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Etiology and Outcome of Convulsive Status Epileptics in Children

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Abstract **Original Research Article**

Objective of study: To review the etiology, clinical profile, and outcome of status epileptics (SE) in pediatric age group. ***Methods:*** Data from 50 cases was obtained prospectively which admitted to intensive care unit Benghazi children hospital from between May, 2019 and May, 2020 Patients aged between 30 days and 15 years with the symptoms of SE were selected for this study exclusion criteria convulsion at neonatal age and patient with non-convulsive status epileptics. ***Results:*** The data show that Male sex of the cases was predominant as they represented 58% complemented by 42% females: Although male gender was greater than female among the cases, the deaths were 50% male and 50% female, so mortality was equal etiology of the status epileptics it was observed that, in 62% of the sample due to acute symptomatic condition, in 26% due to remote symptomatic illness, unclassified reason was reported in 6%, complex febrile convulsion in 4% and epilepsy related in 2%. Type of seizure was generalized tonic-clonic convulsion in 94% and focal in 6%. Of cases Number of drug used for the cases was one drug in 2%, two drugs in 20%, three drugs in 60% and four drugs in 18%. More than have of the cases (52%) were classified as refractory to anticonvulsant therapy, 8% were super-refractory. 40% of the sample responded to two anticonvulsant medications Outcome of death happened in 20% of the cases (10 cases) and transfer to the ward was done for 80%. ***Conclusion***: Patients with younger age and male sex are slightly more vulnerable to develop SE. Longer duration of SE and acute symptomatic an etiology are independent predictors for poor outcome status epileptics.

Keywords: Status epileptics, convulsion, Etiology, outcome.

INTRODUCTION

Status epileptics is a life threading seizure and common pediatric emergency for every 100,000 children, 73 had SE., the higher the incidence of SE will be more in younger children. (Sánchez & Rincon, 2016) The incidence of SE in children aged less than 2 is high at 156 per 100,000 and is at the highest for infants (Qadir *et al*., 2018).

The SE is that the commonest pediatric neurological emergency and a major cause of admission to the pediatric intensive care unit PICU (Alyoubi *et al*., 2021).

Historically, SE was defined as a seizure lasting longer than half-hour or a series of seizures in a period of 30 minutes without return to baseline level of consciousness between attacks of seizures (Costea *et al*., 2016). The new definition has gradually shortened thanks to increasing recognition that most seizures are brief (3–4 minutes) and anticonvulsant administration delays are associated with more refractory seizures.

The most recent guideline of Neurocritical Care Society for SE management in children and adults defines SE as "5 minutes or more of continuous clinical and/or electrographic seizure activity or recurrent attacks of convulsion without recovery (returning to baseline) between seizures.

Immediate aggressive management could also be particularly important in post-operative neurosurgical and cardiac surgical patients, patients with elevated intracranial pressure (e.g. traumatic brain injury, brain tumor , central nervous system infections), and patient with multi- system organ failure.

The terminology want to describe SE timing has evolved over time. During the prodromal or incipient stage (30 minutes), or refractory SE (RSE) (seizures that persist despite treatment with adequate

doses of two or three anticonvulsant). The recent guideline states that "definitive control of status epileptics should be established within 60 min of onset. In contrast to some earlier timing terminology which considered medications as first, second, and third line agents, the new guideline uses the terms "emergent", "urgent", and "refractory" to assist convey a sense of time urgency and that medications should be administered sequentially if seizures persist.

RSE is defined as clinical or electrographic seizures which persist after an adequate dose of a first line of management benzodiazepine and a second appropriate anticonvulsant therapy; no specific time must elapse before initiation of RSE management (Abend & Loddenkemper, 2014).

The most common presentation is generalized convulsive SE (GCSE), the main seizure type for pediatric SE or focal SE with impaired consciousness after failure to initial treatment. Other common clinical presentations are subtler and thus, are implicational non-convulsive SE (NCSE). Within the latter clinical scenario, patients usually present with stupor/coma after a GCSE or after an acute brain insult.

