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CLINICAL PROFILE AND OUTCOME OF CHILDREN ADMITTED WITH STATUS EPILEPTICS IN PICU OF A DEVELOPING COUNTRY

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ABSTRACT

Background: Status epilepticus (SE) is a common, life-threatening neurologic disorder. The exact incidence is not known. The frequency of occurrence of status epilepticus is 17-23 per 100, 000 persons per year, with the higher incidences occurring in developing countries. In children the mortality from SE ranges from 3-10%.

Objective: To describe the etiology, clinical profile and immediate-outcome of children with status epilepticus at a Tertiary Care Hospital in Karachi. **Method:** This is a descriptive and retrospective cohort study on all children admitted in our institution with diagnosis of status epilepticus (ICD 9 code 3453). Demographic, pertinent clinical variables and outcomes were collected on structured questionnaire. **Result:** During the study period, fifty patients were identified. Mean age was 51 months (age range was 1-168 months with $SD \pm 41$ months). There were 29 male and 21 female. Generalized tonic clonic seizures were the most common (86%) form of seizures observed. Twenty-five (50%) patients were newly diagnosed with no prior history of seizure. Acute febrile illness or infections were the most common etiology (52%). No biochemical abnormalities were observed in our study. Abnormal EEG was reported in 62% of patients. CSF abnormalities were observed in 22%. Minimum 2 and maximum 8 anti-epileptic drugs were used (mean = 4.33). The most commonly parenteral drugs included phenytoin, phenobarbitone, levetiracetam and valproic acid. Thirty-one (62%) patients required continuous midazolam infusion. In majority (44%), status was controlled after more than 60 mins. Thirty-three patients (66%) required PICU admission for seizure control. Thirty-one (62%) required mechanical ventilation, twenty-five (50%) required inotropic support. Mean PICU stay duration was 3.89 days (range = 1-15 days).

Survival rate was 92%. The cause of death (n=4) was related to underlying systemic illness. No complications were observed in forty-one (82%) patients. **Conclusion:** In our report, young children had a high incidence of SE and the most common etiology was acute febrile illness. Majority of cases were refractory SE although the mortality rate was low.

INTRODUCTION

Status Epilepticus (SE) is the most common pediatric neurologic emergency and is associated with significant morbidity and mortality^{1,2}. The conventional definition of SE is defined as a seizure lasting 30 min or longer or repeated tonic-clonic convulsions recurring over 30 min without recovery of consciousness between each convulsion³. Lately, an operational definition of SE has evolved that any continuous seizure of 5 minutes or longer to initiate treatment early⁴. SE usually responds well to medications but under or inappropriate treatment can be devastating^{5,6}. There is no precise incidence of SE in pediatric population. A recent systematic review of the epidemiology of SE suggested an incidence of 18-70/10, 0000 children per year^{2,7}.

The objectives of the study were to determine the

clinical profile and immediate outcome of SE in pediatric age group admitted to pediatric intensive care unit (PICU) or Special Care Unit of Pediatric Ward in a tertiary-care hospital.

METHODS

A retrospective analysis of SE patient was done at Aga Khan University Hospital pediatric ICU, Karachi. It was for 4 years duration from January 2007- December 2010. All consecutive patients with discharging diagnosis of status epilepticus were included. SE was defined as seizures lasting for 30 minutes or more or multiple episode of seizures without return of consciousness to base line as per International League Against Epilepsy Group Definitions(3). But in case of non-convulsive status, EEG findings suggestive of status were also taken as status. All patients of 1 month -16 years of

age were included in study whether having clinical or subclinical seizures. Those patients who were found to crossing the age limit of 16 years at discharge were planned to be excluded from study. If someone did not fulfill the criteria of convulsive or non-convulsive SE on file review were also excluded. But none of patients on file review fulfilled the exclusion criteria so all were included. In this study, benzodiazepines were considered first-line drug whereas phenytoin or / and phenobarbitone and levetiracetam were considered second-line AEDs. The third-line AEDs were pharmacologic coma included midazolam infusion or thiopental infusion. If an additional AED was required, it was considered a fourth-line therapy⁸.

Ethical review committee approved the study. Medical record numbers were retrieved using coded system from ISD department and files reviewed to fill the Performa. Demographic variables and clinical parameters were recorded in Performa. These included name, age sex, types of seizures, cause and precipitating factor, number of anti-epileptic drugs required to control seizures, EEG and radio imaging findings, requirement for ventilation, duration of ICU stay, complications and survival or death were recorded. SPSS Version 19 was used for data entry and analysis. Descriptive statistical analyses were done for various demographic, clinical, lab parameters and short-term outcome.

