

A CLINICAL CO-RELATION OF FEBRILE SEIZURE AND IRON DEFICIENCY ANEMIA IN HOSPITALIZED CHILDREN FROM A TERTIARY CARE HOSPITAL OF ODISHA, INDIA.

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ABSTRACT

Background: Febrile seizures (FS) are the most common neurologic disorder in the pediatric age group. Frequency of simple febrile seizure in India is 10-17%, which is higher than the developed countries. Iron deficiency is one of the most prevalent nutritional problems in developing countries. The mean age of presentation of iron deficiency anemia and FS is almost similar. So this study is undertaken to find any association between these two factors.

Materials and methods: This Cross sectional, hospital-based study was conducted in Department of Pediatrics, MKCG Medical College & Hospital, Berhampur, Odisha during the period of October 2018 to September 2020. The case selection was done as per the predesigned proforma. Sample size taken was 105. The p value of less than 0.05 was considered as significant.

Result: Majority of cases belonged to lower socio-economic group. The blood parameters showed that majority of the cases had MCV, MCH and Serum Ferritin level lower than the normal level.

Conclusion: Though FS is a benign condition, identification of the underlying cause is very much essential to prevent morbidity, for planning out of proper management guideline and prevention of future recurrences of FS.

Keywords: Febrile seizure, Iron deficiency anemia, Serum Ferritin

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INTRODUCTION

Febrile seizures are defined as events in infancy or childhood which usually occur between the age group of three months and five years and are associated with a fever, but without evidence of intracranial infection or a defined cause for the seizure ¹. Febrile seizures are the commonest neurologic disorder among the pediatric age group, which affects nearly about 2–5% of children². Frequency of simple febrile seizure in

India is 10-17%, which is higher than the developed countries like Japan (9-10%), Western Europe and USA (2-7%) and in Guam (14%)³. Iron plays a vital role in the metabolism of several neurotransmitters. It has been found that in case of iron deficient state, aldehyde oxidases and monoamine are reduced. The expression of cytochrome C oxidase, which is a marker of neuronal metabolic activity, is decreased in iron deficiency. In developing countries, out of all nutritional deficiency conditions, Iron deficiency is one of the most prevalent nutritional problem. In developing countries 46–66% of all children under 4 years of age are anemic, with half of the prevalence attributed to iron-deficiency anemia.⁴ Many studies have clearly demonstrated the effect of iron on development, cognition, behavior and neurophysiology, and especially on brain metabolism, neurotransmitter function and myelination. It has been seen that, Iron-deficiency anemia is common during the second and third years of life and is mostly associated with different developmental and behavioral impairments; hence it can influence motor and cognitive skills. Because iron is important for the function of various enzymes and neurotransmitters in the central nervous system, low levels of Serum Ferritin may lower the seizure threshold⁴.

MATERIALS AND METHODS

This Cross sectional, hospital-based study was conducted in Department of Paediatrics, MKCG Medical College & Hospital, Berhampur, Odisha during the period of October 2018 to September 2020. The case selection was done as per the predesigned proforma. Sample size calculated as 105 taking into consideration of the formula Sample size = $4pq/n^2$ & [p = prevalence of FS (7%), q = 1-p, n = Permissible error (5%)]. 105 children aged more than 3 months to 60 months admitted to the pediatric episode of febrile seizure were enrolled as cases (As per the inclusion & exclusion criteria).

INCLUSION CRITERIA:

- Aged between 3 months to 60 months
- Fever (Documented by thermometer) $>37^{\circ}\text{C}$ or 99°F in Axilla
- Seizure in infancy & childhood associated with fever.
- Child is otherwise neurologically healthy without any neurological abnormality before and after episode of seizure.

EXCLUSION CRITERIA:

- Children with a history of seizure disorders, central nervous system infections, afebrile seizure
- Children with developmental delay, and/or neurologic deficit.
- On Iron therapy, epileptogenic drug within the past month

STATISTICAL ANALYSIS

The data were analyzed with the SPSS version 21 software. Chi-square is used for discrete variables and unpaired t test for continuous variable. The $p < 0.05$ is considered as significant ($p < 0.05$)

RESULTS**Table-1: Socio-demographic parameters of febrile seizure**

Sl. No.	Parameters		Number	Percentage(%)
1	Gender	Male	75	71.4
		Female	30	28.6
2	Age(month)	3m-<12m	33	31.4
		12m-<36m	61	58.1
		36m-60m	11	10.5
3	Family history	Present	40	38.1
		Absent	65	61.9
4	Socioeconomic status	Upper	6	5.7
		Middle	37	35.2
		Lower	62	59.1

Table-1 shows that out of 105 children, majority were male 75(71.4%). Most of them were in the 1yr-<3yr age group (58.1%) with the mean age of cases being 18.96±12.025 months. Among the febrile seizure patients majority (61.9%) were not having any positive family history & around 62 (59.1%) children belonged to lower socio-economic status.