Although convulsive SE often evolves to NCSE, the excellence between these two phenotypes is crucial as the therapeutic approaches and outcomes are different, being NCSE more often related to medical poor prognosis due to delayed recognition (Vasquez *et al*., 2019).

Neurological complication of pediatric status epileptics (SE) occur in 9%–28% of patients. Outcomes could also be affected by additional clinical factors, including age at onset, etiology, SE duration and time to start treatment of those, SE duration and time to treatment are of particular importance, as they're potentially modifiable (Gaínza-Lein *et al*., 2021).

MATERIALS AND METHODS

We provide a prospective analysis of prospectively collected data performed at intensive care unit Benghazi children hospital we had collected data on children with SE including(Refractory and super refractory status epileptics)and assesses variability of care to delineate strategies for improving management and prognosis in pediatric SE.

Inclusion criteria were (1) age = 1 month to 15 years; (2) admission to intensive care unit Benghazi children hospital between May 1, 2019 and may, 2020, with any cause of SE. Exclusion criteria was non-convulsive SE and neonatal age group and epileptic patients without SE.

The demographic data of participants is presented in descriptive statistic. Standard deviation SD and mean were used to report continuous variables. Statistical Package for Social Science) SPSS was used for all the analyses in the study.

RESULTS

This study analyzed data related to 50 children with status epileptics. The age range of the sample was from one month to 180 months with mean age of 28.3 months (±42.96), median of 10.5 months. The distribution of cases according to age groups (table 1) showed that, 74% of them were aged from one month to two years, 10% were >2-5 years and 16% were > 5years of age. Male sex of the cases was predominant as they represented 58% complemented by 42% females (Table 1). Normal birth history was reported in 88% of the sample, while 12% have history of birth asphyxia. Developmental history was normal in 80% whereas 20% have delayed developmental history (Table 1).

Anthropometry of the sample was normal in 78%, microcephaly in 14%, failure to thrive in 6% and hydrocephalus in 2% (Table 1).

Regarding etiology of the status epileptics it was observed that, in 62% of the sample due to acute symptomatic condition, in 26% due to remote symptomatic illness, unclassified reason was reported in 6%, complex febrile convulsion in 4% and epilepsy related in 2% (Table 2).

Clinical examination of the cases was normal in 56%, abnormal neurological examination in 42% and one patient (2%) was comatose.

Type of seizure was generalized tonic-clonic convulsion in 94% and focal in 6% (Table 2). Number of drug used for the cases was one drug in 2%, two drugs in 20%, three drugs in 60% and four drugs in 18%. More than have of the cases (52%) were classified as refractory to anticonvulsant therapy, 8% were super-refractory. 40% of the sample responded to two anticonvulsant medications (Table 2).

Family history of febrile convulsion or epilepsy was positive in 12% of the cases (6 cases), 88% have negative family history of epilepsy. Drug history of anticonvulsant drug was positive in 16% of the cases 84% not on anticonvulsive treatment (Table 3).

Radiological investigations and EEG was not done for 60% of the cases, 26% have abnormal MRI or CT scan or ultrasound brain, 8% have normal MRI and EEG or ultrasound brain, abnormal EEG was found in 6% of the cases (Table 4).

Normal lab findings were reported in 84% of the cases, sepsis was found in 6%, hypocalcemia in 4%, meningitis in 4% and hypoglycemia in 2% (Table 4).

Outcome of death happened in 20% of the cases (10 cases) and transfer to the ward was done for 80% (Table 4).

Cross tabulation for outcome against some factors was done (table 5) and the results were as the following:

Although male gender was greater than female among the cases, the deaths were 50% male and 50% female.

All the dead cases had no history of birth asphyxia. Regarding etiology seven out of ten deaths were acute symptomatic, two were remote symptomatic and one case was unclassified.

All deceased cases were generalized tonic-clonic seven out of ten deceased cases were refractory cases, two were super refractory and one responded to treatment and died due to sepsis.

Normal lab findings were reported in 84% of the cases, sepsis was found in 6%, hypocalcemia in 4%, meningitis in 4% and hypoglycaemia in 2% (Table 4).

