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A STUDY OF IRON DEFICIENCY ANAEMIA IN CHILDREN BETWEEN 6 MONTHS AND 5 YEARS OF AGE PRESENTING WITH FEBRILE SEIZURE IN A TERTIARY HEALTH CENTRE OF CENTRAL INDIA

Paediatrics

Dr. Ajay Kasumbiwal Associate Professor, Paediatrics, SVNGMC, Yavatmal.

Dr. Keerthi Krishnakumar* Junior Resident, Department of Paediatrics, SVNGMC, Yavatmal. *Corresponding Author

ABSTRACT

Background: Febrile seizures (FS) are the most common type of seizures in children. The relationship between iron deficiency anaemia (IDA) and first FS has been examined in several studies with conflicting results. The present study was undertaken to assess the IDA in children between 6 months to 5 years of age presenting with FS. **Method:** Total 108 children were included in the study during a period of 2 years from January 2021 to December 2022. A detailed history was taken, and laboratory investigations were done. **Results:** The mean age of onset of FS was 24 months, with early onset between 6 months to 1 year (35.2%) with male predominance (56.50%). Simple FS were more common (85.2%) than complex FS (14.8%). The mean length of seizures was 6.42±2.54 min. Upper respiratory tract infection was the commonest trigger of FS (51.90%). Maximum children had temperature between 102 to 103 0F (40.7%). The prevalence of IDA was 58.3%. In children with IDA, recurrent episodes of FS were more frequent, and duration of seizure was longer (7.55±3.56 min). Among 108 cases, 74(68.5%) patients had hypochromic microcytic peripheral smears, while 34(31.5%) had normocytic normochromic peripheral smears. **Conclusion:** IDA was more frequent in children with FS, and which may be a risk factor for development of FS. Screening for IDA should be considered in children with FS. All the laboratory investigations carried out to evaluate IDA were significantly lower, this suggests that iron deficient children are more prone for FS. Early detection and iron supplementation in children who are at risk of developing iron deficiency might prevent FS.

KEYWORDS

Febrile seizures; Iron deficiency anaemia; Upper respiratory tract infection; Complex; Smears

INTRODUCTION

A febrile seizure (FS) is defined by the International League Against Epilepsy (ILAE) as a seizure that occur in association with a febrile illness (FI), in between the ages of 6 and 60 months (peak 12 to 18 months) with a temperature of 38^{0}C (100. ^{0}F) or higher, that are not the result of CNS infection or any metabolic imbalance, and that occur in the absence of a history of prior afebrile seizures [1]. However, febrile seizures are classified as simple or complex. A simple febrile seizure is a primary generalised, usually tonic-clonic, attack associated with fever, lasting for a maximum of 15 min, and not recurrent within a 24-hour period [1, 2]. Frequency of simple febrile seizure in India is 10-17%, which is more than the developed countries like USA (2-7%) and Japan (9-10%) [3, 4]. A complex febrile seizure is more prolonged (> 15 min), and/or is focal, and/or recurs within 24 hours. Febrile status epilepticus is a FS lasting longer than 30 min [1, 2].

Earlier studies have identified various risk factors for FS, including developmental delay, family history of FS, discharge from a neonatal unit after 28 days, day care attendance, viral infections, certain vaccinations, and nutritional deficiencies, including iron and zinc [5, 6]. Moreover, many studies have clearly demonstrated the effect of iron on development, cognition, behaviour, and neurophysiology, and especially on brain metabolism, neurotransmitter function and myelination [7]. IDA is common during the second and third years of life and has been variably associated with developmental and behavioural 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 serum levels of ferritin may reduce the seizure threshold [8]. Neurological symptoms such as poor attention, weak memory, delayed motor developmental and behavioural disturbance caused by iron deficiency anaemia are well-known [9].

Although studies have also observed that fever aggravates the negative effects of iron deficiency on the brain: that is iron deficient children may have an increased risk of occurrence of febrile seizures and may also influence the type and duration or recurrence of seizures [10]. So, it could be possible that IDA may predispose to other neurological disturbances like irritability, weak memory etc. along with FS. The observed percentage of FS is 2 to 4% of all infants and that of recurrence in children with less than 1 year of age is around 50% and 28% for those older than 1year of age [11]. Majority of the cases of FS are found to occur in age group 14 to 18 months, which directly overlaps with the age group of 6 months to 24 months which points to some relationship between both [12].

Several forms of evidence both in animal models and in epidemiological studies led to the hypothesis that iron deficient state could have a role in the onset of FS. However, some studies indicated that iron deficiency with or without anaemia was more prevalent in children with FS [13,14]. While others have found no association between iron deficiency and FS [15, 16]. Keeping in view the difference of opinion, the present study was planned to find out the prevalence of IDA in FS patients in a tertiary health centre of central India.

MATERIALS AND METHODS

After obtaining Institutional Ethical Committee approval and written informed consent from parents/guardians, this prospective observational study was conducted in the Department of Paediatrics at Tertiary Care Centre in central India during a period of 2 years from January 2021 to December 2022. Total 108 patients in the age group of 6 months to 5 years with febrile seizure were included in the study. Children on iron therapy, developmental delay, epileptic syndromes, CNS anomalies, mental or cognitive defects and infections, with seizures due to underlying organic cause (meningitis, metabolic disorders) and children whose parents were not willing to give consent were excluded from the study.

