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CLINICAL SPECTRUM AND EEG FINDINGS OF NON-CONVULSIVE STATUS EPILEPTICUS IN CHILDREN

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ABSTRACT

OBJECTIVE: To determine the clinical spectrum and EEG findings ofnon-convulsive status epilepticus in children.

METHODS: A total of 38 children were included in this prospective cross sectional study, having EEG suggestive of NCSE after taking informed consent from guardians, keeping EEG as gold standard tracings were reviewed according to criteria of non-convulsive status epilepticus. Their clinical features were also noted leading to non- convulsive status epilepticus. Diagnostic workup will be done to find out the underlying cause, according to the suspected etiology of non-convulsive status epilepticus.

RESULTS: There were 26 male and 12 female patients, with ratio of 2:1. Non convulsive status epilepticus was most common between 2-5 years of age being 39.5%. Majority of the children presented with overlap of clinical features i. e, 25 children. The main etiology in non-convulsive status epilepticus was found to be epilepsy which was about 63.2 % (n=24). Most common EEG pattern was found to be Generalized NCSE (continuous or frequent spike, polyspikesharp wavedischarges) pattern1 in 24 children. Majority of the children who presented with non convulsive status epilepticus had normal neuroimaging (n=16), Duration of non-convulsive status epilepticus was also noted , which was more than 72 hours in 63.2% of children.

CONCLUSION: Non convulsive status epilepticus is difficult to diagnose even in specialized training centers, as there are no obvious convulsions. Only way to confirm the diagnosis of non convulsive status epilepticus is keeping high index of suspicion and go for urgent EEG monitoring. There is brain damage at neuronal level which can be minimized by early identification and early intervention. Therefore, we conducted this study to guide us to determine the signs and symptoms and EEG findings of non-convulsive status epilepticus.

KEY WORDS: Non convulsive status epilepticus, overlap of signs and symptoms

INTRODUCTION

Status epilepticus is a clinical condition which results due to failure of the inhibitory mechanisms of the brain leading to continuous seizure activity or evolution of such mechanisms responsible for prolonging seizures.[1] Non-convulsive status epilepticus(NCSE) is an impairment of state of mind with subtle clinical features without convulsive activity of 30 minutes duration associated with EEG findings of continuous or frequent epileptiform discharges in the form of spike, polyspike, sharp and slow wave discharges or high voltage slow wave delta activity with sharp waves.[2]

According to new status epilepticus classification issued by International League against Epilepsy, NCSE is categorized into NCSE with coma and NCSE without coma.NCSE without coma is further classified into generalized and focal (on EEG basis).[1] NCSE can also be classified on the basis of etiology in addition to state of consciousness.[3] Although there are no obvious actual events but NCSE is thought to cause neuronal damage.[4] Few studies have been conducted on status epilepticus as well as on NCSE, especially in children. It's difficult to know the exact incidence and prevalence about non convulsive status epilepticus. Incidence of Status epilepticus is approximately 10-20/100,000. out of which Non convulsive accounts for 25-50% of the cases.[5-9]

Non convulsive status epilepticus can be due to several causes. Most common underlying etiologies in children are central nervous system infection, epilepsy, trauma, tumor, postasphyxial brain damage, cerebrovascular accidents and degenerative brain diseases.[2]Clinically a

child with non-convulsive status epilepticus can present with impairment or fluctuation of consciousness, confusion, agitation, psychomotor retardation, head and eyes deviation, automatisms, starring gaze, repetitive blinking, focal movements, myoclonic jerks, language disturbances, altered sensations and coma/apnea. [10]Non convulsive status epilepticus can be treatedwith Midazolam infusion, intravenous antiepileptic drugs and sometimes may need methylprednisolone pulses followed by oral medication which are equallyeffective.[11] Outcome depends on underlying etiology along with early intervention done at initiation of NCSE.

