

ASSOCIATION OF FEBRILE SEIZURES WITH IRON DEFICIENCY ANEMIA: A PROSPECTIVE STUDY.

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Abstract

Introduction: Febrile seizures are common in pediatric age group. These seizures are benign and self limiting and usually do not recur after 5 years of age. In pediatric patients viral illnesses are commonly associated with incidence of febrile seizures. Family history of febrile seizures may be present in many cases. Many studies have concluded that febrile seizures are more common in children having iron deficiency some other studies have even reported that iron deficiency is less frequent in children with febrile seizures. We conducted this study of iron deficiency anemia in children presenting with febrile seizures.

Materials and Methods: 50 pediatric patients presenting with febrile seizures were included in this study on the basis of a predefined inclusion and exclusion criteria. Demographic details such as age and gender was noted. Previous history of febrile seizure was asked for and noted. Family and past history was noted. Serum Ferritin levels were determined in all the cases. Hemoglobin levels less than 11 gm/dl was taken as cutoff for the diagnosis of anemia. For statistical analysis SSPS 21.0 software was used and p value less than 0.05 was taken as statistically significant.

Results: Out of 50 studied cases 36 (72.00%) were males and 14 (28.00%) were females with a M: F ratio of 1:0.38. The mean age of patients was found to be 18.18 +/- 11.32 months. Majority of the cases (74%) were having first onset of febrile seizures. Second and third episode of febrile seizures was seen in 8 (16%) and 5 (10%) cases respectively. 42 (84%) patients were found to have simple febrile seizures whereas remaining 8 (16%) patients had complex febrile seizures. criteria 36 (72%) patients were found to have iron deficiency anemia defined as serum Ferritin level below 12 microgram/lit.

Conclusion: Iron deficiency anemia is associated with an increased risk of febrile seizures in pediatric age group.

Keywords: Febrile Seizures, Iron deficiency anemia, Serum Ferritin, Hemoglobin.

Introduction

Febrile seizures are defined as “a seizure occurring in childhood after 1 month of age associated with a febrile illness not caused by an infection of the central nervous system (CNS), without previous neonatal seizures or a previous unprovoked seizure, and not meeting the criteria for other acute symptomatic seizures.¹ Various studies have reported that 3-5% children will have 1 or more episodes of febrile seizures below 5 years of their age. A slight male preponderance is seen in febrile seizures. Though the exact association between fever and seizures is not known there are various hypotheses which link activation of cytokine network in febrile children as triggering factor for seizures. Febrile seizures are broadly divided into 2 groups simple and complex febrile seizures. Simple febrile seizures by definition are generalized and last for less than 15 minutes and do not recur within 24 hours.² On the other hand complex seizure may last for more than 15 minutes, may be focal and may recur within 24 hours. Imaging is usually not required in cases of simple febrile seizures but is recommended in cases of complex febrile seizures to rule out intracranial pathologies.³

In pediatric patients viral illnesses are commonly associated with incidence of febrile seizures. Family history of febrile seizures may be present in many cases. The inheritance is reported to be polygenic but small number of cases with

autosomal dominant inheritance pattern have also been identified.⁴ The outcome is better in simple febrile seizures whereas patients having history of complex febrile seizures are more prone for future development of complications such as epilepsy, delayed developmental milestone and various neurological problems.⁵

Various risk factors have been identified with occurrence of febrile seizures that include family history of febrile seizures, high grades of temperature, maternal alcohol intake and smoking during pregnancy. The association between iron deficiency anemia and febrile seizures has also been a topic of great interest amongst researchers.⁶ Various studies have linked iron deficiency anemia to febrile seizures but the exact cause of this association is still needs to be investigated. Fever can worsen the detrimental effects of anemia and may trigger seizure activity in brain thereby making pediatric patients having iron deficiency more vulnerable for occurrence of febrile seizures.⁷ It is a well known fact that iron deficiency is associated with various neurological manifestations such as irritability, poor attention span, learning difficulties and delayed developmental milestones. Iron is known to act as coenzyme in various pathways and various neurotransmitters. Despite all these theories there is no clear cause-effect relationship which could be established between iron deficiency and febrile seizures.⁸ While many studies have concluded that febrile seizures are more

common in children having iron deficiency some other studies have even reported that iron deficiency is less frequent in children with febrile seizures. Hence there are conflicting conclusion reported by various studies about association of iron deficiency and febrile seizures.

Keeping in mind this conflicting outcome of various studies we undertook this hospital based analytical study of iron deficiency anemia in children presenting with febrile seizures.

