

## RESEARCH ARTICLE

### STATUS EPILEPTICUS: ETIOLOGY, OUTCOME AND PREDICTORS OF MORTALITY

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#### **Abstract:**

##### **Objective**

This study was designed to determine the etiology of status epilepticus (SE) and its relation to mortality.

##### **Materials and Methods**

This descriptive study was carried out based on the medical records of 40 patients with diagnosis of SE discharged from pediatric hospital of Bandar Abbas between March 2002 and March 2004. Multivariant analysis was performed to determine the prevalence of the disorder and the relation between SE and other factors such as gender, age, response to treatment, and mortality. We classified the etiology according to international league against epilepsy (ILAE) classification and also uses another classification regarding underlying causes such as fever (non-CNS infection), central nervous system infection, hypoxia, and metabolic causes.

##### **Results**

Status epilepticus was responsible for 0.3% of all hospital admissions during the study period. Based on the ILAE classification, frequencies for acute symptomatic, febrile, progressive encephalopathic, remote, and cryptogenic SE were 42.5%, 32.5%, 10%, 7.5%, and 7.5%, respectively.

The most common underlying causes resulting in SE were fever (45%), metabolic disorders (15%), CNS infection (12.5%), chronic neurologic diseases (7.5%), idiopathic (7.5%), hypoxia (5%), drug withdrawal (2.5%), CNS hemorrhage (2.5%), neurodegenerative disease (2.5%), brain abscess (2.5%), and post DPT (Diphtheria, Pertussis, Tetanus) vaccination (2.5%). Mortality rate was 25% (80% in the patients younger than 5 years and 40% in those aged less than 1 year). Occurrence of SE and its mortality was found to be related to age ( $p < 0.05$ ).

##### **Conclusion**

For SE, if seizures continue for more than 5 minutes, treatment must be initiated. The outcome is determined by etiology, age, seizure duration and management; however, all we can do is enhance the management and increase its effectiveness.

**Keywords:** Status epilepticus, Etiology, Underlying cause

#### **Introduction**

Status epilepticus (SE) is usually a manifestation of an acute precipitating event that affects the central nervous system (CNS) or an exacerbation of symptomatic epilepsy (1). It is a medical and neurological emergency, accompanied with significant mortality and morbidity (1,2). Status epilepticus is internationally classified as a

seizure lasting for more than 5 minutes or two or more separate seizures having a period of incomplete recovery of consciousness (2-4).

Based on the classification of the International League Against Epilepsy (ILAE), etiologies include acute symptomatic SE, cryptogenic SE, remote symptomatic SE, febrile SE, and progressive encephalopathy (5). The other classification of etiologies used by some authors was based on underlying diseases such as fever (non-CNS infection), CNS infection, idiopathic, metabolic, chronic neurologic disease, and tumors (1, 3).

Etiologies of SE, used in children, differ clearly from those used for adults (1). Age has been documented as a risk factor for SE (1, 4). Status epilepticus has a bimodal distribution with the highest value during the first years and the 6<sup>th</sup> decade of life and after that (2). More than 80% of children, under the age of 2 years, have SE of a febrile or acute symptomatic cause, whereas, cryptogenic or remote symptomatic causes were more common in older children (1); in contrast, sub therapeutic levels of antiepileptic drugs, remote causes and cerebrovascular accidents represent the three most common etiologies of SE reported in adults (2).

Status epilepticus is usually underestimated and diagnosis of some types of the condition is not easy. Treatment in diagnosed SE is often initiated with delay or is not enough (1). The most dramatic decrease in morbidity and mortality has occurred in pediatric populations, probably due to more rapid interventions and improved treatment modalities (4). Mortality of SE is reported to range from 3% to 6% among children which is lower than that in adults (1, 4). Prompt diagnosis and management has been associated with improved outcomes (1, 4, 5). Since the etiology of SE in our area has not been clearly defined, this study was designed to determine the etiology of status epilepticus and its relation with mortality.

## Materials And Methods

In this descriptive study, the medical records of all 40 hospitalized SE patients evaluated and managed were collected during a two year period (March 2002 to March 2004) and studied.

The data gathered from medical records included information on underlying causes of SE, etiology, age, gender, duration of hospitalization, previous seizure,

previous SE, family history, type of seizure, duration of SE, response to treatment, outcome of SE as well as paraclinic test results such as ABG, CBC, LP(lumbar puncture), blood sugar, electrolytes, blood culture, BUN, and chest X-ray.