NCSE is difficult to diagnose even by intensivists, neurologists and epileptologists. It is often missed as clinical features are subtle that usually lead to poor neurological outcome in the form of epilepsy, psychomotor retardation or even death. Apart from diagnosis, its treatment and management are difficult and tricky. Few studies were done in adults and pediatric population in this regard.The absolute diagnosis is made on EEG which requires expertise to interpret it according to NCSE EEG criteria. In developing countries, it is a challenging exercise to diagnose NCSE on EEG basis as it is not available in peripheral and rural areas. The clinical spectrum characteristics with underlying diagnosis in this study will help to provide recommendations to our physicians to detect early, go for urgent EEG and intervene, keeping in mind possibility of non-convulsive status epilepticus.

METHODS

Study design: Prospective,Cross-sectional study.

Place and duration of study: Department of Pediatric Neurology, Children Hospital & the Institute of Child Health, Lahore. The study was done for a period of 6 months after the approval of synopsis, from September 2020 to February 2021.

Sample size: Based on incidence of NCSE, in previous studies we took sample of 38 patients.

Sampling technique: Non probability,consecutive sampling.

Sample Selection:

Inclusion Criteria: All patients presented in the Pediatric neurology department, from 1 month to 18 years of age of both genders having EEG suggestive of NCSE with and without coma were included in the study over a period of 6 months.

Exclusion Criteria:

EEG not suggestive of NCSE.
Convulsive StatusEpilepticus.

Etiology: We evaluated following underlying causes

1.Epilepsy. 2. Epileptic encephalopathy.
3.DBD. 4.CNS infection.
5.Post asphyxia brain damage. 6. Stroke
7.Post traumatic brain injury 8. Metabolic causes

Data collection:
After taking written informed consent from parents and guardians, 38 children presenting in the pediatric neurology department, having confirmed non-convulsive status epilepticus on EEG were enrolled in the study keeping EEG as gold standard tracings was reviewed by pediatric neurologist according to the criteria of non-convulsive status epilepticus having typical, frequency, distribution, and type of epileptiform discharges and focus of onset of discharges.

Their demographic data was collected, detailed history was taken with clinical neurological examination to find out the underling etiology of non-convulsive status.Video recording of the patients were taken to identify any abnormal clinical features.

A pre-designed questionnaire was filled by Pediatric Neurology Consultants.

Neuroimaging was done (MRI brain having, T1, T2, Fluid attenuated inversion recovery,Diffusion weighted images and contrast studies). Diagnostic workup was done to find out the underlying cause, according to the suspected etiology of non-convulsive status epilepticus including fundoscopy, CBC, CRP, CSF, ECG, ECHO, ANA, C3, C4, etc.

DATA ANALYSIS.
The results were analyzed by using SPSS version 20. The quantitative variables like age were presented as mean and standard deviation while the qualitative variables like gender were presented by calculating frequencies and percentages. p- Value between the variables of <0.05 were considered significant.

RESULTS
Out of 38 cases of non-convulsive status epilepticus,there were 26 male children and 12 female children with ratio of 2:1. While there was predominance in age group of 2-5 years having 15 children followed by 12,7 and 4 in age groups of 5-10 years,1 month -2 years and 10-18 years respectively.

In our study majority of children were having overlap of clinical features i.e., 25 children. 4 children presented with altered state of consciousness,3 with abnormal behavior and 3 with automatisms. Staring gaze was found in 2 children.1 child presented with complex partial seizures.

Complex partial seizures occurred as manifestation of non-convulsivestatus epilepticus in children from 2-5 years of age.Automatisms were common in ages 5-18 years. Children of ages. 2-18 years old, presented with abnormal behavior. Altered state of consciousness was found in 1-2 years and 5-10 years of children. Staring gaze was present in 2-5 years and 10-15 years old patients.Overlap of sign and symptoms was present in majority of patients i.e., in 12 children between 2-5 years old followed by 7 children in 5-10 years old and 5 children in 1 month -2 years old. (Table 1)

The main etiology in non-convulsive status epilepticus was epilepsy which was about 63.2 %(n=24) .2nd most common cause of non-convulsive status epilepticus was found to be due to CNS infections in 18.4 %(n=7) children.Degenerative brain diseases causing non convulsive status epilepticus was in 13.2 % (n=5) children. While2.6 % (n=1 for each) children were having non convulsive status epilepticus due to epileptic encephalopathy and post asphyxia brain damage respectively.Most of the patients of non-convulsive status epilepticus presented with overlapof sign and symptoms irrespective of their underlying etiology. (p value=0.86). (Table 2)

In children with non convulsive status epilepticus,50% had underlying developmental delay.

