ORIGINAL ARTICLE

Factors Influencing the Outcome of Status Epilepticus in Patients Present to a Tertiary Care Hospital: a Retrospective Cross-Sectional Study

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ABSTRACT

Aim: To determine factors influencing the outcome of status epilepticus in patients present to a tertiary care hospital

Study Design: Retrospective Cross-sectional study

Place and duration: This study was conducted in Jinnah Post Graduate Medical Centre Karachi Pakistan. From January 2019 to January 2020.

Methodology: This study carried out a retrospective review on the patients suffering from Status Epilepticus who were admitted in the hospital of Sindh, Pakistan. Patient details were used to investigate the prognostic values, including demographic, clinical and etiological factors. These factors were determined using statistical tests where a 5% significance level was utilized for these tests.

Results: A study group of 180 patients was analyzed and the mortality rate was determined to be 23 (13%). Morbidity was also analyzed and it was observed in 45 (25%) patients. It was also observed that males had significantly higher mortality rates. It was seen that CNS infections were the most common cause of epilepsy in patients suffering from Status Epilepticus (n=54). A greater morbidity rate was found for patients suffering from acute symptomatic causes of Status Epilepticus (p=0.000).

Conclusion: The key causes for mortality in patients admitted for Status Epilepticus were CNS infections, prolonged seizures and seeking late medical attention. Higher mortality rates were also associated with males and patients who had poor control of their seizures. Acute and symptomatic etiologies were also found to be a common determinant in higher morbidity rates.

Keywords: Status Epilepticus, Central nervous system infections, adults

INTRODUCTION

Status Epilepticus has been defined as a neurological emergency state where the patient suffers from repetitive seizure activity prolonging 5 minutes. These seizures offer no recovery time and this disease may be characterized by continuous seizures which lasts longer than five minutes (1). The occurrence of this disease in patients suffering from status epilepticus (SE) is estimated to vary from 1.29 to 73.7 per 100,000, with substantial variance depending on region and research type. The combined annual crude incidence in developing countries is reported to be 13.8 per 100,000. Medicine has advanced vastly, and multiple breakthroughs have been done in the understanding of Status Epilepticus and the best ways to manage it, short-term mortality can range from 3 to 40%, depending on the center and kind of SE (1).

It is on the basis of semiology that the International League Against Epilepsy (ILAE) proposed on how to identify the different components of SE. ILAE expanded on these by identifying the components of SE based on different factors such as age, using EEG and etiology. This identification led to the need of clinical course and therapy needed (2). This got increased the need for more research into the wide range of prognostic markers that might help identify SE patients who are at high risk and guide

Treatment options. Speaking of therapy and intensive care to the ferocity of SE would not only speed up care delivery, but it would also lessen the risks associated with overtreatment of those with less severe illnesses (3).

In South Asian Region failing to make the correct prognosis for the disease is an issue. This is especially accurate in Pakistan's case, where there is an apparent gap available in the knowledge of diagnosing SE cases existing in pediatric care and very few cases have been published on pediatric studies (6). Given the region's particular demands, this has major implications for the creation of a competent therapeutic strategy.

In order to meet this gap, this paper details an observation study that has stretched out over a period of five years where it observes the number of SE admissions in the capital of Sindh, Pakistan. The patients that come to the tertiary care hospital were evaluated based on their different individual characteristics such as demographic, etiological, and clinical. The outcomes of interest resulted in-hospital mortality as an important predictive variable for both were investigated.

METHODOLOGY

The study was conducted as a retrospective in Jinnah Post Graduate Medical Centre Karachi Pakistan. From January 2019 to January 2020. All patients hospitalized to the

Neurology ICU with status epilepticus were included. Permission was taken from the ethical review committee of the institute.

A standardized treatment protocol was issued for the patients diagnosed with SE where they were injected with an initial IV drip of benzodiazepine (diazepam/midazolam). They were also injected with an IV anti-seizure drugs (phenytoin/valproic acid/levetiracetam) which was followed by another round of IV antiepileptics (4). The last IV drip consisted of midazolam /propofol infusion which were administered in stages as needed. All of these medications were given in a variety of dosages, depending on the patient's weight and reaction to it. The airway provided was secured, and all patients were subjected to constant monitoring.

To identify the correct demographic parameters, the age, gender, and residence of the patients admitted was procured in order to identify and collect the correct data. This information also extended to acquiring the in-hospital treatment of the patient as well as the clinical course they were subjected to, how different patients responded to the therapy was also recorded in order to achieve a successful hypothesis (5). The data collected from the patients was not only limited to their in-hospital treatment rather included the information obtained from the follow up examination conducted after six months.

