ORIGINAL ARTICLE

CLINICAL PRESENTATION, CAUSE, AND SHORT-TERM OUTCOME OF CHILDREN WITH STATUS EPILEPTICUS IN TIKUR ANBESSA SPECIALIZED HOSPITAL ADDIS ABABA, ETHIOPIA: A 5-YEAR RETROSPECTIVE CROSS-SECTIONAL STUDY

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ABSTRACT

Background*: Status epileptics(SE) has an increased incidence and poor out come in resource-limited countries where infectious disease like malaria, meningitis are in higher rates and where also health care system is limited. Researches in this setting are limited particularly in pediatrics .We aimed to see the clinical presentation, causes and short-term outcome of children with SE.*

Methodology*: A 5-year cross- section study was conducted from January 2005 to January 2010. Children with age above 1 one month and age less than 13 years were included. Data entered and analyzed with SPSS version 16.*

Result*: Eighty-nine patients were found during the study period. Generalized tonic-clonic seizure was the commonest type of seizure (74.8%). Only 28% arrive within 2 hours of presentation. There was a previous history of seizure disorder in 34(38.2%) of the cases. Temperature greater than 38oc was documented for 40 (44.9%) patients at presentation. From the febrile group at presentation 26/40(65%) had an acute central nerves system (CNS) infection who were previously neurologically normal.*

Patients with acute CNS infection had pyogenic meningitis in 18(69.2%), CNS Tuberculosis 5 (19%) and viral meningitis 3(11.5%) cases. None of the patients received intravenous anti-epileptic drug except diazepam; 51 (57.3%) patients discharged improved with no squeal, 32 (36.0%) had a neurologic deficit (5 were having a neurologic abnormality at admission), there were 6(6.7%) deaths. All deaths occur in acute symptomatic SE. HIV infection was found to be statically associated with poor outcome p-value < 0.05.

Conclusion and recommendation: *Most of the patients with SE arrived late to hospital and mortality was found to be high in acute symptomatic SE. To improve patient care and outcome there should be health education and improve the care of symptomatic SE like providing intravenous anticonvulsant.*

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INTRODUCTION

Status epilepticus (SE) is a common neurological emergency that is associated with high morbidity and mortality. SE is defined as a condition in which there is either greater than 30 min of continuous seizure activity, or two or more sequential seizures without recovery of full consciousness between the seizures [1]. SE is classified as convulsive (CSE) and no convulsive status epilepticus (NCSE). CSE is a clinical diagnosis while an electroencephalogram (EEG) is required to diagnose NCSE. CSE has better prognosis among the two and can be further classified based on the clinical picture as generalized and partial. [2]

The estimated incidence of childhood status epilepticus (SE) is between 17 to 23 episodes per 100,000 per year. [3] Incidence rates, causes, and prognosis vary substantially by age. The incidence of status epilepticus is said to be higher in children as compared to adults and in younger children as to the older children. [4] There is a higher incidence in developing countries than the developed ones. Status epilepticus is common in patients admitted to hospitals in resource-poor countries (RPC). This is said to be due to lack of health care and a higher incidence of infectious disease. In sub-Saharan Africa, the high incidence of febrile illnesses might influence the incidence and outcome of CSE. The mortality associated with CSE in RPC is greater (11-15%) both in adults and children, but the long-term outcome in terms of premature mortality and neurocognitive sequel are undetermined. [5]

SE can be a complication of acute illness such as encephalitis, malaria or can occur as a manifestation of epilepsy. Between 10 and 20 % of children with epilepsy will have at least one episode of SE. SE occurs as the first seizure in 12% of children with epilepsy. Nearly a quarter of persons presenting with SE have preexisting epilepsy. In one-third of patients with a preexisting seizure disorder, no obvious precipitating factor can be identified for the occurrence of SE. Genetic factors are also risk factors for the development of status epilepticus. [6, 7]

STATEMENT OF THE PROBLEM

Ethiopia is one of the sub-Saharan countries where the incidence of infectious disease is high including meningitis, malaria, HIV, etc. which all contribute to high incidence of SE there is also a limitation in both diagnostic and management modalities of SE. There are no studies done on SE in pediatric patients previously in Ethiopia.