RESULTS

Demographic Data: During four years, 50 children were admitted in our institution with diagnosis of SE. Salient clinical features, seizure pattern and causes are tabulated in Table 1. Of which 29 were male and 21 were female. Average age at presentation was 51 months and age range was 1-168 months with standard deviation of 41 months. Thirty-four (68%) cases were less than five-year old. Infants (1-12 month) were 9 (18%). 25 children (50%) were previously healthy. Thirty-three patients (66%) got admitted to PICU while the rest were managed in Special Care Units, where monitoring of vitals was done closely¹⁷.

Seizure: Generalized tonic clonic status was reported in 43(86%), 5 cases of generalized tonic status and 2 cases of non-convulsive SE were seen. SE was of 30 minutes duration in 9 patients, 31-60 minutes duration in 19 patients and more than 60 minutes duration in 22 patients (Fig.1). Time till control of seizures was as: 18 patients < 1 hour, 9 in 1-2 hours, 13 patients 2-24 hours and 10 patients with more than 24 hours (Fig.2). Twenty-five cases were known cases of seizure disorder or neurological illness. Investigations: Lumbar

puncture was done 19 patients; abnormal results were seen in 11 patients (58%). EEG was done in 49 patients, one patient was shifted out early in course of treatment and EEG was not done on him. EEG was abnormal in 31 cases (63%). 25 patients require multiple EEGs or continuous EEG monitoring which showed burst suppression pattern on pharmacologically-induced coma. CT scan brain and MRI Brain were done in 18 and 14 cases respectively. Abnormal CT and MRI were found in 5 (28%) and 6 (43%) cases respectively. Metabolic profiles were normal in our group of patients. Anti-Epileptic Drugs: Minimum 2 and maximum 8 anti-epileptic drugs were used; with 4.33 mean number of drugs used in each case. The Midazolam infusion was required in 31 patients. The doses range from 6-25mcg/kg/min in our cohort. Mean duration was 1.55 days and range 1-8 days. It was hard to predict that which drug was effective. We can only comment that the combination therapies were helpful in aborting the SE. Etiology/precipitating factors: Etiological review showed 26 cases were febrile, 7 underlying metabolic diseases, 10 other miscellaneous causes and 7 were idiopathic. Status was precipitated by poor compliance of medication in 5 patients, by fever in 26 patients and in 19 no factor was identified. Largest underlying diagnosis was developmental delay in 25 cases, followed by infection 12 cases, including meningitis/viral encephalitis, cerebral malaria, dengue encephalitis and typhoid fever, 3 cases of trauma, 3 cases of autism & ADHD, 2 cases of suspected MELAS, 2 cases of febrile fits presenting first time in status epilepticus and 1 case each of febrile neutropenia, GBS and turner's syndrome. Drug levels were low in those having poor compliance. ICU Therapies: PICU Stay was seen in 33 patients. Mean PICU stay duration was 3.89 days with range of 1-15 days. Ventilation was required in 31 patients. Mean 2.91 days required for ventilation with range of 1-14 days. Inotropic support was required in 25 patients with mean duration of 2.3 days with range of 1 - 15 days. Outcomes: In our cohort, forty-six (92%) children survived and discharged. but only 4 cases (8%) were expired which was unrelated to SE and because of underlying illnesses. Of all survived patients, 2 required CPR, 2 tracheostomy for prolonged ventilation and pulmonary toilet, 1 developed renal failure and required dialysis. The 4 patients died due to their underlying diagnosis. One was GBS with hypoxia during their travel to hospital, one with febrile neutropenia with MODS and was having no code status, one with post-traumatic DI and clinical evidence of brain death and another with meningoencephalitis and no code status.

DISCUSSIONS

In our cohort, SE is more common in young children (less than five-year old) as described in other published reports. The occurrence of SE in infant is highest in other reports as compared to 18% in our series^{2, 9}. There is no gender difference in our study. The female preponderance was seen in few research papers(10). We observed the convulsive form of SE about 96% (48 cases) in our report. It is the most common type of SE in children in the literature^{2, 7, 11, 12}. Like other reports of SE in children, acute febrile illness was the most common cause or precipitating factor in our cohort^{12, 13, 14}. Our data is not different from other reports where SE is seen as the first manifestation of seizure disorders in 30 - 55% of cases^{12, 14, 15}.