Outcome of death happened in 20% of the cases (10 cases) and transfer to another ward was done for 80% (Table 4).

Cross tabulation for outcome against some factors was done (Table 5) and the results were as the following:

Although male gender was greater than female among the cases, the deaths were 50% male and 50% female. All the dead cases had no history of birth asphyxia.

Seven out of ten deaths were acute symptomatic, two were remote symptomatic and one case was unclassified.

All deceased cases were generalized tonic clonic regarding response to treatment: Seven out of ten deceased cases were refractory cases, two were super refractory and one responded to treatment.

Table 1: Basic characteristics of the sample

Characteristics		**Frequency**	**%**
Age groups	Birth - 2years	37	74.0
	>2 - 5years	5	10.0
	> 5years	8	16.0
Sex	Male	29	58.0
	Female	21	42.0
Birth history	Normal	44	88.0
	Birth asphyxia	6	12.0
Developmental history	Normal	40	80.0
	Delayed	10	20.0
Anthropometry	Normal anthropometry	39	78.0
	Microcephaly	7	14.0
	FTT	3	6.0
	Hydrocephalus	1	2.0

Table 2: Clinical characteristics of the sample

Clinical characteristics		**Frequency**	**%**
Age of onset	Birth - 2years	45	90.0
	> 2year -5years	3	6.0
	> 5years	2	4.0
Aetiology	Acute symptomatic	31	62.0
	Remote symptomatic	13	26.0
	Unclassified	3	6.0
	Complex febrile convulsion	2	4.0
	Epilepsy related	1	2.0
Clinical examination	Normal neurological examination	28	56.0
	Abnormal neurological examination	21	42.0
	Comatosed	1	2.0
Type of seizure	Generalized tonic clonic	47	94.0
	Focal	3	6.0
Number of drugs needed to control convulsion	One drug	1	2.0
	Two drugs	10	20.0

	Three drugs	30	60.0
	Four drugs	9	18.0
Response to treatment	Responded to Anticonvulsant	20	40.0
	Refractory	26	52.0
	Super-refractory	4	8.0

Table 3: Family history and drug history of the study cases

Characteristic		**Frequency**	**%**
Family history	No FH or epilepsy	44	88.0
	Positive FH of febrile convulsion Or epilepsy	6	12.0
Drug history	No drug history	42	84.0
	Anticonvulsant drug	8	16.0

Table 4: Investigations done to the cases and the ultimate outcome

Investigations		**Frequency**	**%**
EEG, MRI, Ultrasound, & CT	Not done	30	60.0
	Abnormal MRI or CT scan or ultrasound brain	13	26.0
	Normal MRI and EEG or ultrasound brain	4	8.0
	Abnormal EEG	3	6.0
Lab findings	Normal lab finding	42	84.0
	Sepsis	3	6.0
	Hypocalcemia	2	4.0
	Meningitis	2	4.0
	Hypoglycaemia	1	2.0
Outcome	Transferred	40	80.0
	Died	10	20.0

Table 5: Cross tabulation for outcome against some factors was done

Factor		**Outcome**		**Total**
		Transferred	**Died**	
Gender	Male	24	5	29
	Female	16	5	21
Birth history	Normal	34	10	44
	Birth asphyxia	6	0	6
Aetiology	Acute symptomatic	24	7	31
	Remote symptomatic	11	2	13
	Unclassified	2	1	3
	Complex febrile convulsion	2	0	2
	Epilepsy related	1	0	1
Type of Seizure	Generalized tonic clonic	37	10	47
	Focal	3	0	3
Response to treatment	Responded to Anticonvulsant	19	1	20
	Refractory	19	7	26
	Super refractory	2	2	4

DISCUSSION

The status epileptics in children is a common medical emergency and it needs immediate medical attention (Sánchez & Rincon, 2016) Therefore, epidemiological studies are needed to estimate their etiologies and prevalence, thereby helping in its management. The morbidity rate of SE among infants and youngsters is much higher than that among adults but mortality rate; is more in adult compared to children.