OBJECTIVE

To determine clinical presentation, causes, short-term outcome of status epileptics and its determinants.

PATIENTS AND METHODS

Tikur Anbessa specialized hospital is a teaching hospital for undergraduate and post graduate students. In addition to teaching, the hospital gives both inpatient and outpatient service to patients referred from different parts of the country. The pediatric emergency department is the place for the management of acute and emergency conditions in those less than 13 years a definition for pediatrics age for the Hospital. In addition, patients are also admitted to the wards, based on the need for admission and the diagnosis. Patients who have chronic illness will have their visit from Monday to Friday on the appropriate follow-up a clinic. Neurology and seizure clinic are parts of these follow-up clinics where patients with different neurologic problems or seizure disorders are seen on Tuesday and Thursday respectively.

In this study 89 patients were included who were admitted to pediatric emergency unit , pediatrics ward, intensive care units with diagnosis of SE. Admission diagnosis was taken from the record book of specific wards. The cards of all patients with seizure disorder and neurologic problem on follow up at the neurologic clinic were revised to see if they were admitted for status epileptics in the time of the study period. Data was collected regarding the socio-demographic status, clinical presentation, laboratory result and outcome of patients by trained data collectors using pretested and modified questionnaire. The questionnaires were checked for completeness by the supervisor and principal investigator. Patients excluded from the study are those less than 1 month (since neonatal seizure is different), greater than 13 years (because this age group was seen in adult side), incomplete recording and unclear diagnosis. Data was cleaned and entered using SPSS-16, analyzed by univariate, bivariate, and logistic regression.

OPERATIONAL DEFINITION

Status epilepticus: is defined as a condition in which there is either greater than 30 min of continuous seizure activity, or two or more sequential seizures without recovery of full consciousness between the seizures

Acute symptomatic SE: Status epilepticus in a previously neurologically normal child, within a week of an underlying cause including central nervous system (CNS) infection, encephalopathy, traumatic head injury, cerebrovascular disease, and metabolic derangements or toxic injuries.

Febrile Status epilepticus: that develops in a previously neurologically normal child between the ages of 6 months and 5 years during a febrile illness apart from CNS infection.

Remote symptomatic: Status epilepticus in the absence of an identified acute insult but with a history of a pre-existing neurological abnormality more than 1 week before disorders.

Idiopathic/cryptogenic SE: is SE not symptomatic and occurs in a child with no prior neurological disorder or in a child in whom no neurological findings were detected via history physical examination and investigations.

Unclassified: Convulsive status epilepticus that cannot be classified into any other group.

Short-term outcome: condition of the patient at discharge from hospital

Neurologic squeal: development of neurologic deficit at discharge like hemiplegia or mono paresis which was not there at admission.

Delayed response to treatment: no response after 2 hours of treatment

The level of consciousness at initial evaluation was divided into conscious, lethargic (arousable and responsive), stuporous (arousable but not responsive), and comatose (un arousable).

Outcome at hospital discharge was recorded as improved (returned to baseline), deteriorated (alive but substantially impaired relative to baseline clinical condition), and died.

Ethical considerations

Data collection was started after written legal permission obtained from the department of Pediatrics and Child health and Addis Ababa university-Medical Faculty institutional review board.

RESULT

Data for 89 patients admitted with a diagnosis of SE in 5 years were analyzed. Of this 52 (58.4%) were males. Sixty-eight (76.4%) were from Addis Ababa. The age distribution was 22.5% were 1-12 months, 50.6% were 13-60months and the remaining 27 % were greater than 60 months. Socio-demography and clinical profile are seen in Fig 1 and Table 1.