EEG is the investigation of choice to diagnose a child with non convulsive status epilepticus having variable sign and symptoms. In this study, we carried out multiple EEGs in ICU setting of each patient, and we took the initial 1st EEG to study the non convulsive status epilepticus.

Majority of the children 63.2 % (n=24) had Generalized NCSE (continuous or frequent spike, polyspikesharp wavedischarges) pattern 1 in their EEG. While18.4 % showed GeneralizedNCSE (slow wave delta activity) pattern 2 and Focal NCSE (continuous or frequent spike, polyspikesharp wavedischarges) pattern 3 each in their EEG test.Most common EEG pattern was found to be pattern 1 in 24 children which is mostly seen in patients having overlap of sign and symptoms(n=16) with p value of 0.26.(Table 3& 4)

In epileptic patients, mostly(n=15) they had Generalized NCSE (continuous or frequent spike, polyspikesharp wave discharges)pattern 1 followed by Focal NCSE (continuous or frequent spike, polyspikesharp wavedischarges) pattern 3 (n=6) and then Generalized NCSE (slow wave delta activity)pattern 2 (n=3). Patients with epileptic encephalopathy(n=1) came with pattern 2.Pattern 1 was also common in DBD patients(n=4).CNS infections(n=5) lead to pattern 1. Children with post asphyxiabrain damage showed pattern 2. (Table 4)

Neuroimaging is one of the important investigations to be carried out in any patient with neurological disorder.Majority of the children who presented with non convulsive status epilepticus had normal neuroimaging(n=16),followed by cerebral atrophy (n=9) and gyri form swelling and hyperintensities(n=8).3 children presented with underlying structural abnormalities while ischemic demyelination led to non-convulsive status epilepticus in 2 children.
Clinical spectrum and neuroimaging findings are not statistically significant in relation to each other(p=0.607) (Table 5)

In epileptic patients neuroimaging findings were found to be normal in 13 children .In addition to that 3 showed structural abnormalities ,gyri form swelling and hyperintensities while 5 had cerebral atrophy .CNS infections showed gyri form swelling and hyperintensities in majority of the cases(n=5) whereas DBD patients had mostly underlying cerebral atrophy (n=3).Epileptic encephalopathy and post asphyxia brain damage presented with underlying ischemic demyelination and cerebral atrophy respectively. There is a strong correlation between etiology and neuroimaging findings in patients of non-convulsive status epilepticus with p value 0.001.(Figure 1) (Table 6).

Duration of non-convulsive status epilepticus was also noted in our patients, which was more than 72 hours in 63.2% followed by, 21.1 % who remained in non-convulsive status epilepticus for more than 24 hours. Less number of patients n=6 had non convulsive status epilepticus for more than 48 hours. (Figure 2).

DISCUSSION

Non convulsive status epilepticus is defined as a clinical condition in which a patient has motor movements and subtle signs but no tonic clinic convulsions, fulfilling the EEG criteria of continuous or frequent epileptiform discharges in the form of spike, Polyspike, sharp and slow wave discharges or high voltage slow wave delta activity with sharp waves. [2,12]
Non convulsive status epilepticus is not easy to

diagnose because there are not obvious convulsions as compared to convulsive status epilepticus. Both convulsive and Non convulsive status epilepticus cause neuronal injury, it's just their manifestations which are different.[13-16]

Only way to confirm the diagnosis of non-convulsive status epilepticus is EEG. Therefore, we conducted this study to help us to determine the signs and symptoms of non-convulsive status epilepticus, so that we can keep high index of suspicion and go for urgent EEG keeping in mind non convulsive status epilepticus.

Non convulsive status epilepticus is classified by ILAE into 2 main categories.Non convulsive status epilepticus with coma andnon convulsive status epilepticus without coma. Non convulsive status epilepticus without coma is then further classified into generalized and focal types. [1]

Our study showed that there was male predominance with ratio of 2:1 which is different in another study with female predominance in adolescent age group studied by A M Husain et al. 4 While another pediatric study showed male preponderance with 63.2%.

