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Original Research Article

A study of prevalence of abnormal EEG and its association between various clinical presentations of atypical febrile seizures

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ABSTRACT

Background: Quantitative EEG is a rapidly emerging tool in the diagnosis and follow up of various neurological disorders and can act as predictive marker for subsequent epilepsy in children with complex febrile seizure. The present study aimed to estimate the prevalence of abnormal electroencephalogram (EEG) and to find the association between Quantitative EEG (qEEG) and various clinical features of atypical febrile seizures(AFS).
Methods: EEG was recorded along with clinical features including the age at onset, duration of episode, number of episodes in a day, type of seizure and the recurrences from the children aged between 6-60 months with atypical febrile seizures. EEG recordings were classified into Normal and abnormal EEG with epileptiform changes by the expert interpretation and the distribution of above said clinical features in the both groups were analyzed. It is also attempted to find the association between qEEG and few of the clinical features.
Results: Prevalence of abnormal EEG in atypical febrile seizures was 33.9%. There were no significant differences in the distribution of abnormal EEG and their association with various clinical features of AFS. Significantly increased absolute power of θ and α waves were recorded from the frontal montages in the children with epileptiform changes in the EEG.
Conclusions: qEEG changes can be also considered as marker of severity of febrile seizure episodes. Many prospective studies with long-term follow up are required to establish the predictability of future epilepsy by qEEG.

Keywords: Atypical febrile seizures, Febrile seizures, Prevalence, Quantitative EEG

INTRODUCTION

Febrile seizure (FS) is one of the most common neurological disorders in children. The incidence of FS in India varies between 5-10% and it is 8.8% in Japan, and 14% in Guam.[1-4]

Variation in prevalence relates to differences in case definitions, ascertainment methods, geographical variation, and cultural factors. FS is classified into simple and complex febrile seizures based on various clinical features such as duration, type, number of episodes, post ictal neurological status and so on.[5] As it is primarily based on history obtained from caregivers, it could be eventually subjective. 2 to 10% of children who have febrile seizures will subsequently develop epilepsy, especially atypical febrile seizure is an independent risk factor for future epilepsy.[6-9]

Quantitative electroencephalogram (qEEG) is the mathematical processing and transformation of digitally recorded EEG into a format using various algorithms,

that quantitatively gives the power and peak frequency of different waveforms. qEEG is considered as an evolving adjuvant tool in the diagnosis and follow up of various neurological disorders. Changes in the pattern and parameters in quantitative EEG are well established and consistent in various neurological disorders.[10,11]

Changes in theta and alpha waves of qEEG has been reported in atypical febrile seizures.[12] It has also been reported that EEG abnormality in frontal region act as predictive marker for subsequent epilepsy in children with complex febrile seizure.[13]

Hence this study aims to find the distribution of various clinical features of atypical febrile seizures and their association with qEEG by spectral analysis.

METHODS

The present study was conducted as a prospective observational study, among children with atypical febrile seizures who were admitted in the Department of Pediatrics, Rajiv Gandhi Government Women and Children Hospital, Puducherry, between September 2017 to May 2018. The sample size was calculated using open Epi software V3.055, based on the previous studies with abnormal EEG in atypical febrile seizures with 80% power and 95% confidence interval.[14,15]

The sample size was 180 including 10% drop out anticipated. Children aged 6-60 months with atypical febrile seizures were included and children with simple febrile seizure, diagnosed with CNS infections, who were on chronic medication including antiepileptic drugs and having developmental delay or any CNS structural anomalies, syndrome, Inborn errors of metabolism were excluded. Children were given syrup Triclofos (phosphorylated derivative of chloral hydrate) 30 mg/kg for sedation which has been studied to be the most effective and safe sedation for recording EEG in children.[16]

EEG was recorded using 'RMS maximus-32' for a duration of 20 minutes as per American clinical Neurophysiology guidelines for EEG recording in pediatrics.[17]

Silver-Silver Chloride (Ag-AgCl) disc type electrodes of 5-7 mm diameter with long flexible lead were placed on the scalp according to the 10-20 international system with the help of "Elefix" paste.

EEG thus recorded was analyzed for abnormal epileptiform activity such as sharps, slowing and spike wave by our neurologist and a written report of the same was obtained. Guidelines for acquiring quantitative EEG as mentioned in American Association of Neurology guidelines were followed and quantitative EEG obtained.[18] EEG v54.2 software provided with RMS maximus -32 was used to estimate power spectral analysis of qEEG from the selected epoch of 2 second duration with artifact free region. Results are given in absolute power (Abs) in (μV^2) and relative power (Rel) in percentage.

RESULTS

In the present study, EEG was found to be abnormal in 33.9% with epileptiform discharges. Age and gender were comparable between the groups with normal EEG and abnormal EEG based on t-test, Chi-Square tests respectively (Table 1).