Table-2: Febrile seizure related parameters

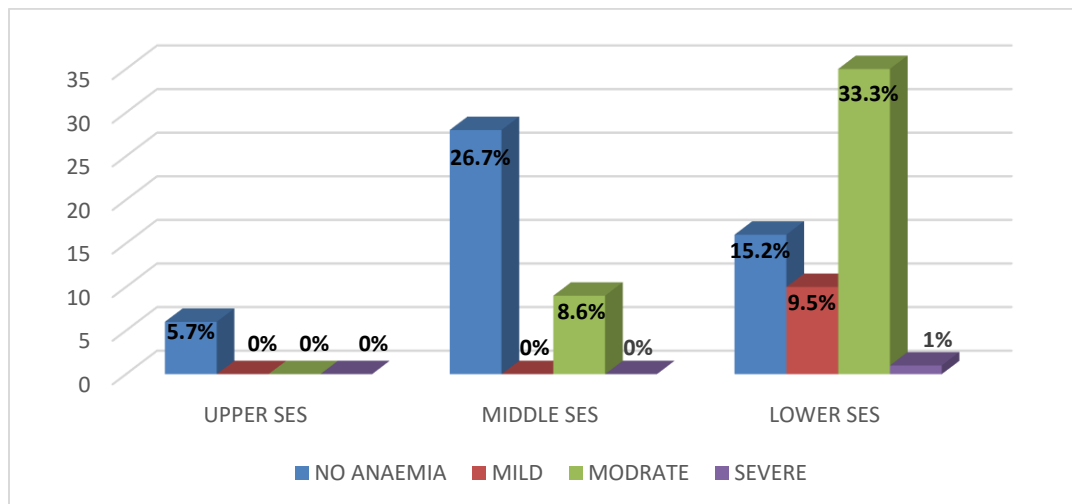
Sl. No.	Parameters		Number	Percentage(%)
1	Temperature(⁰ F)	100-<101	5	4.8
		101-<102	31	29.5
		102-<103	48	45.7
		103-104	21	20
2	Time of FS from onset of fever(Hr)	<24hr	58	55.2
		24-72hr	43	41
		>72hr	4	3.8
3	PEM wise FS distribution	NORMAL	76	72.4
		MAM	27	25.7
		SAM	2	1.9

Table-2 shows that out of 105 children, most of them i.e. 48(45.7%) were having temperature of 102-<103⁰F & most of them i.e. 58 (55.2%) children developed seizure within 24hr of fever onset. Majority of the children i.e. 76 (72.4%) children were having normal nutritional status.

Table-3: Blood parameters

Sl. No	Parameters	Number	Percentage(%)	MEAN \pm SD	
1	ANAEMIA IN FS	50	47.6	8.91 \pm 1.12	
		55	52.4	12.172 \pm 1.12	
2	MCV	<70	55	52.4	62.10 \pm 4.54
		>70	50	47.6	81.88 \pm 2.98
3	MCH	<27	78	74.3	23.56 \pm 2.07
		27-33	27	25.7	30.08 \pm 1.94
4	Ferritin	<30	56	53.3	12.18 \pm 6.08
		>30	49	46.7	75.15 \pm 24.16

Table-3 shows that majority of febrile seizure cases i.e 55 (52.4%) children were having haemoglobin level >11 gm/dl with a mean \pm SD of (12.17 \pm 1.12) & majority of cases 55 (52.4%) were having MCV <70 fl with a mean \pm SD MCV of 62.10 \pm 4.5. Out of all cases most of the children 78 (74.3%) were having MCH <27 pg with mean \pm SD MCH of 23.56 \pm 2.07 and majority of the cases i.e. 56 (53.3%) children were having S. ferritin <30 with mean \pm SD of Serum ferritin of 12.18 \pm 6.08.

Fig-1:**SES wise distribution of anaemia in febrile seizure**

The above fig shows that most children (33.3%) were having moderate anemia. 9.5% and 1% of low SES were having mild and severe anemia respectively. p value was significant (<0.05).