The etiologies of Status Epilepticus were classified as cryptogenic or chronic, and as acute (caused by an unknown source) or symptomatic (caused by a known factor). According to the most recent ILAE categorization and recommendations, SE was classed by semiology.

Patients of age 12 years and older who were admitted to the study setting with status epilepticus throughout the trial period. Whereas exclusion criteria based on patients who were first treated in another department or who were discharged against medical advice before completing treatment.

Status Epilepticus has been defined as a neurological emergency state where the patient suffers from repetitive seizure activity prolonging 5 minutes (2). These seizures offer no recovery time, and this disease may be characterized by continuous seizures which lasts longer than five minutes. SE episodes that were not handled by first or second-line AEDs, necessitating IV anesthetics, were referred to as refractory status epilepticus. Super refractory SE was defined as SE that lasted for 24 hours or more after anesthetic delivery (6). In this study, patients who had cognitive impairment, motor impairments, or active epilepsy because of SE were classified as morbid. Scar epilepsy is epilepsy that develops later because of a past brain injury such as a tumor, trauma, surgery, or stroke. Statistical Analysis: IBM SPSS version 21 was used to conduct the statistical analysis. Frequencies and descriptive statistics were computed. The Kolmogorov-Smirnov test was used to determine if the variables had a normal distribution (8). The categorical variables were compared using the Chi-squared test with a 95% confidence range.

Fisher's Exact Test or Likelihood Ratio were used to analyze variables with tiny cell scores, if applicable (7). To examine differences in continuous variables between groups, non-parametric tests were performed. Throughout the investigation, a 5% significance threshold was applied.

RESULTS

Total 180 individuals with SE were admitted to the hospital throughout the research period. Mortality was observed in 22 (12.5%) instances, whereas the intensity of morbid was documented in 44 (25.0%) cases (As shown in figure 1). All Morbid sequelae are further divided into groups based on their frequency. Our study had a median age of 24 years (IQR=15.0-31.75). Mortality (p=0.002) was highly related with male gender, but not morbidity (p=0.356). The vast majority lacked formal schooling (60%). A prior history of status epileptic episodes was linked to a higher risk of death (p=0.004). Other sociodemographic factors were not found to be substantially linked to mortality or morbidity (p>0.07) (As shown in table 1).

Gender was revealed to be a major predictor of mortality among men (25.6 percent vs 19.4 percent in females) (As shown in figure 2)

The CNS infections (n=54) were identified as the main reason that our SE patients were suffering from epilepsy, like idiopathic epilepsy (n=34). SE's etiology (As shown in figure 3). Many SE cases140 (79.5%) occurred among patients who had suffered from epileptic attacks in the past. De novo SE instances were linked to higher morbidity (p=0.00), but not to higher death (p=0.853). The age of the patient was found to be a major factor in the development of de novo SE (0.047). In comparison to cryptogenic SE, symptomatic causes of SE were related with higher morbidity (p=0.008), but no such connection was seen with death (p=0.172)). (As shown in table 2) Acute causes of SE were linked to a greater risk of morbidity (p=0.00), but not fatality (p=0.137). SE related to an acute etiology (p=0.000) and symptomatic SE were both linked with a prolonged hospital stay (p=0.000) (0.003).

The most prevalent provoking factor was noncompliance with medications/under dosing 68 (38.6%), followed by infectious etiologies 55 (31.3%). Infectious etiology had the highest death and morbidity rates (54.5 percent and 27.2 percent). The most prevalent kind of SE was generalized tonic clonic seizures with significant motor phenomena (87.9 percent). Most patients with SE (58%) reported poor seizure control in the previous three months, which was linked to increased morbidity at follow-up (p=0.000). Most SE patients (85.9%) were found to respond to medical treatment, while the rest were classified as refractory or super-refractory status epilepticus (As shown in figure 4).

