

The clinico-etiological profile of febrile seizure and its association with serum ferritin level

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Abstract

Background: Febrile seizures are defined as an event in infancy or childhood, usually occurring between 6 months and 5 years of age, associated with fever but without evidence of intracranial infection or other definable cause. Thus, the present study was conducted to determine any association between serum ferritin level and first febrile seizure. **Methods:** A cross sectional study was conducted among the infants of age group 6 months to 5 years with complaints of fever with seizures attending Department of Pediatrics, GSVM Medical College, Kanpur for Feb. 2017 to Oct. 2018. After approval from Institutional Ethics Committee. Data was collected on pre designed case sheet consisting of general information history, clinical examination, temperature recording and relevant laboratory investigation such as hemoglobin, total leucocyte count, differential leucocyte count and serum ferritin levels. Statistical analysis was done using SPSS (version 24.0; SPSS Inc., Chicago, IL, USA). **Results:** Study found that among 50 children, 40% children of febrile seizure belonged to age group 1 year to 2 years; febrile seizure was predominantly present in male population. Type of febrile seizure was predominantly simple febrile seizure (72%) and complex febrile seizure (28%). Results of GTCS clearly indicate that there is statistically significant association of GTCS with low serum ferritin level of less than 10 ng. **Conclusions:** In ferritin less than 10 ng, 29(90.6%) patients had GTCS and which was statistically significant. Association of cause of fever vs. serum ferritin was statistically significant. Larger studies are needed to confirm the present findings.

Keywords: Febrile seizure, Serum ferritin, Association

Introduction

Febrile seizures are seizures that occur between the age of 6 and 60 months with a temperature of 38.0°C (100.4°F) or higher, that are not the result of central nervous system infection and that occur in the absence of a history of prior afebrile seizures. A simple febrile seizure is a primary generalized and tonic-clonic in nature, lasts a few seconds and rarely up to 15 min, is followed by a brief postictal period of drowsiness, and occurs only once in 24 hours [1,2].

The incidence of febrile convulsions is 2-5% in neurologically healthy child. The peak incidence of febrile seizure is at the age of 14 to 18 months [2]. Iron

deficiency anemia is one of the most prevalent micronutrient deficiencies in young children in India and other parts of the world, and it is strongly associated with persistent cognitive and motor delays even after the anemia and iron deficit have been repaired. Most iron in neonates is in circulating hemoglobin.

As the relatively high hemoglobin concentration of the newborn infant falls during the first 2-3 months of life, considerable iron is recycled. These iron stores are usually sufficient for blood formation in the first 6-9 months of life in term infants. In term infants, anemia is caused solely by inadequate dietary iron usually occurs at 9-24 months of age and is relatively uncommon thereafter [3,4]. Iron deficiency anemia was defined as

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the Hb concentration falls 2 standard deviation (SD) below the mean for age as presence of the indexes. Serum iron concentration 430 mcg/dl in children, confirm this status [1,2,4]. Owing to their association with epilepsy in future, various studies have attempted to identify the risk factors associated with them viz, family history of febrile seizures, epilepsy, perinatal factors and temperature peak. Pisacane, et al. reported that low iron level is associated with febrile seizure, whereas Kobrinsky, et al. reported that iron deficiency raises the threshold for seizures [5,6].

As iron is important for function of neurotransmitters and various enzymes, low level of serum ferritin may lower the seizure threshold [7]. Fever can worsen the negative effects of low serum ferritin on the brain and trigger seizure [5]. Considering the age prevalence of iron deficiency anaemia and febrile convulsion which are the same, the role of iron in the metabolism of neurotransmitters (such as GABA and serotonin) and some enzymes (such as monoaminoxidase and aldehydeoxidase), the function of hemoglobin in conveying oxygen to the brain and since fever can exacerbate symptoms that result from anaemia, a relationship between iron deficiency anaemia and febrile convulsions is probable. This study was conducted to determine any association between serum ferritin level and first febrile seizure.

Material and Methods

To conduct the present cross-sectional hospital based study, a total of 50 children were studied in the Department of Pediatrics, GSVM Medical College, Kanpur for Feb. 2017 to Oct. 2018 following setting were made and most standard methods were applied.

Inclusion criteria: The study group comprised of children having febrile seizure in age group 6 month to 5 year.

Results

Table-1: Age wise distribution of Serum ferritin levels.