Fig 1 Sex and age distribution of Frequency of SE

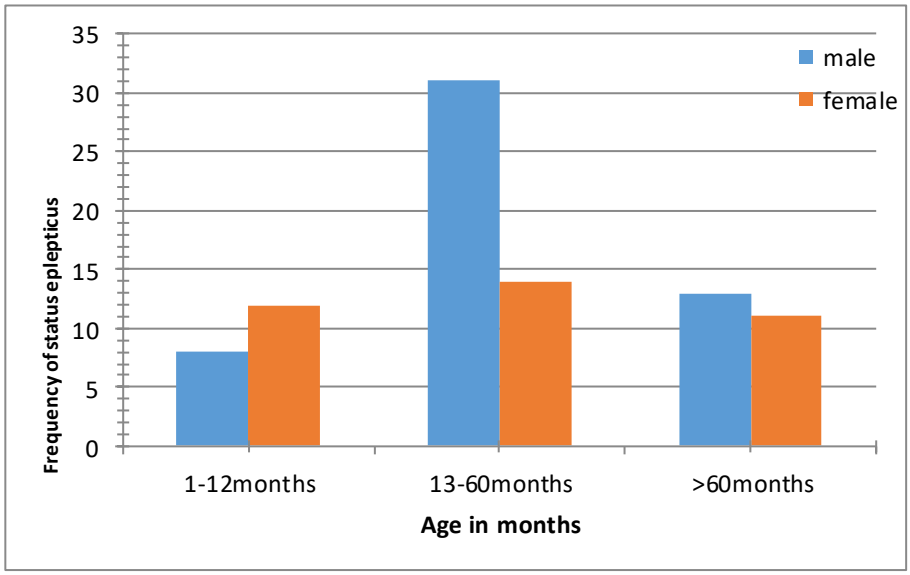

Table 1: clinical presentation and outcome of children with status epilepticus who presented to Tikur Anbessa Specialized Teaching Hospital, Addis Ababa, Ethiopia

Clinical profile		Total	improved	Neurologic sequelae	died
Age in months	1-12	20	8(9%)	9(10.1%)	3(3.4%)
	13-60	45	26	16	3
	>60	24	17	7	0
Time to treatment in hours	<2	25	13	8	1
	2-12	46	29	16	2
	>12	17	9	7	3
Type of seizure :	Generalized	66	43	19	4
	Partial	13	6	6	1
	Partial with secondary generalization	8	2	5	1
Condition on arrival	Conscious	7	2	4	1
	Convulsing	32	15	15	2
	Lethargic	23	18	5	0
	Comatose	26	15	8	3
Glasgow coma scale on arrival	≤8	45	23	19	3
	9-12	28	21	5	2
	≥13	8	4	4	0
	unknown	7	2	4	1
Previous history of Seizure disorder	Yes	34	21	12	1
	No	55	30	20	5
Preceding neurologic deficit	Yes	5	0	5	0
	No	84	51	27	6
HIV	positive	3	0	2	1
	negative	25	8	15	2
	not done	61	43	15	3

Table 2: Organic causes identified in children with status epilepticus who presented to Tikur Anbessa Specialized Teaching Hospital, Addis Ababa, Ethiopia

	Causes	frequency	Percent (%)
Acute symptomatic	Pyogenic meningitis	18	20.2
	Tb meningitis	5	5.6
	Viral meningoencephalitis	3	3.4
	Traumatic brain injury	3	3.4
	Hypoglycemia	1	1.1
	ALL with CNS metastasis	1	1.1
	Hypoxic brain injury	1	1.1
Remote symptomatic	Suspected perinatal insult	11	12.4
	Hypoxic encephalopathy	3	3.4
	Congenital brain abnormality	1	1.1

Time of arrival for treatment was less than 2 hours in 25(28.1%) of cases, 2-12hours in 46 (57%), greater than 12hrs in 17(19.1%) of cases and unknown in 1(1.1%) case. The most common seizure type observed was generalized seizure 66(74.2%) followed by partial 13(14.6%), partial with secondary generalization 8(9%) of cases and 1(1.1%) unknown.

ETIOLOGY

The most common cause of SE identified was idiopathic/cryptogenic 36(40.4%) cases, followed by acute symptomatic 27(30.3%), remote symptomatic 19(21.3%), febrile seizure 6(6.7%) and one case was unclassified. Among the acute symptomatic cases pyogenic meningitis was the commonest 18(20.2%), TB meningitis 5(5.6%), viral meningitis and traumatic brain injury each 3 cases (3.4%) and hypoxic brain was the cause in one patient secondary to intraoperative cardiac arrest and hypoglycemia was also seen in one patient who has prior history of seizure and one patient had intracranial metastasis as cause for one patient with acute lymphoblastic leukemia. Among patients with remote symptomatic cases 11(12.4%) perinatal insult was suspected as a cause based on history and physical examination they had also clinically suspected cerebral palsy. (Table 2 causes)

In children, less than 12 months acute symptomatic status epilepticus was seen in 55% of cases followed by a febrile seizure. Remote symptomatic and idiopathic/cryptogenic SE

was the commonest for children greater than 12 months 41.4% and 96.7% respectively.