Non convulsive status epilepticus was most common in children between 2-5 years of age being 39.5% followed by 5-10 years being 31.6%. In another study, carried out in pediatric population showed mean age of 5.5 years. [2]

In our study mean duration of symptoms was found to be 12.6 hours as compared to another study in which it was 19.8 hours. [4] Most of the children had longer duration of Non convulsive status epilepticus i.e.,> 72 hours(63%) in our study.

Study done by Stacy.K.H. Tay et al showed median duration of Non convulsive status epilepticus to be 48 hours. [2]

Mostly patients with non convulsive status epilepticus present with variety of signs and symptoms. They can range from staring gaze to altered sensorium. [17] In this study many children presented with overlap of different symptoms which makes the diagnosis more difficult (65%). Next most common symptom was altered state of consciousness (10.5%) which is also common in another study to be 83%. [4] Automatisms were also common in our study (7.9%) as compared to other studies in which this percentage is less. [18]

Our patients who had Non convulsive status epilepticus had underlying epilepsy as the most common cause (63.2%) which is same in another pediatric study to be 52.6%.[2]

CNS infections were 18.4% in our study leading to Non convulsive status epilepticus as the second most common etiology.

In adolescent patients, remote risk factors are found to be common etiology leading to non convulsive status epilepticus (75%) such as previous strokes, brain tumors, etc. as compared to pediatric population in which epilepsy, CNS infections and DBDs are more common etiologies.[4]

If we know the different clinical patterns of Non convulsive status epilepticus and underlying etiologies leading to Non convulsive status epilepticus then we can do urgent EEG and it would be more accurate and cost effective as well. In majority of our patients, we suspected Non convulsive status epilepticus on clinical grounds and then they underwent the EEG.

EEG morphology has different patterns of wave forms in patients with non convulsive status epilepticus. Some present with typical generalized or focal, continuous, or frequent spike, poly spike and sharp wave discharges while others show slow wave delta activity.
In our study 63% of patients had generalized spike, sharp and slow wave discharges as compared to another pediatric studies in which focal distribution is more common. (78.9%) [(2)].

Majority of our patients had normal neuroimaging (42.1%) followed by cerebral atrophy(23.7%) and features consistent with CNS infections(21.1%).In another study by Stacy et al, most common underlying neuroimaging in patients with Non convulsive status epilepticus was brain atrophy(47%) followed by CNS infections (26%) and less patients had normal brain imaging (15%).

This study was carried out with careful history and examination by pediatric neurologists. In addition to EEG other ancillary tests were also done to find out the cause.

Our findings and strong clinical suspicion guided us to let these patients undergo urgent EEG for Non convulsive status epilepticus.

There are some limitations of this study as well, like small number of patients which needs another multicentered, prospective study to see how quick and vigilant our neurologists are in picking up this common yet complex diagnosis.

TABLE 1
Age in groups * Clinical spectrum Cross tabulation

Age in groups	Clinical spectrum						Total
	Complex partial seizure	Automatisms	Abnormal behaviour	Altered state of consciousness	Staring gaze	Overlap	
1 month- <2 years	0	0	0	2	0	5	7
>2 years-5 years	1	0	1	0	1	12	15
>5 years10 years	0	2	1	2	0	7	12
>10 years - 18 years	0	1	1	0	1	1	4
Total	1	3	3	4	2	25	38

TABLE 2Clinical spectrum * Etiology Cross tabulation

Clinical spectrum	Etiology					Total
	Epilepsy	Epileptic encephalopathy	DBD	CNS infection	Post asphyxia brain damage	
Complex partial seizure	0	0	1	0	0	1
Automatisms	3	0	1	0	0	3
Abnormal behavior	2	0	0	0	0	3
Altered state of consciousness	2	0	1	1	0	4
Staring gaze	2	0	0	0	0	2
Overlap	15	1	2	6	1	25
Total	24	1	5	7	1	38