In SE, the kind of seizure had no significant relationship with death or morbidity (p>0.05). An SE status of refractory and super-refractory (p=0.000) was identified to be associated with a higher mortality rate. According to the temporal nature of seizures, the median hospital stay was reported to be of seven days (IQR=4.35-11.05). Patients having a greater seizure duration and a longer time between seizures and admission to the hospital had a higher fatality rate (p=0.000) and (p=0.000) (As shown in table 3).
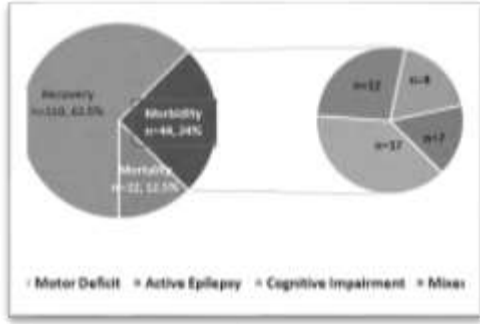
Figure 1: Prognosis determined for study population suffering from SE.
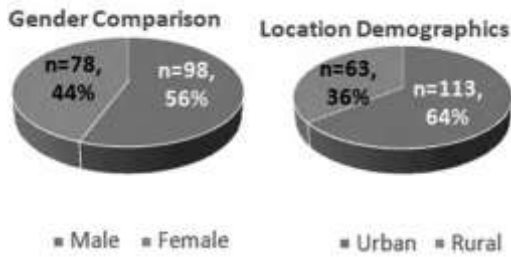

Figure 2: Characteristics determined of a study population based on their gender and location demographic
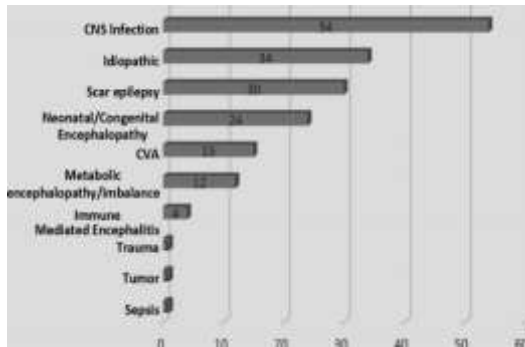

Figure 3: Etiology of epilepsy found in study population suffering from SE.
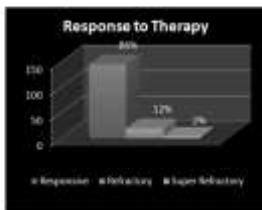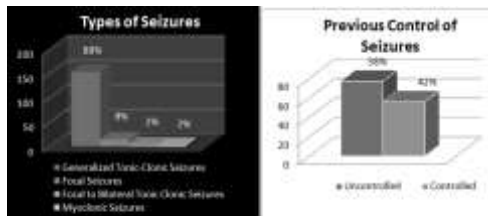

Figure 4: Types of seizure, seizure control and response to therapy

Table 1: Characteristics determined of a study population based on their socio-demographic

Characteristics identified	n (%)	Morbidity Association (p-Value)	Mortality Association (p-Value)
Males	98 (55.7)	0.356	0.002
Illiterate	41 (23.2)	0.110	0.791
literate	2 (1.1)	0.402	0.116
Hereditary history	9 (5.1)		
Historical status of epilepticus	24 (13.8)	0.808	0.004

Table 2: Etiological characteristics of study population.

Characteristics	(n)	(%)	Association with Morbidity(p-Value)	Association with Mortality(p-Value)
History of prior seizures	De novo status epilepticus History of epilepsy	36 140	20.4 79.5	0.00 >0.05
Type of etiology	Cryptogenic Symptomatic	38 138	21.5 78.4	>0.050.
Time course of etiology	Acute Chronic	56 120	31.8 68.1	009 0.00 >0.05

Table 3: Seizure Temporal Profile.

Characteristics	Median (IQR)	Association with Morbidity (p-Value)	Association with Mortality (p-Value)
Duration of the seizure	53 minutes (30-65)	0.841	0.00
Duration of hospital admission	7 days (4.35-11.70)	0.00	0.114
Time to Hospital Arrival	45 minutes (30-120)	0.712	0.001

DISCUSSION

Status epilepticus has been identified as one of the most prevalent neurological emergency. When it comes to this potentially fatal disorder that affects patients and their families, the phrase "time is brain" is more than just a cliché (9). During the dealing with an opponent, it is critical to be aware of the weapons at their disposal. This is where this research comes in, by laying out not only the prognostic markers in SE, but also the clinical, etiological, and demographic profile of SE patients who presented at a tertiary care hospital in Karachi during a five-year period (10).

In this retrospective study, the case fatality rate was 12.5 percent. This corresponds to a 15.6 percent case fatality rate in underdeveloped nations, according to a meta-analysis on the issue. Many possible variables implicated in the prognosis of SE were documented in our investigation, as well as the importance of the underlying etiology in SE outcomes. Gender was revealed to be a major predictor of mortality among men (25.6 percent vs 19.4 percent in females).