Table 1: The demographic and electroencephalogram data of atypical febrile seizure patients studied (n=180).

	Normal EEG	Abnormal EEG	P value
Age (years)	2.77±1.6	2.55±1.3	0.361
Gender			
Male	69	39	0.44
Female	50	22	
Total	119	61	

Age in years (mean±SD); Gender distribution are given as numbers.

Prevalence of EEG abnormality in children with age at onset of seizure less than 3 years and more than 3 years were 78.7% and 21.3% respectively. There was no significant difference in the prevalence in children with normal EEG (75.6% in less than 3 years; 24.4% in more than 3 years) (Table 2). Prevalence of normal EEG, among the children with three different duration of seizure episodes (0-15 minutes, 15-30 minutes and >30 minutes) were 72.3%, 9.2% and 18.5% respectively. These prevalence were similar to the groups with abnormal EEG (68.9%, 8.1% and 23% respectively; p=0.772). (Table 2).

Out of 180 children, 35.5% children had 1 episode, 53.3% had 2 episodes, 7.77% children had 3 episodes and 3.33% had 4 or more episodes in 24 hours duration. There was no significant difference in the prevalence of EEG abnormalities in various groups classified according to the number of episodes in 24 hours (chi square 3.223, p=0.358) (Table 2).

In our study only 10% had focal seizures while the rest 90% had GTCS. Prevalence of abnormal EEG was found to be only 14.8% in children with focal seizures and was not statistically different from the children with normal EEG (chi square 2.317; p=0.128) (Table 2).

An abnormal neurological assessment (post ictal encephalopathy) was reported in only 1 child following an episode of seizure, while the other 179 children had no such abnormalities. (Table 2). EEG was found to be abnormal in 41% in 1st episode group, 21.3% in 2nd

episode group and 37.7% in 3rd episode group. There was no statistical significance (chi square 1.573, p=0.455) between the prevalence of EEG abnormality and recurrence of seizures. (Table 2).

Table 2: Distribution of various clinical features and its association with EEG findings in AFS patients studied.

Clinical feature		Normal EEG	Abnormal EEG	X^2	P value
Age at onset	<3 years	90	48	0.211	0.646
	>3 years	29	13		
Duration of seizure episode	0-15 min	86	42	0.518	0.772
	15-30 min	11	5		
	>30 min	22	14		
Episodes in 24 hours	One	38	26	3.223	0.358
	Two	69	27		
	Three	8	6		
	Four and above	4	2		
Type of seizures	Generalised	110	52	2.317	0.128
	Focal	9	9		
Post-ictal neurological state	Normal	118	61	0.515	0.473
	Abnormal	1	0		
Recurrence of seizures	1st episode	57	25	1.573	0.455
	2nd episode	28	13		
	3rd episode	34	23		

Table 3: Comparison of qEEG (absolute power of theta, alpha waves) in frontal montages with the manual interpretation of EEG in atypical febrile seizure patients (n=180).

qEEG	Normal EEG (n=119)	Abnormal EEG (n=61)	Mann-Whitney U Test ZScore	P-value
FP1-θ (Abs)	14.69 (7.44-56.34)	33.13* (12.1-310.635)	-3.268	0.001
FP1-α (Abs)	4.34 (2.17-63.01)	21.82* (4.52-144.035)	-3.235	0.001
FP2-θ (Abs)	12.98 (5.36-67.77)	30.24* (10.45-272.855)	-2.990	0.003
FP2-α (Abs)	4.99 (2.06-58.55)	17.69* (4.44-131.14)	-3.299	0.001
F7-θ (Abs)	4.74 (1.54-128.11)	33.47* (3.24-314.065)	-2.572	0.010
F7-α (Abs)	1.56 (0.39-95.95)	5.42* (1.025-232.76)	-2.724	0.006
F3-θ (Abs)	4.79 (1.54-140.6)	23.05* (3.15-393.115)	-2.614	0.009
F3-α (Abs)	1.84 (0.43-124.22)	5.84* (1.05-171.945)	-2.454	0.014
FZ-θ (Abs)	3.92 (1.53-107.93)	32.67* (3.335-315.04)	-2.925	0.003
FZ-α (Abs)	1.98 (0.41-101.44)	5.98* (1.245-221.785)	-2.764	0.006
F4-θ (Abs)	3.83 (1.51-116.59)	42.86* (3.075-541.825)	-3.235	0.001
F4-α (Abs)	1.79 (0.4-93.95)	5.82* (1.45-252.68)	-3.007	0.003
F8-θ (Abs)	4.52 (1.57-141.85)	32.99* (3.01-577.105)	-2.850	0.004
F8-α (Abs)	2.81 (0.4-127.19)	5.84* (1.03-220.15)	-2.728	0.006