DISCUSSION

Our study shows 75(71.4%) children are male compare to female 30(28.6%); boys have consistently emerged with higher frequency of febrile seizures. However present study finding are in contrast to another set of large studies by Yerushalmy et al⁵, 1969 and Verity et al⁶, 1985 who found no sex

difference. Most of the children i.e. 61(58.1%) are in 1yr-<3yr comparable to the other studies. Alfredo Piscane et al ⁷ and studies done by Vasvani RK et al ⁸ who found the mean age of FS as 15 & 18 months respectively. Several studies done by Iwasaki N et al, Nakayama J et al and Audenaert D et al suggest a dominant mode of inheritance of FS, but our study found that majority of cases were having no family history of FS which need to be further studied. This study shows 62(59.1%) children belongs to lower socio-economic status in contrast to study conducted by Eden AN et al in an urban setting with an equal mix of lower and middle SES groups ⁹.

Majority of cases 48(45.7%) admitted with an initial temperature of 102⁰F-103⁰F. Animal studies suggest a possible role of endogenous pyrogens such as interleukin 1 by influencing neuronal excitability, may link fever and seizure activity ¹⁰. In most of the children, seizure started within 24 hrs of fever onset i.e. 58(55.2%) cases. The shorter the duration of recognized fever, the higher is chance of recurrence. A study done by Margriet van Stuijvenberg et al ¹¹, shows that half of the recurrences of febrile seizure during a subsequent episode of fever occur within the first 2 hours of fever. Accordingly, other studies on febrile seizure show that a substantial part of the seizure recurrences occurs early in the episode of fever and recurrences of febrile seizure are often the presenting symptom of a feverish illness¹¹

Most of the children i.e. 76(72.4%) children with FS were having normal malnutrition. Hendrickse et al¹² and Familusi et al¹³ noted that convulsion was more frequent in well-nourished than in malnourished children.

Our study shows that most of the cases i.e. 50(47.6%) have haemoglobin distribution of Hb <11gm/dl. The mean Hb level found to be 10.46±1.97 among total FS cases which corroborates with study done by Nigade et al¹⁴.

Among 105 cases, 55(52.4%) children had MCV <70 fl & Mean 62.10 ± 4.54. The Mean Total was found to be 71.2±11.72. Distribution of MCH among 105 cases shows 78 (74.3%) children had MCH <27 pg & Mean 23.5679 ± 2.07 with a Mean Total MCH of 25.24±3.51.

The percentage distribution of Serum Ferritin among 105 cases shows that 56 (53.3%) children had <30ng/ml & Mean 12.18 ± 6.08. The Mean Total Serum Ferritin is found to be 41.57±35.85. In the present study, IDA in children with FS is more frequent than those with Febrile illness, thus suggesting Iron deficiency as risk factor for first FS. Daoud et al¹⁵ observed a significantly lower plasma ferritin level in the first FS group than in the reference group proving that Plasma Ferritin is a sensitive, specific and reliable measurement for determining iron deficiency at an early stage, and it may be the best indicator of total body iron status. Vaswani et al¹⁶ observed significant low serum ferritin levels in children with FFS than in controls. Similar results were observed by Pisacane et al. Kumari PL et al¹⁷ found highly significant association between iron deficiency and simple FS.

The relationship of anameia in different socio-economic status shows that out of 32 children of

lower SES 16(15.2%) children, 10(9.5%) children, 35(33.3%) children, 1(0.9%) had no anaemia, mild, moderate & severe anaemia respectively. Similarly, out of 37 children of middle SES 28(26.6%) children, 0 children, 9(85.7%) children, 0 children had no anaemia, mild, moderate & severe anaemia respectively. Similarly out of 6 children of upper SES all 6(5.7%) children had no anaemia. P value found to be significant for this study.

CONCLUSION-

Febrile seizure is a benign convulsive disorder. Still identification of the underlying cause of FS is very much essential. Though Iron deficiency anemia has an important correlation with febrile seizure, incidence is more associated with low age group from 1yr – 3yr with mean age of about 19 month. There is a male preponderance among the FS cases. Maximum FS cases (55.2%) developed seizure within 24 hrs of fever onset. Higher incidence of FS is among low SES children. Most FS children are having normal nutrition 53.3% children are having IDA. Patients with febrile seizures were more likely to have low Hb%, MCV, MCH Sr. ferritin (ng/ml) were significantly higher among the children of febrile seizure.

Limitations of this study:

- Small sample size.
- Anemia other than IDA weren't found in this study. So further study may be required to know the real association of anemia % FS.
- S.ferritin is a non-specific acute phase reactant can rise in any inflammatory diseases.
- S.transferrin, TIBC, Serum Fe couldn't be done.
- Other causes of IDA not evaluated.

The result suggests that Iron deficiency anemia may be a risk factor for febrile seizures. Screening for IDA should be considered in children with febrile seizure. Iron deficiency is a significant risk factor for simple febrile seizures in children of age group 3 months to 60 months. Early detection and timely correction of iron deficiency may be helpful for prevention of simple febrile seizures in children of this age group.

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