A male preponderance in the prevalence of SE has been found in many investigations. However, the research on the influence of gender on outcomes is mixed, with some studies indicating no effect, on increased fatality rate in females, a higher mortality rate in men (9). Acute symptomatic etiologies are clearly connected to poorer outcomes in SE patients, and the increased prevalence of these etiologies in men may explain both the higher incidence in the literature and the lower outcome in this study.

In our study, as people became older, they had worse functional results. It was observed that there was an obvious correlation between patients as they aged and the worsening outcomes off SE. This led to age being a factor in various prognostic scoring systems which could be used to determine the severity of SE within a patient or determining the morality rate of a patient. Age can be seen as a factor in the status epilepticus severity score (STESS). The Epidemiology-based Mortality Score in Status Epilepticus (EMSE) also uses the age of the patient to determine the prognostic score for SE (12).

In this study, it was discovered that patients who suffered from a prolonged attack of SE and a longer delay between SE and hospital presentation were both related with a higher risk of death (11). Trinka, E., Höfler, J., & Zerbs, A. presented much research demonstrating the same in a recent review. They stressed that the underlying etiology had a significant impact on the duration of SE

More than one-third of our SE presentations were from rural regions since our hospital serves as a major tertiary-care referral institution for the city and province. This highlights the absence of facilities in remote regions, forcing referral to our hospital, lengthening the time it takes to obtain adequate treatment and negatively impacting results (14). More research of the frequency of SE in rural areas, as well as the implications for prompt care, is needed.

At six months, de novo episodes of SE and SE developing from a symptomatic illness period reported to be both linked to inferior functional outcomes. De novo incidences of SE were also linked to being older. These findings are similar to those described in 'Status epilepticus in the elderly: Comparison with younger adults in a comprehensive community hospital' and are most likely due to the acute symptomatic etiologies that follow de novo and symptomatic SE (14).

CNS infection discussed is more related with poorer outcomes than SE owing to cryptogenic epilepsy or non-compliance with medications (p0.005), based on a more thorough assessment of the underlying etiologies during our research period. According to a recent meta-analysis, CNS infections are a major cause of SE in the poor countries, owing to filthy circumstances and uneven healthcare treatment (12). It contains major substance for the development of a regional action plan in poor nations, as plans to alleviate the burden of SE must take into account the region's overall infection-control strategies. The next most important cause of epilepsy among our SE patients was scar epilepsy. Scar epilepsy is frequently caused by a co-morbid illness such as diabetes, obesity, hypertension, or lifestyle factors like as smoking, riding a bike without a helmet, and so on (13).

Death was connected to the refractoriness of SE episodes, but the length of hospital stay was linked to poor functional outcomes. While the most prevalent causes of SE may vary depending on the situation, the etiology of refractory SE appears to be comparable to that of non-refractory SE (13).These observations are supported by our experience and analysis. Super refractory SE, according to the same analysis, may have a distinct etiological profile and is most typically seen in the context of encephalitis. This is particularly concerning because, according to a recent study conducted at our facility, in both pediatric and adult patients the cause of symptomatic epilepsy was identified as CNS infections. Three of the four instances of extremely refractory SE found in this investigation were caused by CNS infections. The need of the hour is to avoid super-refractory status epilepticus by reducing population risk factors, as fatality rates in these situations vary from 30 to 50%.

The research limitations of the retrospective study were limited to one tertiary care facility. Furthermore, our setup it's not sufficient enough to provide the resources needed for monitoring the EEG of ICU patients continuously. Studies have shown that epileptic activity can be caught and prevent it earlier in ICU patients through the use of EEG by continuous monitoring this has been particularly proven true for the case of patients suffering from non-convulsive seizures (8).

CONCLUSION

In our study, male gender, poor seizure management, infections of the central nervous system, prolonged seizures, late hospital visit, were the most common and identifiable predictors of morality where the refractory and super-refractory nature of status epilepticus play it a part in determining the morality as well. Subjects having a previous history of status epilepticus, as well as instances with etiologies that were in nature acute and symptomatic had higher morbidity. More local research on prognostic markers are needed to give high sensitivity and specificity in predicting status epilepticus outcomes.

Conflict of interest: None
Funding Source: None
Permission: It was taken from the ethical review committee of institute

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