Materials and Methods:-

This was a hospital based analytical study conducted in the department of pediatrics in a tertiary care medical college. 50 pediatric patients presenting with febrile seizures were included in this study on the basis of a predefined inclusion and exclusion criteria. Demographic details such as age and gender was noted. Previous history of febrile seizure was asked for and noted. Family and past history was noted. Developmental study was reviewed with a view to find out cases having developmental delay. A detailed clinical examination was done. Neurological examination was done to rule out presence of any focal deficit. Complete blood count and peripheral blood smear was done in all the cases. Serum Ferritin levels were determined in all the cases. Hemoglobin levels less than 11 gm/dl was taken as cutoff for the diagnosis of anemia. Neuroimaging was not done in patients with simple febrile seizures whereas in cases of complex febrile seizures neuroimaging such as computerized tomography or magnetic resonance imaging of brain was done. Electroencephalography (EEG) was done in all the cases. For statistical analysis SSPS 21.0 software was used and p value less than 0.05 was taken as statistically significant.

Inclusion criteria:-

1. 50 pediatric patients with febrile seizures
2. Age between 6 months to 5 years.
3. Informed written consent obtained from parents.

Exclusion criteria:-

1. Age less than 6 months.
2. Patients known to be having pre-existing neurological disorders.
3. Children with delayed developmental milestones, various syndromes or neurodevelopmental disorders such as cerebral palsy etc.
4. Those have hematological disorders including thalassemia, leukemia or lymphomas.
5. Cases in whom parents refused consent to be part of study.

Results:-

This study included 50 pediatric patients with febrile seizures. Out of 50 studied cases 36 (72.00%) were males and 14 (28.00%) were females with a M:F ratio of 1:0.38.

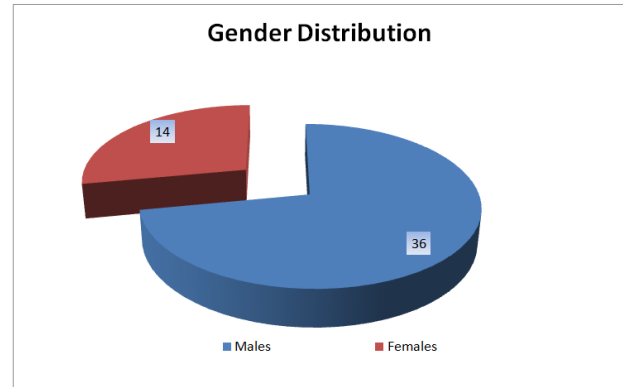


Figure 1: Gender Distribution of studied cases.

The analysis of age distribution of studied cases showed that the most common affected age group was found between age group of between 6-12 months (36%) followed by 13-24 months (28%) and 3-4 years (18%). Relatively less number of patients were found in between the age groups of 2-3 years (12%) and above 4 years (6%). The mean age of patients was found to be 18.18 +/- 11.32 months

Table 1: Age Distribution of studied cases.

Age Group	No of Patients	Percentage
6m-12 months	18	36.00%
13 months-24 months	14	28.00%
25 months-36 months	6	12.00%
36 months – 48 months	9	18.00%
> 48 months	3	6.00%
Mean Age	27.68 +/- 11.32 months	

The analysis of cases on the basis of episode of febrile seizures showed that majority of the cases (74%) were having first onset of febrile seizures. Second and third episode of febrile seizures was seen in 8 (16%) and 5 (10%) cases respectively.

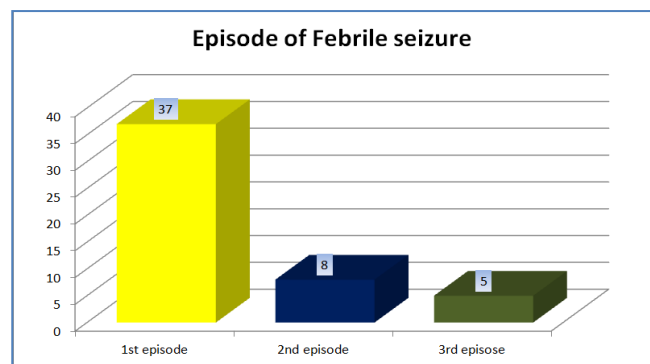


Figure 2: Episode of Febrile Seizures.

Out of 50 studied cases 42 (84%) patients were found to have simple febrile seizures whereas remaining 8 (16%) patients had complex febrile seizures.

Table 2: Simple Vs Complex Febrile Seizures.

Type Of Seizures	No Of Patients	Percentage
Simple Febrile Seizures	42	84.00%
Complex Febrile Seizures	8	16.00%
Total	50	100%

The analysis of hemoglobin levels of the studied cases showed that out of 50 cases hemoglobin level less than 6 gm/dl was found in 6 (12%) patients. Hemoglobin was found to be 10-11 gm/dl in 12 (24%) cases. Hemoglobin levels between 9-10 gm/dl, 8-9 gm/dl, 7-8 gm/dl and 6-7 gm/dl was found in 6 (12%), 6 (12%), 4 (8%) and 5 (10%) patients respectively.

Table 3: Hemoglobin Levels in Studied cases.