TABLE 3 EEG SPECTRUM OF NCSE

	Frequency	Percent
Pattern 1 Generalized NCSE (continuous or frequent spike, polyspikesharp wave discharges)	24	63.2
Pattern 2 Generalized NCSE (slow wave delta activity)	7	18.4
Pattern 3 Focal NCSE (continuous or frequent spike, polyspikesharp wave discharges)	7	18.4
Total	38	100.0

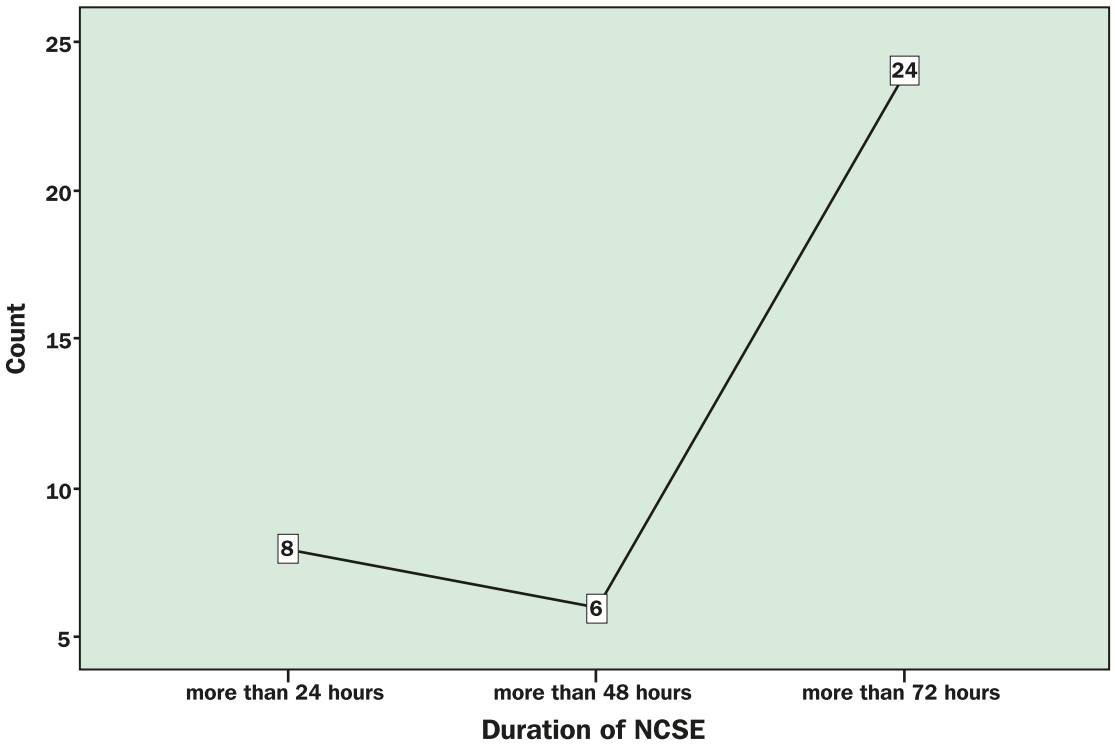


FIGURE 2 Duration of NCSE

TABLE 4CLINICAL SPECTRUM * EEG CROSS TABULATION

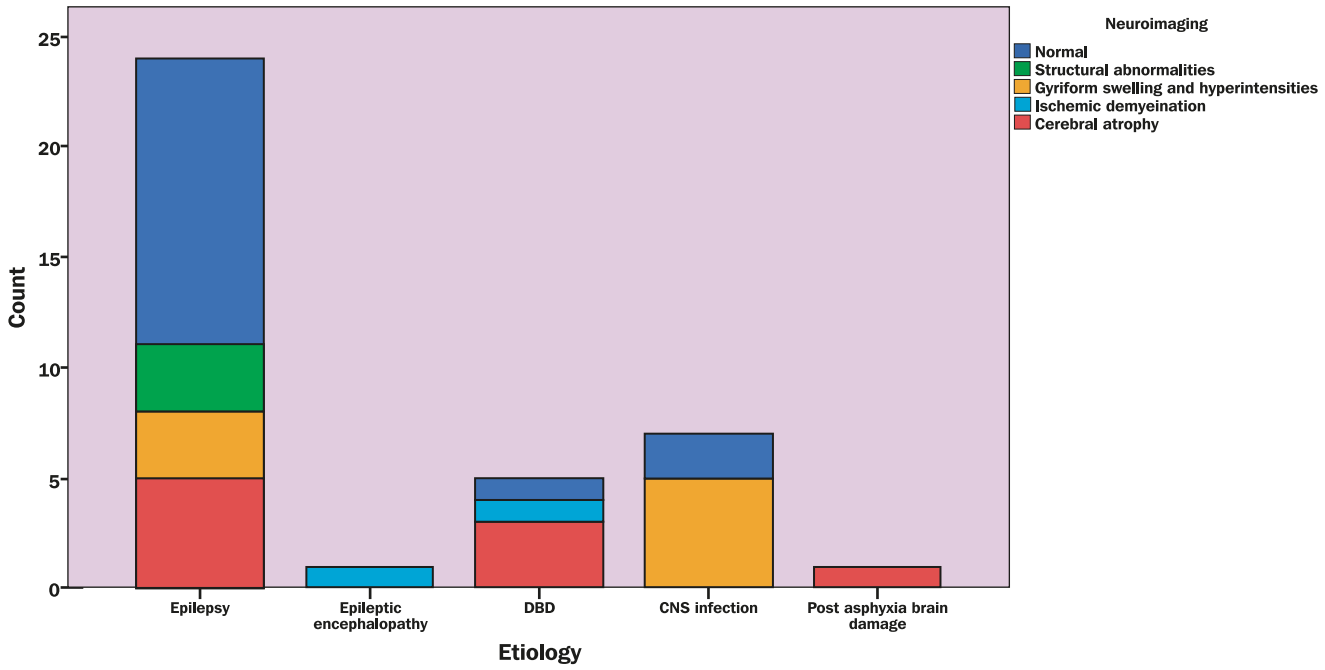
Clinical spectrum		EEG before treatment			Total
		Generalized NCSE (continuous or frequent spike, polyspikesharp wave discharges)	Generalized NCSE (slow wave delta activity)	Focal NCSE (continuous or frequent spike, polyspikesharp wave discharges)	
	Complex partial seizure	1	0	0	1
	Automatisms	2	0	1	3
	Abnormal behavior	2	0	1	3
	Altered state of consciousness	1	3	0	4
	Staring gaze	2	0	0	2
	Overlap	16	4	5	25
Total		24	7	7	38

Table 5 Clinical spectrum * Neuroimaging Cross tabulation

Clinical spectrum	Neuroimaging					Total
	Normal	Structural abnormalities	Gyri form swelling and hyperintensities	Ischemic demyelination	Cerebral atrophy	