The prevalence of status epileptics from 10 to 73 per 100,000 people, and thus the majority of the reported cases are reported among children less than 2 years.

Predominant involvement of younger age group has been reported in many previous studies In our study 74% patients were below of 2 years. The reason for this predominance of SE in younger children is not known. Probably, mechanisms for control of seizure activity are fragile in younger children and should get disrupted with minimal abnormalities in neurofunction (Kumar *et al*., 2014) we classified the etiological factors

as complex febrile seizure, acute symptomatic infections, Remote symptomatic Epilepsy, and unclassified.

Acute symptomatic (CSE in previous neurologically normal child, within a week of an identified acute neurological insult including head trauma, infection (CNS, GIT, respiratory) enephalopathy, cerebrovascular disease and metabolic or toxic derangement. were found to be the commonest cause of status epileptics in our study 62% of cases

In a Japanese study, children below the age of 15 year 49.3% were found to be affected by SE due to febrile seizure on the other hand, some European researches shown that 34-60% of SE was because of cerebrovascular accident.

Results of our study suggest that etiologies are directly affecting the outcomes of status epileptics suggested by a previous analysis (Uzair *et al*., 2019).

Children with febrile SE or epilepsy related SE had a 0 % mortality while children with acute symptomatic SE have 22%mortality mortality was related to the age of the patients, cause of status epileptics and EEG findings that were taken after admission (Sahin *et al*., 2001).

Male sex of the cases was predominant as they represented 58% complemented by 42% females This is in line with a study done in Kenya and Ethiopia (Samia *et al*., 2019) (Adal *et al*., 2021).

Although male gender was greater than female among the cases, the deaths were 50% male and 50% female so mortality rate is equal. GTCS was the most common type of epileptic seizure encountered in 94% of patients was higher than that was reported by studies done in Malaysia (40.0%), and Ethiopia (48.6%) (Arul Kumaran *et al*., 2009) (Rishe *et al*., 2015).

The possibility for this could be due to difference in qualification of expertise and diagnostic tools used which can facilitate the classification of seizure type.

More than have of the cases (52%) were classified as refractory status epileptics. It is defined as clinical or electrographic seizures which persist after an adequate dose of an initial benzodiazepine and a second appropriate anti-seizure medication in our study mortality rate was 20% most of them were refractory and super refractory.

In some patients, refractory status epileptics may last many weeks despite treatment with multiple medications, which has been referred to as malignant refractory status epileptics or super-refractory status epilepticus (Holtkamp *et al*., 2005) in this study we have 4 patient diagnosed as super refractory and 2 of them were died.

In many studies in children and adult have shown that a longer duration of SE is one of the factors associated with poor outcome.

Antiepileptic drug regimen is defined as a trial of either a single drug (mono-therapy) or combination of two or more of anticonvulsive drugs.

Intravenous midazolam, phenytoin, and phenobarbital were common antiepileptic drugs used for control of SE in our study.

Combination of phenytoin and Phenobarbital was found to be most effective in controlling SE. The most important adverse effect of combination therapy is sedation and respiratory depression. Because of this life-threatening adverse reaction of drugs used in control of SE it is always recommended to manage these patients in pediatric ICU setting.

Iv midazolam infusion used if patient not controlled by first and second line of treatment. Mortality rate in our study was (20%) in line with other studies mortality rate ranged between 10.5 to 28% (DeLorenzo *et al*., 1996).

This study's main limitation is the study's relatively small sample size study. Despite this limitation, we think it provides useful insight into SE's etiologies common gender, and mortality rate.

CONCLUSION

Status epileptics is severe life threating emergency with substantial morbidity and mortality. The combined effects of SE, disease complications and adverse effect associated with treatment generate a complex situation for the patient. Patients with younger age and male sex are slightly more vulnerable to develop SE. Longer duration of SE and acute symptomatic an etiology are independent predictors for poor outcome.

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ETHICS

The study was approved by the Benghazi Children Hospital committee for scientific research and obtained from the Research and consulting Department at the Faculty of the Medicine-University of Benghazi

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