After resuscitation of the patients, checking of vital signs, insertion of IV line, and blood sampling for laboratory tests, they were treated according to the following protocol:

1. A bolus of 25% glucose was given during the first 5 minutes and afterwards diazepam was infused with the dose of 0.3 mg/kg.
  2. If seizure persisted, a repeat dose of 0.3 mg/kg diazepam was infused in 10 minutes of seizure onset.
  3. If seizure persisted, in 15 minutes of onset, a loading dose of phenytoin (10mg/kg) was started and if the seizure was controlled, phenytoin was administered with a maintenance dose.
  4. If not, another dose of phenytoin (10mg/kg) was given within 30 minutes of seizure onset.
  5. If seizure persisted, after 45 minutes of onset, an IV infusion of phenobarbital (20 mg/kg) was administered. If the seizures were controlled during each step, a maintenance dose of phenytoin (5mg/kg/day) was started.
  6. If not, after 60 minutes of seizure onset, a midazolam drip was administered with the initial bolus dose of 0.15 mg/kg followed by 1 to 5 micrograms/kg/min infusion.
- The etiology of SE was determined according to the two types of classifications (ILAE and underlying disease). Data was analyzed using Epi Info software,  $p < 0.05$  being considered statistically significant.

## Results

Of all the patients hospitalized, 0.3% were diagnosed as SE cases, of which 62.5% were male; mean age of the patients was 26.6 months and mean duration of hospitalization was 6.5 days.

The most common etiologies based on ILAE classification were acute symptomatic (47.5%), febrile (32.5%), progressive encephalopathic (10%), remote symptomatic (5%), and cryptogenic SE (5%) (Figure 1). The most common underlying causes were fever (45%), metabolic disorders (12.5%), and CNS infection (12.5%). Other etiologic causes classified were, chronic

neurologic disease, idiopathic, hypoxia, brain abscess, neurodegenerative diseases, intracranial hemorrhage, drug withdrawal, and post DPT-vaccination (Figure 2). In 77.5% of the patients, seizure lasted more than one hour. Four patients (10%) had previous history of SE. Mortality rate was 25% (10 cases, 4 males and 6 females). The most common etiologies leading to death were acute symptomatic SE (42.1%) (Table 1). Eighty percent of mortalities occurred in those aged under 5 years, of which, 40% were younger than 1 year (Table 2). There was also a significant relationship ( $p < 0.05$ ) between etiology and response to the treatment (Table 3). Statistical analysis of the results shows that etiology based on ILAE classification and mortality, etiology and response to treatment were significantly related ( $p < 0.05$ ).

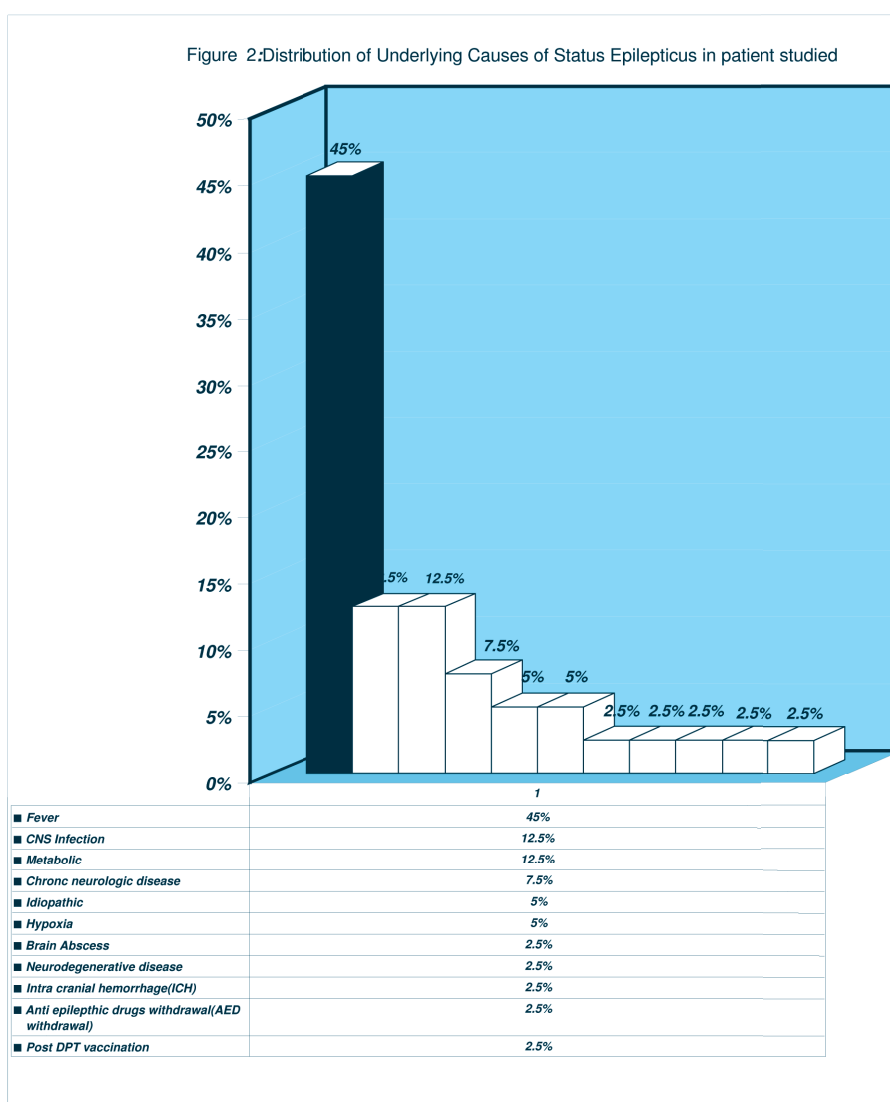
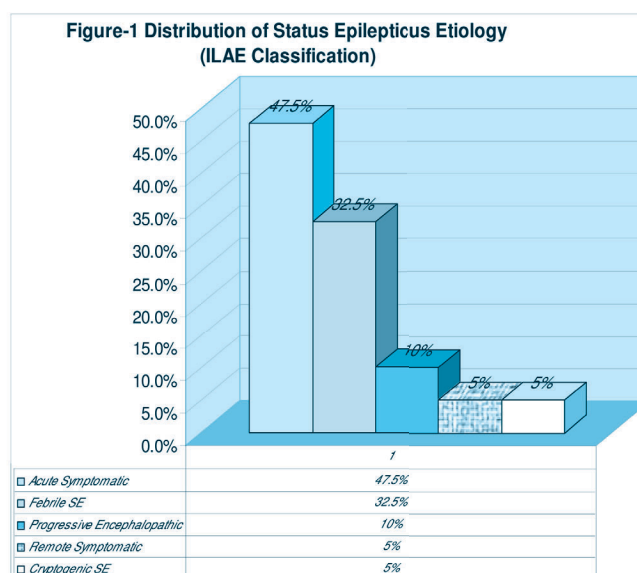