The previous history of seizure disorder was seen in 55(61.8%) of the cases where 5(9.1 %) discontinue their medication, 3(5.4%) were taking a low dose of anticonvulsant, 5 (9.1%) presented with status epilepticus for the first and the rest 42(76.3%) were taking the recommended drug and dose when they develop SE.

INVESTIGATIONS

Lumbar puncture was done for 61(68.5%) patients the result was abnormal in 16(26%). Random blood sugar was normal for 78 (87.6%), 1 patient has hypoglycemia and in the rest of (11.2%) not done. Serum electrolyte was done for 40(44.9%) and 4 patients were having an abnormal result. Blood film was done for 41 patients all are negative. EEG was done for 21 patients after control of seizure and 19 (21.3%) has abnormal finding. CT was done for 20 cases and abnormal in 5 (25%) of cases. MRI was done only for 3 cases and all were abnormal. Serum anticonvulsant level was not determined for all of the patients.

OUTCOME AND COMPLICATIONS

Of the total number 51(57.3%) discharged improved with no squeal at discharge, 32 (36.0%) had a neurologic deficit of which 5 were having a neurologic abnormality at admission, there were a total of 6(6.7%) deaths. Complications were seen in 11 patients aspiration pneumonia 9(10.1%) and renal failure in 2(2.2%).

Outcome neurologic squeal and death were analyzed for different variables. Neurologic squeal occurred in 9(45%) occur in age group less than 12month, 16(35.6%) in age group 13-60month and 7(29.2%) in greater than 60 months. Death occurs in 6 patients all less than 60 months.

Generalized CSE occurred in 74.2% of cases, partial seizure occurred in 13(14.6%) the least common identified was partial seizure with secondary generalization accounting 8 (9%) of cases both neurologic squeal and death were high in this group 5(62.5%) and 1 (12.5%) respectively. Patients who presented with convulsion and coma neurologic squeal occurred in 15(46.9%) and 8(30.3%) of cases. Fifty percent of patients who presented with coma had died. A total of 40(44.9%) patients had fever on arrival and 5(83.3%) of the deaths were febrile. Neurologic squeal and death occurred in 50% of cases whose seizure control took greater than 12 hrs. Acute symptomatic cases and remote symptomatic were associated with high neurologic squeal contributing 13(40.6%) and 15 (46.9%) of cases. All deaths occur in the acute symptomatic group. No neurologic squeal or death occurred in prolonged febrile SE and idiopathic/cryptogenic cases.

TREATMENT

Drugs used for the management of SE were diazepam and Phenytoin in 45(50.6%) of cases, diazepam and Phenobarbitone in 18 (20.2%) and diazepam, Phenytoin and Phenobarbitone in 19(21.3%) cases in the rest of the cases carbamazepine, valproate or clonazepam was also added. In all 89 cases, diazepam was given intravenously and Phenobarbitone, Phenytoin, and the other anticonvulsants were given via NG tube. We tried to analyze time taken for the control of seizure it showed that >12hrs in 38(42.7%) of cases, 2-12 hrs in 35(39.3%) of cases, 30min-2hrs in 13(14.6%) and 2 cases less than 30minute.

DISCUSSION

The objective of the study was to analyze the clinical presentation, causes, outcome and determinants of outcome. In the definition of status epilepticus, there were different controversies the currently accepted definition for epidemiological studies is the 30-minute criteria. (8) The higher incidence is seen in those less than 12 months followed by 12-60 months the age difference was also seen in other studies. (9, 10) in our study, there is male sex predominance which is also seen in other studies. (9-11)

Duration of seizure before arrival to treatment was greater than two hours in 65 (76.1%) of cases delay in treatment was also seen in the research done in Ethiopia on adult patients in 1997. (12)

The most common seizure type seen was generalized seizure followed by partial seizure this finding is consistent with other studies where generalized convulsive SE is also seen being the commonest. (13)