Serum ferritin			
Age	10ng-300ng	<10 ng	Chi-square value; p-value:
6 month -1year	8(44.0)	8(25.0)	10.0694; 0.0393
1- 2 years	6(33.3)	14(43.8)	
2- 3years	0(0.0)	8(25.0)	
3- 4years	2(11.1)	2(6.3)	
4- 5years	2(11.1)	0(0.0)	

Exclusion criteria

a) Consist of children between age group 6 month to 5 year. Through history taking, clinical examination and routine investigation were done to exclude any disease condition conformation of the fact that the children have not suffered in past from any condition such as meningitis, any convulsion, encephalitis and other neurological illness.

b) The study group comprised of cases of seizure, having temperature at least 37.8°C within emergency department as in history within age group 6 month to 5 yrs all cases having CNS infection like meningitis, encephalitis, serum electrolyte imbalance and other acute neurological illness, or that of drug containing elemental supplement as with other condition known to alter serum ferritin levels are excluded from the study.

Tools of data collection: After approval from Institutional Ethics Committee data was collected on pre design case sheet consisting of general information history, clinical examination, temperature recording and relevant laboratory investigation such as hemoglobin, total leucocyte count, differential leucocyte count and serum ferritin levels.

Statistical Analysis: For statistical analysis data were entered into a Microsoft excel spreadsheet and then analyzed by SPSS (version 24.0; SPSS Inc., Chicago, IL, USA) and Graph Pad Prism version 5. Data had been summarized as mean and standard deviation for numerical variables and count and percentages for categorical variables without other qualification, 'chi-squared test' often is used as short for Pearson's chi-squared test.

Unpaired proportions were compared by Chi-square test or Fischer's exact test, as appropriate. P-value ≤ 0.05 was considered for statistically significant.

Table 1 shows that 8(44.4%) patients aged between 6 months-1year 6(33.3%) patients aged between 1-2 years, 2(11.1%) patients aged between 3-4years and 2(11.1%) patients aged between 4-5yearshad serum ferritin level of 10ng-300ng). While 8(25.0%) patients who were aged between 6 months-1year, 14(43.8%) patients aged between 1-2 years, 8(25.0%) patients aged between 2-3 years and 2(6.3%) patients aged between 3-4years had serum ferritin level <10 ng. Association of age and serum ferritin was found to be statistically significant ($p=0.0393$) (Table 1).

Table-2: Gender wise distribution of Serum Ferritin levels.

Serum Ferritin			
Gender	10ng-300ng	<10 ng	Chi-square value; p-value:
Male	14(77.8)	21(65.6)	0.8102;0.3680
Female	4(22.2)	11(34.4)	

Table 2 shows that among patients with Serum ferritin levels10ng-300ng, 14(77.8%) were males and 4(22.2%) were females while among patients with serum ferritin levels<10 ng, 21(65.6%) were males and 11(34.4%) were females. Association of gender and serum ferritin was not statistically significant ($p=0.3680$)(Table 2)

Table-3: Association of type of Seizure with Serum Ferritin levels

Serum Ferritin			
Type of seizure	10ng-300ng	<10 ng	Chi-square value;p-value:
GTCS	7(38.9)	29(90.6)	15.2950;<0.0001
Focal	11(61.1)	3(9.4)	

Table 3 shows that in ferritin 10ng-300ng, 7(38.9%) patients had GTCS and 11(61.1%) patients had focal seizure. In ferritin <10 ng, 29(90.6%) patients had GTCS and 3(9.4%) patients had focal seizure. Association of type of seizure vs. serum ferritin was statistically significant ($p<0.0001$)(Table 3)

Table-4: Distribution of causes of fever according to Serum Ferritin levels.

Serum Ferritin			
Cause of fever	10ng-300ng	<10 ng	Chi-square value;p-value:
Respiratory	6(33.3)	10(31.3)	8.2610;0.0409
GIT	4(22.2)	16(50.0)	
UTI	0(0.0)	2(6.3)	
Other	8(44.4)	4(12.5)	

Table 4 shows that in ferritin 10ng-300ng, 6(33.3%) patients had respiratory, 4(22.2%) patients had GIT and 8(44.4%) patients had other cause of fever. In ferritin <10 ng, 10(31.3%) patients had respiratory, 16(50.0%) patients had GIT, 2(6.3%) patients had UTI and 4(12.5%) patients had other cause of fever. Association of cause of fever vs serum ferritin was statistically significant ($p=0.0409$) (Table 4).

Discussion

Febrile seizures are the most common type of seizures, occurring in 3 to 4% of children [8]. Various studies have attempted to identify the risk factors associated with them viz, age gender, family history of febrile seizures, epilepsy, perinatal factors and temperature peak. Pisacane, et al. [5] reported that low iron level is associated with febrile seizure, where as Kobrinsky, et al[6] reported that iron deficiency raises the threshold for seizures. The present study was conducted on 50

children of between age group 6 month to 5 years from with febrile seizure. Found that among 50 children, 40% children of febrile seizure belonged to age group 1 year to 2 year (Mean $17.4 \pm SD 5.3$ months) similar result was shown in study of Moruskar et al[9], 62.6%, Potdar et al[10] age (18.9 ± 9.01) and Ghosal et al[11] 51.7% no study showing result different then the present study with respect to incidence of febrile seizure in age group of 1 year to 2 year.

