



## "NEUROIMAGING & ELECTROPHYSIOLOGICAL STUDY IN FEBRILE CONVULSION"

**Dr.Aparna Mitra**

Department of Pediatrics, Ramakrishna Mission Seva Pratisthan and Vivekananda Institute of Medical Sciences ,University of Health sciences, Kolkata, West Bengal.

**Dr. Tapabrata Chattopadhyay\***

Department of Pediatrics, Ramakrishna Mission Seva Pratisthan and Vivekananda Institute of Medical Sciences ,University of Health sciences, Kolkata, West Bengal. \*Corresponding Author

### ABSTRACT

**BACKGROUND:** Febrile convulsions are very common within six months to five years of age. Often there is a family history. Normally we do not do any electrophysiological studies or neuroimaging for febrile convulsion. However, with a change in social structure, we need to revisit the area again and again.

**AIMS AND OBJECTIVES:** To find out any neurophysiological abnormalities and neuroimaging and its relevance in febrile convulsion.

**MATERIAL AND METHOD:** Fifty three children with febrile convulsion were studied in our 550 bedded hospital and post-graduate medical college in the pediatric ward between 1st January 2020 to 31<sup>st</sup> December 2020. We did neuroimaging during admission after stabilizing the patient. EEG was done two weeks later after the febrile convulsion.

**RESULTS:** Boys with febrile convulsion are more than girls. EEG changes were more in boys compared to the girls. Positive family history of febrile convulsion was significantly more in those who had EEG changes. EEG changes were more in those in the age group of one to five years than those in less than one year. No abnormality of neuroimaging were detected in the study.

**CONCLUSION:** EEG changes were more in boys, especially when there is a positive family history. No abnormality of neuroimaging were found in the present study.

**KEYWORDS :** Febrile convulsion, EEG, Neuroimaging.

### INTRODUCTION

A febrile convulsion is the most common seizure disorder during childhood. A simple febrile convulsion is a generalized tonic-clonic convulsion that may last upto 15 minutes, associated with a temperature more than equal to 39C, followed by a brief postictal phase. This type of convulsion commonly occurs in children between 6 months to 5 years of age and, there is usually not more than a convulsion in the same episodes of fever<sup>1</sup>.

A febrile convulsion is described as complex or atypical when duration is more than 15 minutes, repeated episodes of convulsions within 24 hours, focal seizure activity, or focal findings are present during post-ictal phase<sup>1</sup>.

The conventional approach towards simple febrile convulsion is masterly inactivity. However, we are often tempted to rethink the policy because of changing epidemiology, socio-economic factors, a single child in a nuclear family, of greater importance, the association of mesial temporal sclerosis, associated with febrile convulsion ,and hidden epilepsy precipitated by fever. In one study, children with febrile convulsions were followed up for more than five years with EEG not less than five times. EEG abnormality was noted frequently in febrile convulsion. There were abnormal EEGs even after the first EEG being normal. However, this study failed to conclude whether EEG's is of any prognostic value in febrile convulsion<sup>2</sup>.

In other studies, we found out that abnormal EEGs were more common when the age of onset of febrile convulsion is less. However, this study also failed to conclude whether abnormal EEG translates future epilepsy<sup>3,4</sup>.

Neurological examination of complex febrile convulsion patients is often normal after their clinical status were stabilized. EEG should be performed seven to ten days after children with complex febrile convulsion<sup>5</sup>.

EEG is of enormous importance in an apparent febrile convulsion of a child with developmental delay or other

evidence of neurological impairment before the occurrence of a febrile convulsion.

Phenobarbitone and Valproic acid can prevent febrile convulsion<sup>6,7,8</sup>. Oral Benzodiazepine also effective when used as intermittent prophylaxis during febrile episode<sup>9</sup>.

Mesial temporal sclerosis and other hippocampal abnormality after prolonged convulsion were noted in some MRI study<sup>10,11</sup>. However, the role of prolonging febrile convulsion in the genesis of hippocampal sclerosis is controversial. Prolonged seizure duration is the most important predictor of temporal lobe change after febrile seizure<sup>12,13,14</sup>. Statistical analysis and data from epilepsy surgery suggest a casual relationship of prolonged febrile seizure in the genesis of hippocampal sclerosis<sup>11</sup>.

