciousness [5]. The mortality rate in SE is 16-43.5%; therefore, treatment should be initiated at the earliest and most effective dose to save the patient's life and reduce possible morbidities [6]. The seizure control rate with benzodiazepines, one of the most frequently used agents in first-line treatment from past to present, is 59-65%. For this reason, second-line and third-line treatments are often required in refractory SE patients [7]. Despite all treatment options, the high mortality and morbidity risk of SE underscores the importance of determining the etiological factors and comorbid conditions that cause SE. This study aims to examine the etiological factors, treatments, EEG findings, and comorbid conditions in SE patients.

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## Materials and Methods

The patients who were followed up in the neurology clinic and diagnosed with SE between January 2014 and June 2020 were reviewed retrospectively. All SE patients who were followed up in our clinic or evaluated in the emergency department and then referred to intensive care were included in the study. A total of 62 patients met these criteria, but the study was continued with 45 patients due to missing data in the files of 17 patients.

Demographic information of the patients, type of seizure, previous diagnosis of epilepsy and regular use of anti-seizure medications, EEG findings during hospitalization, medications used during SE treatment, hospitalization time, and comorbid conditions were evaluated.

The ethics committee of the hospital approved the study (2022/KK/129). The study was conducted in accordance with the Declaration of Helsinki. SPSS 20.0 was used for the statistical analysis. Descriptive statistical methods (mean, percentage, minimum, maximum) were used to evaluate the study data.

## Results

A total of 45 patients (24 female, 21 male) participated in the study. The mean age was 54±20.6 years in women and 39±16.3 years in men. The type of seizure at presentation was non-convulsive status epilepticus (NCSE) in 5 patients and convulsive SE (CSE) in 40 patients. Focal seizures were observed in only 7 of the CSE cases, while generalized seizures occurred in 33 patients. It was determined that 38 patients had a previous diagnosis of epilepsy, and only 7 patients presented with a first seizure. Anti-seizure drugs used by patients with epilepsy were levetiracetam in 20 patients, valproic acid in 11 patients, and 15 patients were receiving polytherapy. The most common comorbidity was infection (35.5%), and no documentable comorbidity was found in 17 patients (Fig. 1). It was observed that 6 patients were referred to the intensive care unit, and 39 patients were followed up in our neurology service for an average of 11.7 days (range: 1-60 days).