Table 4: Comparison of qEEG from frontal montages among three different duration of seizure episodes in atypical febrile seizure patients with abnormal EEG findings (n=61).

qEEG	0-15Min (n=42)	15-30Mins (n=5)	>30Mins (n=14)	P-value
F7-θ (Rel)	16.95(9.35-27.675)	3.9(1.9-6.25)	12.9(8.425-24.9)	0.007
F3-θ (Rel)	16.8(9.1-24.95)	3.8(0.35-8.05)	17.65(10.475-24.25)	0.015
FZ-θ (Rel)	18.25(12.575-27)	3.7(1.95-9.1)	13.25(7.05-25.3)	0.011
F4-θ (Rel)	17.9(9.675-28.675)	7.3(3.9-9.65)	18.2(11.7-25.5)	0.021
F8-θ (Rel)	15.85(9.35-27.55)	4.1(2-10.8)	15.75(11.575-26.55)	0.023

In our study, all the montages from frontal region had significant increase in absolute power in those groups with epileptiform discharges in EEG. Both θ and α waves had increase in absolute power in abnormal EEG group compared to the normal EEG group by manual interpretation. The analysis of data was done by Mann-Whitney U Test. *p<0.05 was considered significant. In all frontal montages, the difference between absolute

power of α and θ waves between normal and abnormal EEG interpretation groups were statistically significant with p value ranging from 0.001-0.01 (Table 3).

Table 5: Comparison of qEEG from frontal montages among the number of episodes per day in atypical febrile seizure patients with abnormal EEG findings (n=61).

	Number of episodes/day	Number of episodes/day	Number of episodes/day	Number of episodes/day	P-value
qEEG	One (n=26)	Two (n=27)	Three (n=6)	Four and above (n=2)	
FP1- α(Abs)	21.625(5.08-77.88)	21.34 (4.29-147.78)	206.83 (92.07-715.4375)	1.76	0.05
FP2-θ (Abs)	19.49 (6.90-78.65)	32.44 (12.11-352.68)	1123.73 (166.98-4477.29)	14.38	0.03
FP2-α (Abs)	15.63 (4.08-71.66)	36.04 (4.42-151.67)	214.445 (100.2025-705.2)	3.35	0.05
F3-θ (Abs)	9.86 (2.18-91.76)	31.44 (3.44-649.56)	1398.85 (133.33-5836.06)	5.99	0.05
FZ-θ (Abs)	14.685 (2.28-75.11)	32.67 (3.79-455.6)	2915.895 (275.32-6650.38)	6.32	0.04

In comparison of qEEG, among three different duration of seizure episode, significant difference among 3 groups were noted in F7,F3,FZ,F4,F8 montages especially in relative power of θ waves with statistical significance of $p<0.05$, by Kruskal Wallis test (Table 4). Even though statistical significances were noted in few montages, a negative correlation coefficient is found in all frontal montages.

In comparison of association between number of episodes per day and qEEG in AFS, though 4th group with ≥4 episodes/ day was comparatively very less, other 3 groups clearly depict increase in qEEG absolute power with increase in number of episodes. This was also reflected with positive correlation coefficient in Spearman's correlation test with p values of 0.031, 0.037, and 0.042 in absolute power of θ waves in FP2, F3 and FZ respectively (Table 5 and 6).

Table 6: Correlation between qEEG from frontal montages and the number of episodes in 24 hours in atypical febrile seizure patients with abnormal EEG findings (n=61).

qEEG	Number of episodes in 24 hours	
	Correlation Coefficient	P value
FP1-θ (Abs)	0.195	0.132
FP1-α (Abs)	0.062	0.638
FP2-θ (Abs)	0.277*	0.031
FP2-α (Abs)	0.167	0.197
F7-θ (Abs)	0.252	0.05
F7-α (Abs)	0.175	0.178
F3-θ (Abs)	0.268*	0.037
F3-α (Abs)	0.172	0.184
FZ-θ (Abs)	0.261*	0.042
FZ-α (Abs)	0.188	0.148
F4-θ (Abs)	0.185	0.154
F4-α (Abs)	0.195	0.132
F8-θ (Abs)	0.167	0.197
F8-α (Abs)	0.141	0.279

In evaluating the association between number of recurrence of seizures and qEEG in AFS, there was no significant difference among the 3 groups, and the p value by Kruskal Wallis test was >0.05.