According to one review, abnormal neurological examination was associated with imaging abnormality in complex febrile seizure but not in simple febrile convulsion<sup>15</sup>.

One study has shown that MRI brain has no advantage over CT-Scan of the brain in managing a complex febrile convulsion<sup>5</sup>.

### AIMS AND OBJECTIVE

- To find out the incidence of Electrophysiological (EEG) changes in febrile convulsion and its relevance.
- To find out the utility of Neuro-imaging (CT-Scan or MRI of the brain) after an episode of febrile convulsion.

### MATERIAL AND METHOD

This study was conducted in the Department of Pediatrics at Ramakrishna Mission Seva Pratisthan and Vivekananda Institute of Medical Sciences, a 550 bedded general hospital and post-graduate medical college located in the heart of the city of Kolkata.

All cases admitted in this hospital with febrile convulsion from 1st January 2020 to 31st December 2020 has been included in the study.

Neuroimaging and EEG were done in all cases. EEG were done after 14 days since the last episode of convulsion.

Neuroimaging were done at any time after the patient was stabilized. During this period, 84 children who were evaluated had been treated for febrile convulsion in our hospital and who had no previously known neurological disorder. Age, sex, timing of EEG, and EEG result were recorded for each patient. These patients had been followed up in the outpatient department.

Blood glucose, urea, creatinine, aspartate, aminotransferase (AST) level, alanine, aminotransferase (ALT) level electrolytes including calcium and magnesium, complete blood count, blood culture, urine culture, and chest X-Ray tests were performed for all patients. These investigations were done to rule out associated another factor which may precipitate seizure-like hypoglycaemia, hypocalcemia, hypomagnesemia or any underlying infection which need separate treatment. The Cerebrospinal fluid examination were performed in all patients admitted with fever with convulsion after being clinically stabilized. Children who had hypoglycemia (6 patients), electrolyte imbalance (5 patients), central nervous system infection (8 patients), hepatic or renal failure (3 patients), intoxication (1 patient), trauma (1 patient), or known neurologic disorder (4 patients) were excluded from the study. Two children with a positive Covid 19 RT PCR test and one child who was admitted with seizures but later diagnosed to be a symptom of Multisystem inflammatory syndromes in children (MISC) were also excluded from the study. After exclusion 53 children were considered for the study.

One of the neurologist, with a special interest in pediatric neurology, of this hospital, interpreted the ground activity and paroxysmal epileptiform discharge at EEG. EEG were interpreted based on wave forms, whether normal or abnormal in terms of different paroxysmal changes in the wave forms and background activity. Paroxysms of the spike, spike waves and multiple spike waves at EEG was interpreted as abnormal EEG findings.

MRI of the brain were performed in all patients. Statistical analysis of the results of EEG and neuroimaging was performed by statistician; Chi-Square test is done to obtain "p" value.  $P < 0.005$  was accepted as a statistically significant result. Permission from the ethical committee were obtained. Written consent of the parents were taken about the investigation.

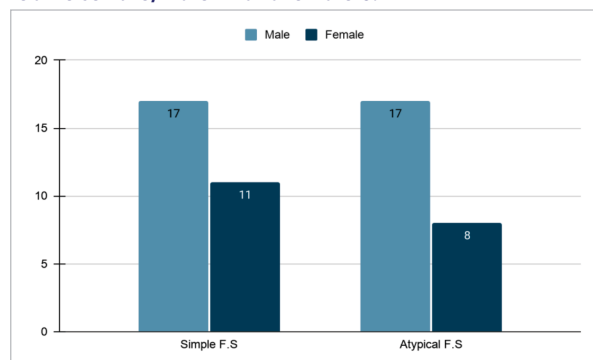
## RESULTS

Table: 1

Sex wise distribution of febrile seizure

Parameter	Simple F.S	Atypical F.S	Total
Febrile seizure	28	25	53
Male	17	17	34
Female	11	8	19

In this study, 28 patients with simple febrile seizure, among them male 17, female 11 and 25 patients with atypical febrile seizure, male-17 and female-8.