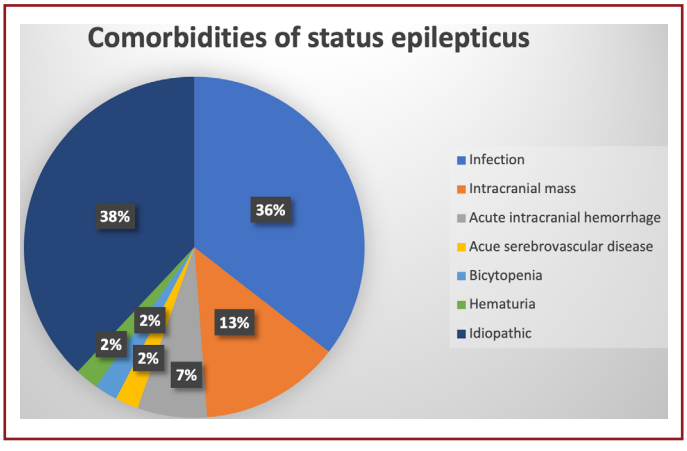


**Figure 1.** Comorbidities of status epilepticus.

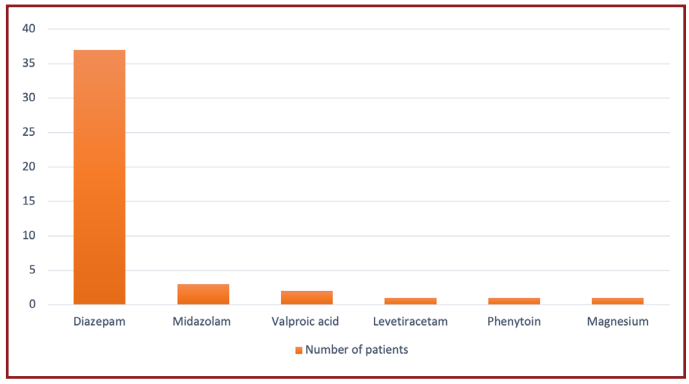


**Figure 2.** First-line drug treatment in status epilepticus.

The drugs used in first-line treatment in SE are shown in Figure 2. During SE treatment, 32 patients were given a second drug, and 16 patients were given a third drug. Levetiracetam was the most common second-line drug, and phenytoin was the most common third-line drug. It was shown that 4 patients with a history of infection and 3 patients with a history of acute intracranial bleeding died after an average of 19.2 days of hospitalization.

When the EEG findings of the patients were evaluated, paroxysmal slow waves were the most common finding. EEG could not be performed in 4 patients due to technical reasons and in 6 patients due to referral from the emergency department to the intensive care unit (Table 1).

**Table 1.** Clinical characteristics of the patients

| | Number (%) |
|---|---|
| Seizure type | |
| Convulsive SE | 40-88.2 |
| Non Convulsive SE | 5-11.8 |
| Presence of epilepsy | |
| Yes | 38-84.4 |
| Anti-seizure drugs for epilepsy patients | |
| Monotherapy | 30-66.6 |
| Polytherapy | 15-33.4 |
| -Two drug combination | 13-28.8 |
| -Four drug combination | 1-2.3 |
| -Five drug combination | 1-2.3 |
| EEG findings | |
| Paroxysmal slow waves | 10-22.2 |
| Abnormalities of the background activity | 9-20 |
| Focal epileptiform discharges | 3-6.7 |
| Generalized epileptiform discharges | 3-6.7 |
| Normal | 10-22.2 |
| Not recorded | 10-22.2 |

SE: Status epilepticus; EEG: Electroencephalography.

## Discussion

In our study, it was observed that SE was more common in women, and the age of onset was later compared to men. The most common type of seizure at presentation was convulsive SE (CSE) with generalized seizures. The most common comorbidity was infection (35.5%), and no documentable comorbidity was found in 17 patients.

There is no clear consensus on the relationship between gender and age in the literature. Although many studies have found that SE is more common in men, it has been reported that it can occasionally be more frequent in women [8]. In the study by Knake et al, [9] no difference was found between the sexes, but the incidence of SE in individuals aged 60 years and above was significantly higher compared to younger age groups.

In our study, CSE was observed more frequently than non-convulsive SE (NCSE), and the most common seizure type was generalized seizures. CSE accounts for 37-70% of all SE cases, and its annual incidence rises to 40/100,000 [10]. In a study evaluating the clinical features of SE, generalized onset seizures were the most common, focal to bilateral tonic-clonic seizures were the second most common, and focal seizures were rarely observed in patients [8]. In our study, 84% of the patients had a known diagnosis of epilepsy. There are different study results in the literature regarding the rate of SE in epilepsy patients. Compared to studies showing that the rate of epilepsy detection in SE patients was below 50% [11] or at around 50% [9], our results appear to be higher.

In a study of 119 patients evaluating SE comorbidities, the most common cause of SE was central nervous system infections (36%) [8]. Metabolic disorders and central nervous system tumors were the second most common causes [12,13]. In hospital-based studies, discontinuation of anti-seizure drugs led to SE in 10.4%-22.5% of cases, while 3-18% of cases were idiopathic [14,15]. Stroke, tumors, and dementia, which are more common in older populations, are the main reasons for the differences in SE etiology between pediatric and adult populations [4]. In our study, infection was found to be the most common cause in 35.5% of the patients, while no documentable cause was found in 17 patients, who were evaluated as idiopathic (Fig. 1).