The mortality rate in our cohort was 8% which was improved from 25% which was previously published from same institution¹⁶. The mortality rate in children with SE has been reported different, with a tendency toward a decrease during the last decades. It is probably multifactorial, being helped by advances in childhood medical and nursing practices with acute life support, critical care management and evolving antiepileptic drug therapies^{12, 15, 17, 18}.

The frequency of refractory SE in our series was >60% (>30cases) which is relatively higher than other published reports (25-50%)^{12, 14, 15}.

Several reports revealed that the prolonged SE is associated with higher neurological morbidity and mortality^{6, 9-21}. Therefore, rapid control of SE should be achieved with rapid escalation of antiepileptic drugs. High-dose midazolam infusion has shown efficacy in termination of refractory SE²¹. Our experience with use of high-dose midazolam with rapid escalation was safe. We can only comment that the combination of therapies achieved in terminating SE in our series. Over the last decade, the early intravenous use of valproic acid and levetiracetam and topiramate were effective in terminating seizure²².

There were several limitations in this study which were retrospective, single center and small sample size.

CONCLUSION

In our report, young children had a high incidence of SE and the most common etiology was acute febrile illness. Majority of cases were refractory SE although the mortality rate was low.

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Table1. Salient Features of Patients with Status Epilepticus (n--50)

Age of Presentation	1months -168 months
Mean age	51months
Male/Female	29/21
Seizure type	
Generalized tonic clonic	43
Generalized tonic	5
Non- convulsive status	2
Patients with prior history of seizures	25
Patients with no prior history of seizures	25