DISCUSSION

Prevalence of abnormal EEG

In the present study, EEG was found to be abnormal in 33.9%. In previous studies in children of AFS, prevalence of EEG abnormalities varied from 2% to 86%.[17,18] In our study, age and gender differences were not significant between the groups with normal EEG and abnormal EEG, unlike a report from Joshi C, where children with abnormal EEG were older than those with normal EEG.[19]

Age at onset

Prevalence of EEG abnormality in children with age at onset of seizure less than 3 years and more than 3 years was not statistically significant in our study. Other studies have reported that there was a linear trend for the detection of higher rates of epileptiform patterns with increasing age.[20-24] Epileptiform discharges were rare in children less than 3 years of age and more common in children aged more than 3 year at the onset of seizures.[19,25]

Duration of seizure

Our study did not find any significant difference in the prevalence of EEG abnormalities, among the children with three different duration of seizure episodes, unlike other observations reporting EEG abnormality and increased risk of subsequent epilepsy in patients with prolonged duration of seizure.[18,26]

Number of episodes

In a study of Clinical and EEG risk factors for subsequent epilepsy in patients with complex febrile seizures by Kim et al, epiletpiform discharges and subsequent epilepsy

was more frequent in children with multiple seizures in 24 hours.[27] In our study, there was no such significant difference in the prevalence of EEG abnormality with various number of seizure episodes in 24 hours.

Type of seizures

In a study of febrile seizures by Annegers et al, there was increased incidence of EEG abnormality and subsequent epilepsy in all cases of focal seizures.[7] Conversely in the present study, there was no significant difference in prevalence of abnormal EEG in children with focal seizures compared to children with generalized seizures.

Postictal neurological state

An abnormal bedside neurological exam in children with AFS was a predictive variable of the likelihood of an abnormal EEG, as they are approximately four times more likely to have abnormal EEG results.[21] In the present study, since abnormal neurological assessment was reported in only 1 child, correlation between abnormal EEG pattern with post ictal neurological state could not be elicited.

Recurrence

There was no statistical significance between the prevalence of EEG abnormality and recurrence of seizures. Previous study by Wo SB, also showed no significant correlation between the recurrence rate of febrile seizures in patients with normal EEG findings and that of patients with epileptiform discharges.[28]

qEEG in Atypical febrile seizures

qEEG is a transformation of digitally recorded EEG from various montages into a spectral analysis of various waveforms(α, β, θ, δ) with absolute power and peak frequency of the waveform range. Even though qEEG can be calculated from various montages, Kuang YQ found that frontal paroxysmal EEG abnormalities were an important predictor of future epilepsy in children with AFS.[13]

We have also observed a similar finding, with all the montages from frontal region having significant increase in absolute power in those groups with epileptiform discharges in EEG. In a study on quantitative analysis of EEG in northern Japan by Koyama A, changes were noted in θ waves.[12]

But in our study both θ and α waves had increase in absolute power in abnormal EEG group compared to the normal EEG group by manual interpretation. In all frontal montages, the difference between absolute power of α and θ waves between normal and abnormal EEG interpretation groups were statistically significant with p value ranging from 0.001-0.01.

Association between duration of seizure episode and qEEG in AFS

Significant difference among 3 groups were noted in F7,F3,FZ,F4,F8 montages especially in relative power of θ waves with statistical significance of $p < 0.05$, by Kruskal Wallis test. Even though statistical significances were noted in few montages, a negative correlation coefficient was found in all frontal montages.

As the sample size in one group was only 5, it will not be appropriate to conclude the association. But the negative correlation between the duration of episode and qEEG can be explained as follows. EEG is a recording of synaptic potential property and synaptic potential is based on quantal release of neurotransmitter at the synaptic level. Quantal cycle varies with different population, so people with small and prolonged quantal cycle release may have prolonged discharge at synaptic level, which is reflected in prolonged duration and decreased amplitude in synaptic potential.[29]

Association between number of episodes per day and qEEG in AFS

We observed an increase in qEEG absolute power with increase in number of episodes of seizures in 24 hours. This was also reflected with positive correlation coefficient in Spearman's correlation test with p values of 0.031, 0.037, and 0.042 in absolute power of θ waves in FP2, F3 and FZ respectively. In previous study on manual EEG interpretation, as the number of episodes per day increase, there was more chance of detecting epileptiform activity in EEG.[27] Hence, qEEG changes can be also considered as marker of severity.

Association between number of recurrence of seizures and qEEG in AFS

There was no significant difference in qEEG, among the 3 groups of various recurrence episodes. This may be possibly due to the small sample size in the subgroups and the data were obtained from recall of incidence from the remote memory of the caregivers.

CONCLUSION

Prevalence of abnormal EEG in atypical febrile seizures was 33.9%. There were no significant differences in the distribution of abnormal EEG and their association with various clinical features of AFS namely, age at onset, duration of episode, number of episodes per day, type of seizure, post-ictal neurological status and number of recurrences.

There was significantly increased absolute power of θ and α waves recorded from the frontal montages in the children with epilptiform changes in the EEG group compared to the group with normal EEG. The differences in qEEG were not statistically significant with the

duration of seizures. A positive correlation was observed between absolute power in qEEG and the number of seizure episode per day in children with epileptiform changes.

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