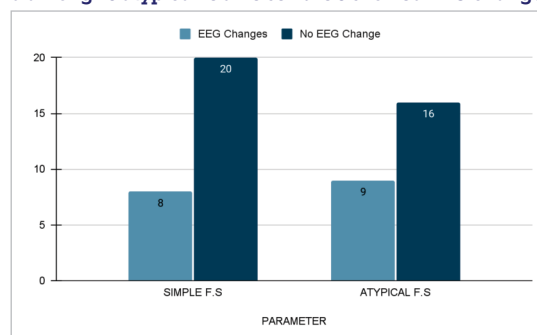
## STATISTICALLY SIGNIFICANT

Table:2

EEG changes in different types of febrile seizure

PARAMETER	SIMPLE F.S	ATYPICAL F.S	TOTAL
Febrile Seizure	28	25	53
EEG changes	8	9	17

Among 28 febrile seizure 8 patient showed EEG changes and among 25 atypical febrile seizure 9 showed EEG changes.



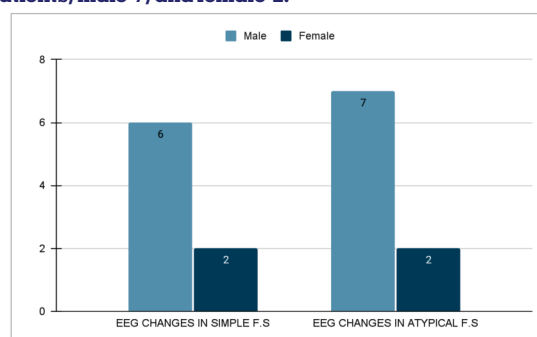
## STATISTICALLY SIGNIFICANT

Table: 3

EEG changes in different type seizure with sex distribution

PARAMETER	SIMPLE F.S	ATYPICAL F.S	TOTAL
Febrile seizure	28	25	53
EEG changes	8	9	17
Male	6	7	13
Female	2	2	4

Among 28 simple febrile seizure, EEG changes noted in 8 patients of them, male-6, female-2 and among 25 patients with atypical febrile convulsion EEG change noted in 9 patients, male-7, and female-2.



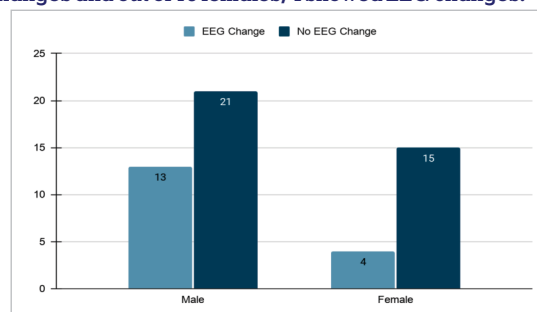
## STATISTICALLY SIGNIFICANT

Table: 4

EEG change between male and female child with febrile seizures

Parameter	Total No. Of Patients	EEG Change	No. EEG Change
Male	34	13	21
Female	19	4	15
Total	53	17	36

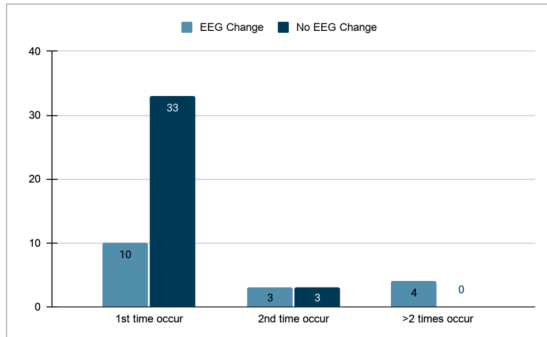
In this study there were 34 male patients, 13 showed EEG changes and out of 19 females, 4 showed EEG changes.



**STATISTICALLY SIGNIFICANT****Table: 5****Number of episode of febrile seizure with EEG change**

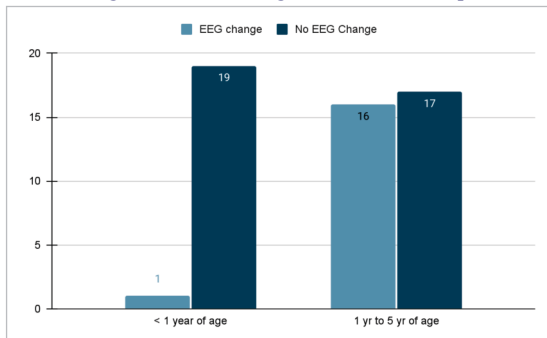
Parameter	1 <sup>st</sup> time occur	2 <sup>nd</sup> time occur	> 2 times occur	total
Febrile Seizure	43	6	4	53
EEG Changes	10	3	4	17

Among 43 first time occurring febrile seizure patient 10 shows EEG changes, among 6 with 2 times febrile seizure, 3 shows EEG changes, and all 4 patients with > two episodes of febrile seizure showed EEG changes.