Figure1. Duration of Status Epilepticus

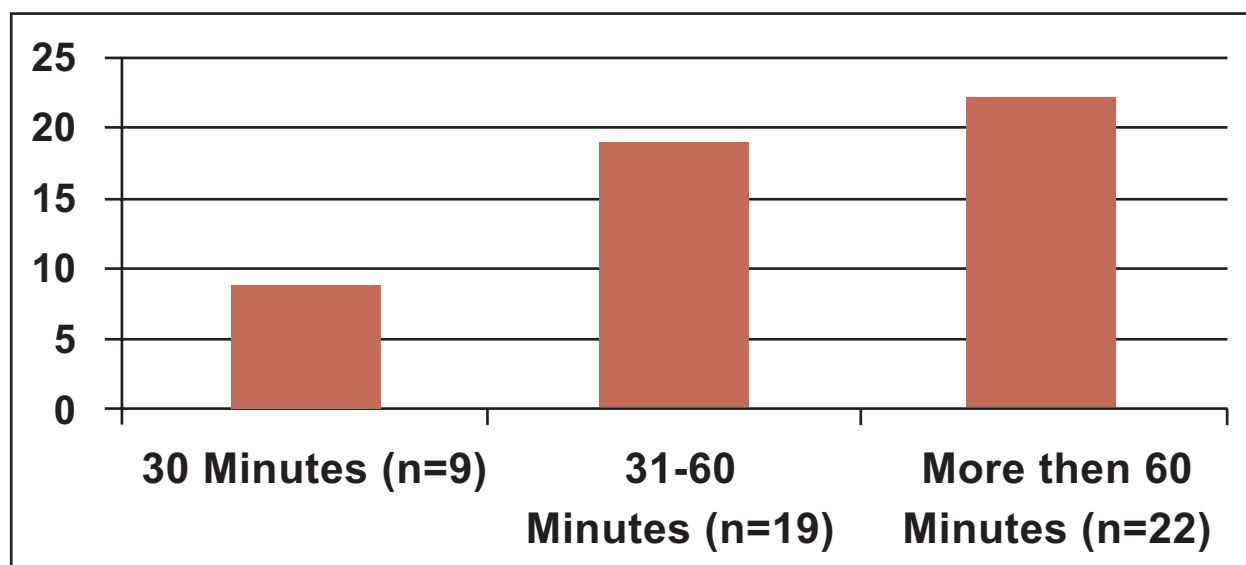


Figure2. Time require to control seizures

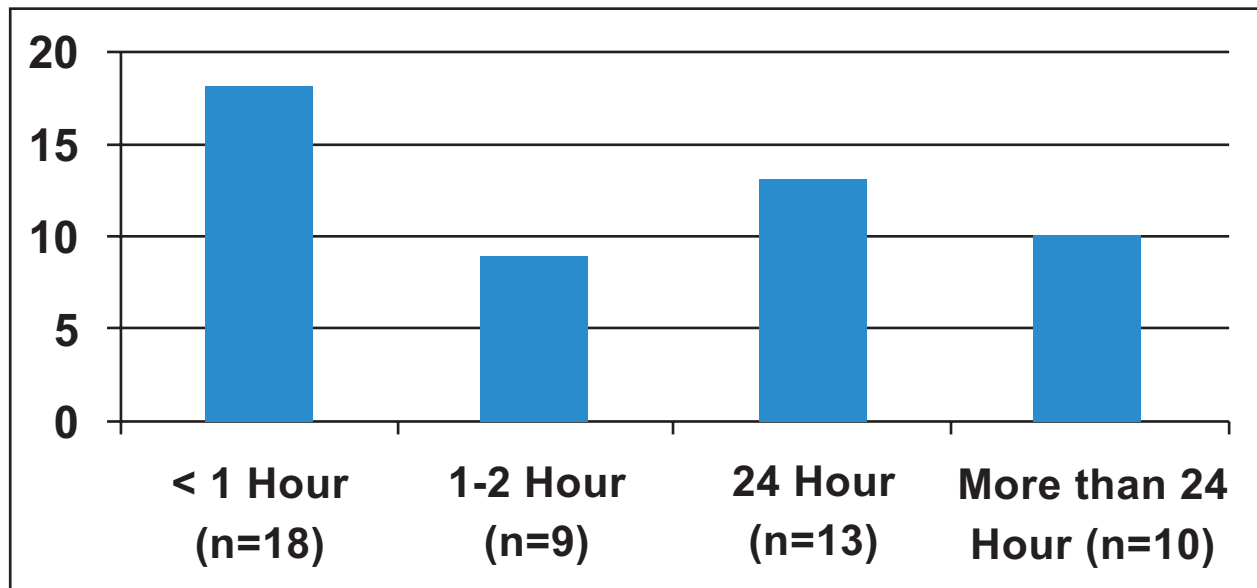


Figure3.

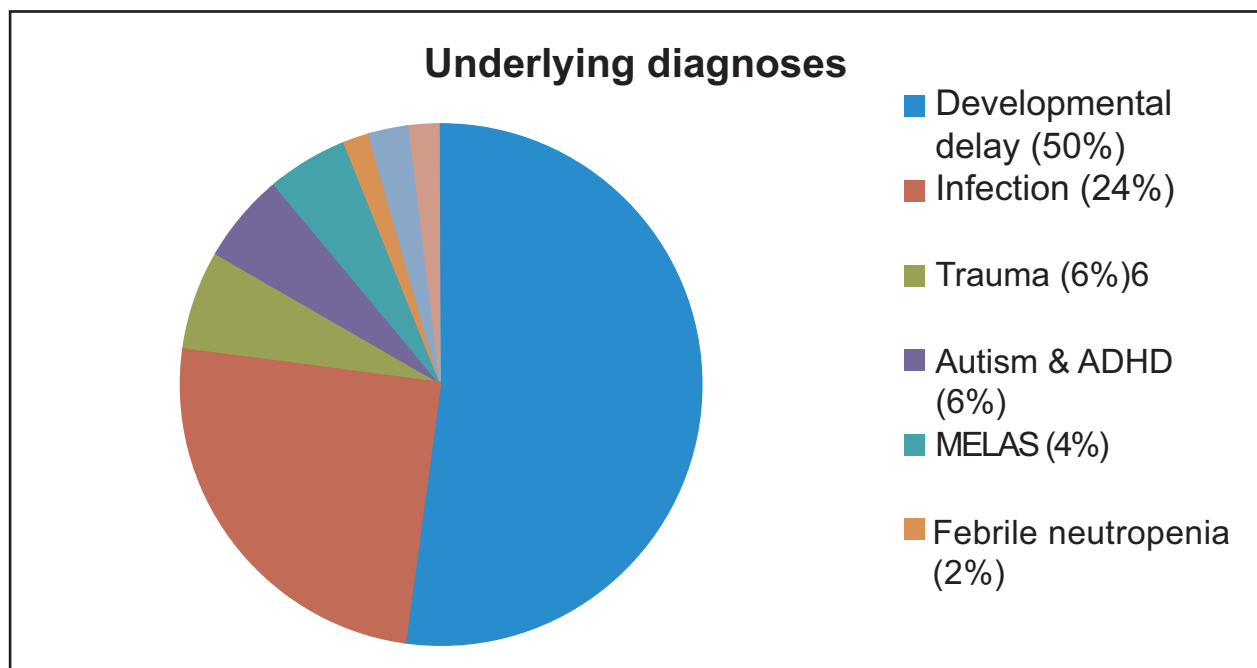


Figure4. Precipitating Factors