Complex partial seizure	0	0	0	0	1	1
Automatisms	1	0	1	0	1	3
Abnormal behavior	3	0	0	0	0	3
Altered state of consciousness	3	1	0	0	0	4
Staring gaze	2	0	0	0	0	2
Overlap	7	2	7	2	7	25
Total	16	3	8	2	9	38

TABLE 6Etiology * Neuroimaging Crosstabulation

Etiology		Neuroimaging					Total
		Normal	Structural abnormalities	Gyri form swelling and hyperintensities	Ischemic demyelination	Cerebral atrophy	
	Epilepsy	13	3	3	0	5	24
	Epileptic encephalopathy	0	0	0	1	0	1
	DBD	1	0	0	1	3	5
	CNS infection	2	0	5	5	0	7
	Post asphyxia brain damage	0	0	0	0	1	1
Total		16	3	8	2	9	38



Etiology and Neuroimaging Bar chart

Figure 2

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Author's contribution:
Shaila Ali; data collection, data analysis, manuscript writing, manuscript review
Natasha Ghani; data collection, data analysis, manuscript writing, manuscript review
Ather Khalily; concept, data analysis, manuscript review
Zia-ur-rehman; data analysis, manuscript writing, manuscript review
Tipu sultan; concept, data analysis, manuscript review