There is a significant difference on etiologies based on the age of the patient in our study. In children, less than 12 months acute symptomatic and febrile seizure were the commonest causes and in those greater than 12 months idiopathic/cryptogenic and remote symptomatic are the causes frequently seen. In our study, 55% of causes of status epilepticus were due to acute symptomatic followed by prolonged febrile seizure. Whereas for the older age group remote symptomatic and idiopathic/cryptogenic causes dominate. For the remote symptomatic the precipitating factors seen were fever with no CNS infection and in most not identified. In idiopathic/ cryptogenic cases SE was found to be the entry for diagnosis where some patients having seizure disorder didn't request health service, most are taking properly their medication and others came after discontinuation of their medication. On those who are said to be taking drugs the information was taken from the cards which were documented based on the patients or attendants since serum level is not determined it is difficult to depend on this report.

The age variation in etiologies was also seen in different studies. In a retrospective study done in New York status epilepticus was found to be common in less than 2 years>40% with more than 80% of the cases having acute symptomatic or febrile origin whereas in children greater than 2 years remote symptomatic and idiopathic where the commonest cause. (15) In an observational study done in Turkey also showed acute symptomatic cases are more common in age group less than 2 years. Among acute symptomatic CNS infection was the commonest top being pyogenic meningitis 20.2%, followed by TB meningitis 5.6% and viral in 3.4%. This is also seen in other studies that CNS infections are common causes in especially in sub-Saharan Africa where there is a high incidence of malaria and other infectious causes due to low socioeconomic status. (5) The absence of malaria in our study could be due to since most patients are from Addis Ababa which said to be malaria free or the other factor may be the preventive methods which are being done against malaria.

There was descriptive study done in Pakistan which showed acute symptomatic epileptic being commonest cause of SE, its specific causes being viral meningoencephalitis (32%), pyogenic meningitis(3.2%) a tubercles meningitis 2.4% which is also the cause for our set up even if pyogenic meningitis is the leading in our set up 20%.

All deaths occur in age group less than 60 months. And high death rate is found in those less than 12 months. No death was seen in greater than 60 months. The higher death rate in this age group is related to the etiologies where most of the cases are due to acute symptomatic. There was no also death in the remote symptomatic, idiopathic and PFS. Neurologic squeal were also high in acute symptomatic and age less than 12 months. Statically significance association with the p value less than 0.05 was seen between etiologies and outcome. Similar studies done in different areas had also demonstrated the same association. In the Korean study, neurologic squeal and death were strongly associated with seizure type. (14) Also in research was done in France death and neurocognitive squeal were dependent on age and etiology. (16) We have a clinical association with age, duration of seizure, type of seizure, condition at presentation and time to control seizure with the poor outcome but no statistically significant association is seen.

The drug most commonly used was diazepam in almost all patients and it was administered IV in all cases. Followed by Phenytoin loading and maintenance 50.6%, in 20% phenobarbital was used, in patients whose response was longer Phenobarbitone and Phenytoin were used 21.3%. Based on our finding 82% of cases took greater than 2hrs to control their seizure. The explanation may be due to the use of oral anticonvulsants which are less effective the other is a

recording problem since progress notes are not written frequently especially in the pediatric emergency OPD and follow up sheets are not attached when patients are discharged. Due to these factors, this finding doesn't go with research done in south Africa to analyze the efficacy of oral phenobarbitone which showed Seizure control was documented within 1 h (n= 8), 11/2 h (n= 1), 3 h (n= 1) and 4 h (n= 5) following enteral phenobarbitone loading. No adverse effects were apparent from the enteral phenobarbitone administration Patients tolerated enteral loading with phenobarbitone. A single enteral loading dose resulted in adequate phenobarbitone exposure.

CONCLUSION AND RECOMMENDATION

The commonest age group with status epilepticus in our set up is children less than 1 year. Idiopathic SE is frequently seen cause. Mortality was found to be higher in children less than 1 year. Acute symptomatic causes are most frequently in less than 12 months with high mortality. Meningitis was the common cause for acute symptomatic cases. Delayed response to treatment more than 2 hours is seen in 82% of patients. Accessibility to parenteral anticonvulsants (phenytoin and phenobarbital) is vital to improving the response. Measuring serum antiepileptic drugs is important for patients with status epilepticus and it would be good if it is done in TASH.

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