**Table: 6****EEG change among <1 yr & > 1 Yr (upto 5 years) of child with febrile seizure**

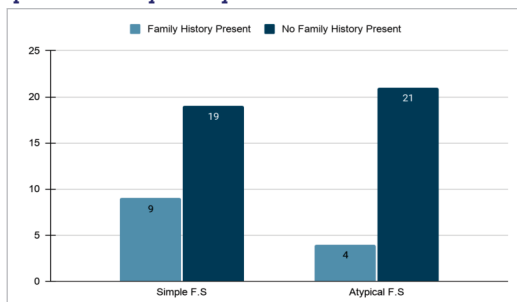
Parameter	EEG change	EEG not changed	Total
< 1 year of age	1	19	20
1 yr to 5 yr of age	16	17	33
Total	17	36	53

In this study there was 20 children < 1Yr of age with febrile convulsion, one patient shows abnormal EEG, there was 33 patients with febrile seizure who were between 1 year to 5 years, among them EEG change was noted in 16 patients.

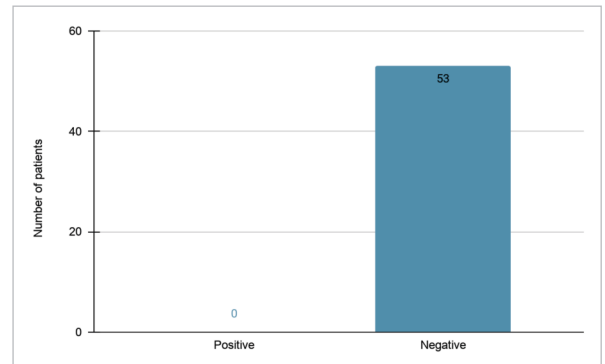
**STATISTICALLY SIGNIFICANT****Table: 7****Distribution of febrile seizure with Positive Family History**

Parameter	Simple F.S	Atypical F.S	Total
Febrile seizure	28	25	53
Family history present	9	4	13

Among 28 simple febrile seizure patients, 9 had positive family history and out of 25 atypical febrile seizure patient 4 had positive family history.



DONE	53
POSITIVE	0

**NEUROIMAGING****DISCUSSION**

The conventional approach towards a simple febrile convulsion is not to do any neuro-imaging or EEG. However, the approach to this common condition needs to be revised again and again with the changing epidemiology, socioeconomic status, position of the child in the family, and availability of more advanced investigation modalities and treatment and prevention options.

Though the courses of most febrile convulsions are benign, there is evidence of occasional patients where prevention and appropriate treatment can alter the prognosis. For example, there are cases of epileptic seizure, which may precipitate by fever. Though an abnormal EEG is not gold standard for diagnosing epilepsy, it may be an important index of suspicion of an epileptic disorder. Like this present study, other studies<sup>2,3</sup> show that EEG changes in febrile convulsion are more prevalent in older children. It is impossible for us to come to any conclusion if the normal initial EEG is followed by abnormal follow-up EEGs. Tachibana et al.<sup>1</sup> in their study, showed that follow-up EEGs were done for more than five consecutive years, and EEG abnormalities were detected after normal initial EEG. However, the present study did not have the scope to similar follow up the patients. In the present study that EEG changes were significantly increased ( $p < 0.05$ ) with complex or atypical febrile convulsions. Another study<sup>5</sup> with complex febrile convulsion has shown an increased incidence of EEG change when done 7-10 days after convulsion. There is no evidence that abnormal EEG is a predictor for further development of epilepsy<sup>2,3</sup>. A large number of children with complex or atypical febrile convulsions and EEG change were diagnosed as epileptic patients later, according to one study<sup>5</sup>. According to some studies<sup>4,16</sup> however EEG finding lacked the predictive value for the later occurrence of either febrile or afebrile seizure. Mesial temporal lobe sclerosis is probably the only dreaded complication of febrile convulsion. This can be detected most efficiently by MRI<sup>10,11</sup> after a febrile convulsion. Some studies<sup>16,17</sup> have shown that temporal lobe changes are more common, if the child in younger age group<sup>12</sup> or if there is febrile status<sup>12,13,14</sup>. However, the only child in the present study, with temporal lobe EEG changes had a simple febrile convulsion and was around five years of age. MRI-scan was normal.