Alfredo Piscane et al [5] found the mean age for FS was 15 months. Separate studies done by Vasvani et al [15], Waruiru et al[16] and Daoud et al[17] also found that FS peaks at 18 months. Naveed-urRehmann et al[13] found mean age was 22.97 ± 9.52 months. Susan et al [18] found average age of 39 ± 15.92 months. It is generally noted that the febrile convulsion are more common in second year.

Moreover, Febrile seizure was predominantly present in male population 70% in the present study, similar result was found in study of Moruskar et al[9] 71.76% and Potdar et al[10] 60.1% and Ghoshal et al[11] majority of cases were male (66.7%) no study showing result different then the present study with respect to predominance of febrile seizure in males Type of febrile seizure was predominantly simple febrile seizure (72%) and complex febrile seizure (28%) in the present study ,similar result was found in study of Moruskar et al[9] simple febrile seizure (69.41%) and complex febrile seizure (30.59%) and Potdar et al[10] simple febrile seizure (80.2%) and complex febrile seizure(19.2%) no study showing result different then the present study with respect to type of febrile seizure.

Regardless of the era of the study or particulars of the design; boys have consistently emerged with higher frequency of febrile seizures. Incidence ratios of boys: girls have ranged from 1.1:1 to 2:1 according to Nelson and Ellenberg [19], however in the present study; findings are in contrast to another set of large studies by Verity et al [20] 1985 who found no sex difference. Amir Salari also found no gender difference between cases and controls. NCPP study showed male predilection only among black population [19] whether there is a biological basis for the gender specific differences in febrile seizure susceptibility or whether boys just contract more fevers and therefore are at greater risk, is currently not established.

Type of febrile seizure was predominantly simple febrile seizure (72%) and complex febrile seizure (28%) in the present study, similar result was found in study of Moruskar et al[9] simple febrile seizure (69.41%) and complex febrile seizure (30.59%) and Potdar et al[10] simple febrile seizure (80.2%) and complex febrile seizure(19.2%) no study showing result different then the present study with respect to type of febrile seizure. Serum ferritin level was found less than the range 10ng in 64% of population, within the range (10-300 ng), in 36% of population, no one had serum ferritin level more than range (300 ng) in the study population of febrile seizure similar result was seen in study of

Potdar et al[10], Ghoshal et al[11], Fallah et al[12], Rehman et al[13] Bidabadi et al[14] shows serum ferritin level more than 300 ng in study population of febrile seizure. Family history in children having serum ferritin level 10-300 ng(33.3%) had positive family history seizure where has in children having serum ferritin level of less than 10 ng 10 (31.3%) had positive family history having association seizure so serum ferritin level with family history is not statically significant (p value .87)

In addition, Zareifar et al [21] indicated that in Shiraz, Iran, iron deficiency (56.6% vs. 24.8%) was more frequent in children with FS and in the FS group; Hb levels were lower than in febrile children without seizure. Akbayram et al [22] indicated that in Turkey, in children with FS, serum iron levels were lower than in the healthy children group. Kumari et al [23] indicated that in India, in FS children, iron deficiency was more frequent than in febrile children without seizure. In another Indian study, the mean of serum ferritin levels were significantly lower in FS children than in children with febrile illness but without convulsion[24].

Sherjil et al[25] indicated that in Pakistan, in children with FS, iron deficiency anemia was more frequent than in febrile children without seizures (31.58% vs. 19.6%). In a study conducted in Islamabad, children with FS had hemoglobin, hematocrit, and serum ferritin level that were significantly lower than in febrile children without seizures [13]. In a Canadian study, iron deficiency (9% vs. 5%) and iron deficiency anemia (6% vs. 4%) were more frequent in children with FS and the odds ratio for iron deficiency in patients with FS was 1.84[26]. In present study children with serum ferritin level of less than 10 ng 29 (90.6%) had GTCS where as 3 (9.4%) had focal seizure in children with serum ferritin level of 10 - 300 ng, 11 (61.1%) had focal seizure and 7 (38.9%) had GTCS it clearly indicate that there is statically significant association of GTCS with low serum ferritin level of less than 10 ng.

Conclusion

Age, association of type of seizure (GTCS versus Focal) and cause of fever were significantly related to serum ferritin levels. Larger studies are needed to confirm the findings.

Author's contribution

First and second author were major contributor in the collection of data and planning of study, while third and fourth author helped in compilation of data.

What this study adds to existing knowledge?

Present study adds that association of type of seizure (GTCS versus Focal) and serum ferritin levels have a significant relationship.

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