Table 1: Relation between etiology and mortality among patients

Etiology	Relieved	Death
Acute Symptomatic SE	57.9%	42.1%
Remote Symptomatic SE	100%	0%
Cryptogenic SE	100%	0%
Febrile SE	92.3%	7.7%
Progressive Encephalopathic	75%	25%

P value is less than 0.05.

Table 2: Relation between age and mortality in patients

Age	Percent of the SE patients	Relieved	Death
<1 year	47.5%	78.9 %	21.1 %
1-3 year	22.5%	88.9%	11.1 %
3-5 year	17.5%	57.1%	42.9 %
>5 year	12.5%	60%	40 %

P value is less than 0.05.

Table 3: Relation between etiology and response to treatment among patients

Etiology	Response to first line treatment	NO response to first line treatment	Refractory to all drugs
Acute Symptomatic SE	78.9%	21.1%	5.2%
Remote Symptomatic SE	100%	0%	0%
Cryptogenic SE	100%	0%	0%
Febrile SE	84.6%	15.4%	0%
Progressive Encephalopathic	25%	75%	25%

P value is less than 0.05.

## Discussion

Acute symptomatic SE was the most common type in our study (42.5%). Acute symptomatic, cryptogenic, and febrile SE were the most common causes before (35%, 30%, and 25%, respectively). In another study, symptomatic SE, idiopathic, and progressive SE (60%, 11%, and 11%) were more common (7). In our study, the most common underlying diseases leading to SE, were fever (45%), metabolic disorders (12.5%), and CNS infection (12.5%); however in the study of DeLorenzo, they were infection (non-CNS) and idiopathic (36% and 24% to 39%) (3).

In our study, SE occurred in 62.5% of the cases in males which is in accordance with the results of Phillips and Shanahan (61%) and Ibrahim and colleagues (66.7%) (8,9). Previous history of seizure was 37.5% in our study, similar to the finding of 35% in the Kwong and associates study (7). Ten percent of our patients had more than one attack of SE which was reported to be 10.8% and 12% in previous studies (7,9).

Mean duration of hospitalization was 6.5 days in our study, as compared to 5.5 days in the study conducted by Ibrahim, whose mortality rate was similar to ours of 25% (9) and in contrast to the study of Kwong (11%) (6), Coeytaux (7.6%), and Philips (6%) (8); the high mortality rate in our study may be due to the fact that our study was performed in a referral pediatric hospital.

According to our results, SE is age dependent. The most common etiologies in childhood are acute symptomatic (47.5%) and febrile SE, similar to the results of Phillip's study performed on 193 patients aged from 1 month to 14 years. The most common etiologies in children younger than one year were acute causes [bacterial meningitis (27%), electrolyte disorders (30%), idiopathic (23%), and fever (19%)]. In children aged below 3 years, acute causes were responsible for 47% of the cases (8). In a study conducted by Coeytaux, 108 cases had acute symptomatic SE (10), whereas in the Kwong study, the most common etiologies were anti-convulsant drug withdrawal, metabolic derangement, and cerebrovascular diseases (7).

These studies show that SE etiology is age dependent and in the lower age ranges, acute symptomatic (especially CNS infection) and febrile SE are the two common etiologies (1, 4, 8, 10). In our study, 10% of the patients had more than one episode of SE which is similar to the results of a prospective study performed by Berg (9.5%) (11).

## Conclusion

Identifying the underlying etiology plays an important role in the management of patients with SE and in reducing mortality. Our study shows a high mortality rate in young children especially those aged less than one year. Physicians must be aware of and emphasize the importance of SE in this age group.

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