In this study there were 20(twenty) young children (< 1 year of age) with febrile seizures, three among them only one had EEG change. But EEG change was not temporal lobe EEG changes.

In this study, there were five patients with febrile status; again no one had temporal lobe EEG change. According to one study<sup>13</sup> temporal lobe EEG changes develop in more patients with prolonged febrile convulsions, where the mean duration of the convulsion is 100 minutes or more. The only patient in

our present study who developed temporal lobe EEG change, did not have prolonged convulsion and had a normal MRI. Those who had a prolonged convulsion in our study did not have any temporal lobe EEG changes.

The present study has shown significantly more EEG changes in male children as compared to female. None of the available literature showed similar sex statistics. But it will be interesting to explore the issue further.

In the present study, EEG abnormality is significantly higher when a family history of febrile convulsion is present. We could not find out similar evidence after an extensive literature review. However, the incidence of febrile convulsion is definitely more, when family history of convulsion (febrile or afebrile) is present<sup>17,18</sup>.

If there is fever and convulsion and positive family history, we are more confident that this episode is a febrile convulsion. However, our finding open a new horizon against conventional wisdom.

Does this mean the children with febrile convulsion and positive family history are at a greater threshold of developing epilepsy?

Do they need special follow up?

Our study is not adequately powered to answer these questions. We could not find adequate evidence in the literature to these questions with certainty. EEG changes are not significantly (statistically) different in the group where only one episode or any episode of febrile convulsion occurred. This may suggest that multiple episodes of convulsion in the same episode of fever may not pose a special risk of epilepsy in later life. We could not get any other study supporting this finding as reviewed literature in our favor or against.

Neuro-imaging change (CT-SCAN of the brain and MRI brain) in febrile convulsion (both simple and atypical febrile convulsion) is the aim of this study. There are many studies where MRI brain shows mesial temporal sclerosis after a prolonged febrile convulsion<sup>12,13,14</sup>. This study also showed changes in MRI brain occurred when there is significant postictal neurodeficit.

Should EEG be performed in all cases of febrile convulsion? Though initial EEG changes are present in a significant number of patients, there is no significant recurrence of convulsion either febrile or afebrile in the same patient or group of patients. Even if EEG changes occur, it is not a predictor of further risk for epilepsy. Therefore probably at this stage, it will not be justified to recommend EEG for a simple case of febrile convulsion or even atypical (complex) febrile convulsions. In the present study, children with complex or atypical febrile convulsion had greater chance of EEG changes. However, this EEG change would not predict the risk of epilepsy, and therefore is of no value in deciding the consideration of prevention. Though the prophylactic medications are effective in prevention, they often have severe side effects.

Our study also shows that a child in febrile status also does not pose a special threat towards the development of temporal lobe changes. Whether preventive strategy towards a subsequent episode of febrile convulsion decrease the risk of mesial temporal sclerosis is only open to speculation.

The neuroimaging, similarly may not add any significant diagnostic advantage in either simple or complex febrile seizure.

Thus our clinical judgment based on the common sense

approach should be most useful for interpreting whether a convulsion is febrile or not. Only when we clinically suspect epilepsy or space-occupying lesion associated with seizure and fever should we contemplate further investigations.

This statistically significant incidence of EEG changes in certain groups, for example those who are a male child or when there is a positive family history, in this series does not mean that adverse consequences will be more in these groups.

Therefore further investigation of either EEG or any neuro-imaging modes is not justified, when there is a high degree of clinical suspicion of febrile convulsion.

## Conclusion and Summary

- EEG changes are common in children with both simple and atypical or partial febrile seizures, especially in the case of a male child and is positive family history of febrile seizure are present. As there have been no recurrences of febrile seizure or epileptic fit, it is impossible to understand the clinical significance of this abnormal EEG. Our present policy will be not to do EEG in simple or even atypical febrile convulsion
- No abnormality in neuro-imaging or MRI of brain was detected.

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