A study evaluating the efficacy of levetiracetam, fosphenytoin, and valproic acid has shown that the efficacy of these drugs, frequently used in the treatment of SE, is similar [16]. In this study, which included patients whose seizures continued after treatment with benzodiazepines, the primary endpoint was defined as the cessation of seizures and improvement in the consciousness levels of the patients. SE could be controlled in 47% of patients taking levetiracetam, 45% of patients taking fosphenytoin, and 46% of patients taking valproic acid [16]. In our study, diazepam was the most frequently used drug from the benzodiazepine group (82.2%) (Fig. 2), while levetiracetam was the most frequently used second drug, and phenytoin was the most common third drug. According to the literature, one of the most important reasons for the inability to control seizures is the insufficient dose of benzodiazepines in SE treatment [17]. In our study, although the dose of benzodiazepines administered to the patients in the emergency room is not known, it was determined that 40 patients were given benzodiazepines as the first-line treatment, and 32 patients were given a second anti-seizure drug in addition to benzodiazepines. A third anti-seizure medication was given to only 16 patients. Studies show that in SE treatment, benzodiazepines and first-line anti-seizure drugs are sufficient to stop seizures in many cases, and a third anti-seizure treatment is rarely required. In the study by Orlandi et al., [18] 436 SE attacks were evaluated, and it was determined that 24 attacks were stopped with benzodiazepines alone, 67 with first-line anti-seizure drugs, and 210 with first-line anti-seizure drugs in addition to benzodiazepines.

The presence of SE in the pediatric (21%) and adult age groups (34%) was associated with inadequate doses of anti-seizure drugs, and the most important reason for SE was the non-compliance of patients with their treatments [19,20]. In our study, 84.4% of the patients with SE were diagnosed with epilepsy, and 33.3% were receiving polytherapy, suggesting that our patients' compliance with anti-seizure treatments may have been insufficient. However, a clear assessment cannot be made due to missing data in the patient files.

It has been reported that the mortality rate in SE is approximately 20% [21]. Permanent changes may develop in patients due to modifications in neuronal networks, such as neuronal damage and death [2,22]. Mortality associated with SE is higher in adults than in the pediatric age group [23]. The fact that SE is resistant to treatment is also an important factor associated with mortality. The mortality rate in super-refractory SE is higher than in refractory SE [24]. In our cases, it was determined that 4 patients with a history of infection and 3 patients with a history of intracranial bleeding died on average 19.2 days after hospitalization. As in our patients, mortality rates are higher in acute symptomatic SE than in untriggered SE, and death occurs in a shorter time [25]. This finding emphasizes

the importance of early and rapid initiation of treatment, especially in acute symptomatic SE. The recurrence rate of SE in all age groups ranges from 13.3% to 18%. Recurrence rates are highest, especially within 2 years following the first SE episode [26]. No recurrence was observed in our cases, which may be due to insufficient follow-up data as patients were transferred to intensive care units.

In patients with convulsive seizures or CSE, NCSE (also called electrographic SE) is suspected when there is no improvement in consciousness after controlling motor activity. The incidence of CSE is between 37-70% [27], and NCSE was observed at a rate of 14% with continuous EEG monitoring [28]. Continuous EEG monitoring is recommended in patients diagnosed with NCSE and when there is clinical suspicion of NCSE following CSE. In cases where continuous EEG monitoring is not possible, it is recommended that patients undergo routine and serial EEG recordings. In our study, EEG findings were obtained from routine EEG recordings after hospitalization. In a study where 70 patients had EEG recordings one hour after receiving anti-seizure drugs for the treatment of SE, paroxysmal slow waves were the most common finding, similar to our findings [29]. When the EEG recordings of our patients were evaluated, it was observed that most of them had routine EEGs taken only once. In NCSE patients, serial routine EEG recordings (3 or 4) were performed.

The small sample size and retrospective design are limitations of our study.

## Conclusion

In our study, it was found that the majority of SE patients were diagnosed with epilepsy, CSE was more common, and the most important comorbidity was infection. Knowing the etiological factors in SE, which is one of the most important neurological emergencies due to the high risk of mortality and morbidity, is crucial for initiating rapid and effective treatment.

**Ethics Committee Approval:** The study was approved by Haydarpaşa Numune Training and Research Hospital Clinical Research Ethics Committee (No: 2012-KAEK-47, Date: 13/06/2022).

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**Conflict of Interest:** The authors declare that there is no conflict of interest.

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