Hemoglobin levels	No Of Patients	Percentage
< 6gm/dl	6	12.00%
6-7 gm/dl	5	10.00%
7-8 gm/dl	4	8.00%
8-9 gm/dl	6	12.00%
9-10 gm/dl	6	12.00%
10-11 gm/dl	12	24.00%
> 11 gm/dl	11	22.00%
Total	50	100%

The diagnosis of iron deficiency anemia was done on the basis of serum Ferritin levels and a level of serum ferritin less than 12 microgram/lit was taken as diagnostic of iron deficiency status. By using this criterion 36 (72%) patients were found to have iron deficiency anemia.

Table 4:- Serum Ferritin levels in studied cases.

Serum Ferritin	No Of Patients	Percentage
=/> 12 microgram/Lit	14	28.00%
< 12 microgram/Lit	36	72.00%
Total	50	100%

The analysis of cases of febrile seizures on the basis of whether or not they had iron deficiency anemia showed that iron deficiency anemia was present in 36 (72%) of the cases where as 3 patients had anemia but iron deficiency was not present in those cases. 11 patients were not having anemia. An overwhelming majority of the children presenting with febrile seizures were found to have iron deficiency status.

Table 5: Febrile Seizures and anemia.

Serum Ferritin	No of Patients	Percentage
Febrile Seizures With Iron Deficiency anemia	36	72 %
Febrile Seizures with Anemia other than due to iron deficiency	3	6.00%
Febrile seizures with no anemia	11	22.00%
Total	50	100%

Discussion:-

We undertook this study to find out whether febrile seizures are more common in children with iron deficiency status. There are many studies which tried to find out the association between iron deficiency anemia and febrile seizures and many of them have found that iron deficiency status predisposes children for development of febrile seizures. We undertook this study to find out iron deficiency status of children presenting with febrile seizures.

Out of 50 studied cases 36 (72.00%) were males and 14 (28.00%) were females with a M: F ratio of 1:0.38. Many other studies have also found that febrile seizures are more common in boys as compared to girls. Agarwal J et al conducted a study of febrile seizures. 92 children with febrile seizure were enrolled in study. Males accounted for 70% and females 30%. Simple febrile seizure was present in 48% and complex febrile seizures were seen in 52%. Recurrence of seizure was seen in one third of cases.⁹ the male preponderance in cases of febrile seizures have also been reported by the authors such as Habib Z et al¹⁰ and Esegibe EE et al¹¹.

In our study the most common affected age group was found to be between 6 months to 1 year of age followed by above 1-2 year of age. The mean age of patients in our study was found to be 18.18 +/- 11.32 months. Similar mean age of the children presenting with febrile seizures was also reported by many other studies. Biyani G et al conducted a study of children with febrile seizures in which the authors found that the mean age of children presenting with febrile seizures was 21.1 months.¹² Majority of children presenting with febrile seizures were reported to be below 2 years in studies conducted by Leung Ak et al¹³ (mean age 20.59±7.93 months) and Lee SH et al¹⁴ (mean age, 21.8±13.8 months). These results were found to be similar to the results seen in our study.

Simple febrile seizures are more commonly seen as compared to complex febrile seizures. In our study out of 50 studied cases 42 (84%) patients were found to have simple febrile seizures whereas remaining 8 (16%) patients had complex febrile seizures. Delpisheh A Conducted a study to analyze epidemiological and clinical characteristics as well as risk factors associated with febrile seizures. The authors found that Prevalence of simple and complex febrile seizure was 69.3% (95% CI: 19.6–31.0) and 28.3% (95% CI: 59.5– 79.0), respectively.¹⁵ Similarly predominant simple febrile seizures were reported by the studies conducted by Al-Eissa YA¹⁶ and Esmaili Gourabi H et al¹⁷.

Finally we found that majority of the children presenting with febrile seizures had iron deficiency status. IN our study diagnosis of iron deficiency anemia was done on the basis of serum Ferritin levels and a level of serum Ferritin less than 12 microgram/lit was taken as diagnostic of iron

deficiency status. By using this criterion 36 (72%) patients were found to have iron deficiency anemia. In a study conducted by Nigade RM et al patients with febrile seizures and having iron deficiency accounted for about 85.88% of all the patients and the patients with febrile seizures with no iron deficiency accounted for 14.12%. p value was found to be significant for this study.¹⁸ Similar results were also reported by the authors such as Papageorgiou V et al¹⁹ and Kwak BO et al²⁰.

Conclusion:-

Febrile seizures are common in pediatric age group. They are usually benign and self limiting. The association of iron deficiency anemia and febrile seizures have been a topic of immense interest amongst researchers. Our study found that iron deficiency anemia is a common occurrence in cases of febrile seizures and hence our study concludes that iron deficiency anemia is associated with an increased risk of Febrile seizures in pediatric age group.

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