A detailed history was taken which include antenatal, natal, and post-natal risk factors history, drug history, developmental history, dietary history, onset of first seizure with its duration and type were recorded in pre structured case record form (CRF). Under aseptic precaution 2ml of blood was collected in EDTA bulb and send for following investigation and their finding was recorded in CRF. Anaemia was defined as haemoglobin, red cell indices, i.e., mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH), and mean corpuscular haemoglobin concentration (MCHC) lower than normal for age, a widened red cell distribution width (RDW) below the acceptable level for age and a peripheral smear with features s/o iron deficiency anaemia [17]. First line investigation was done in all cases. Complete blood count (CBC), haemoglobin (Hb), mean corpuscular haemoglobin (MCH), mean corpuscular volume (MCV), mean corpuscular haemoglobin concentration (MCHC) and peripheral smear, TLC and differential leukocyte count, CRP were noted.

Serum electrolytes (Na+, k+, Ca 2+) and glucose levels were measured within 12 hours of the convulsion. Normal serum sodium, potassium, and calcium levels reported by our laboratory were in the range of 137-147 mmol / L, 3.5-5.3 mmol / L, and 2.11- 2.52 mmol / L respectively. Normal serum glucose level was in the range of. 3.9-6.1mmol / L.

Statistical Analysis

The collected data were analysed using SPSS version 21.0 for

windows. For comparison of quantitative data Student 't' was used and for the comparison of qualitative data, Chi-square or Fishers exact test were used. The confidence limit for significance was fixed at 95% level with p value <0.05. P value <0.05 was considered as statistically significant.

OBSERVATIONS AND RESULTS

During the study period, a total of 108 children between 6 months to 5 years of age admitted with FS were enrolled in the study. Majority of children (40.7%) were from the age group of 1 to 3 years. The mean age and weight of children was 2.05±1.26 years and 9.78±2.33 kgs respectively with male predominance (56.50%). Maximum 46(42.6%) of children belongs to upper-lower class followed by lower-middle class 42 (38.9%) as shown in table 1.

Table 1: Socio-demographic Profile Of The Patients

Socio-demographic		No. of patients	Percentage
Age group (Years)	6 months to 1 year (Infants)	38	35.2
	1 to 3 years (Toddler)	44	40.7
	3 to 5 years (Pre-school)	26	24.1
	Mean Age	2.05 ± 1.26 years	
Gender	Male	61	56.5
	Female	47	43.5
Weight (Kgs)	<10 kg	68	64.8
	>10 kg	40	37.0
	Mean ± SD	9.78±2.33	
Socioeconomic status	Lower	03	2.8
	Upper-lower	46	42.6
	Lower middle	42	38.9
	Upper middle	13	12.0
	Upper	04	3.7

Among 108 children, 92 children were presenting with simple febrile seizures (85.2%) and 16 children were presenting with complex febrile seizures (14.8%). The mean length of seizures was 6.42±2.54 min. 19 children (17.6%) had presented with family history of FS and 7 children presented with family history of epilepsy with FS as shown in table 2. Most of the children had temperature between 102 to 103 0F (40.7%) followed by 100 to 101 0F (27.8%), 101 to 102 0F (25.9%) and 103 to 104 F (5.6%).

Table 2: Types, Duration, And Family History Of Febrile Seizure

Types and of seizures			No. of patients	Percentage
Type of febrile seizure		Simple	92	85.2
		Complex	16	14.8
Length of febrile seizure		<5 mins	75	69.4
		5 to 10 mins	22	20.3
		>10 mins	11	10.2
Family history	Febrile seizures	Present	19	17.6
		Absent	89	82.4
	Epilepsy	Present	07	6.5
		Absent	101	93.5

Upper respiratory tract infection (URTI) was the commonest trigger of febrile seizure (51.90%) as depicted in figure 1. With respect to nutritional status, it was seen that 67.6% of the children had no malnutrition whereas 23.1% of children had grade moderate acute malnutrition and 9.3% had grade severe acute malnutrition.

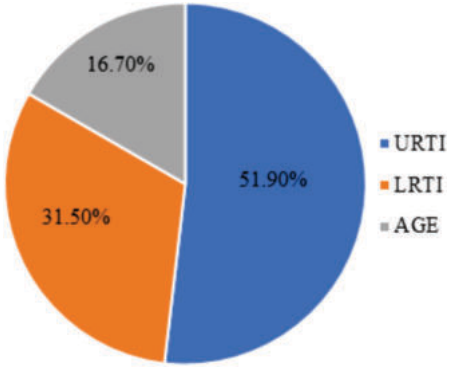

Figure 1: Etiology of fever

URTI-Upper respiratory tract infection; LRTI-Lower respiratory tract infection; AGR-Acute gastroenteritis

In the present study children with FS, all laboratory parameters were analysed documenting for iron deficiency anaemia were significantly lower as shown in table 3.

Table 3: Mean Haematological Parameters Among Children.

Variables	Mean	SD
Haemoglobin (g/dL)	9.4	1.2
Haematocrit (%)	34.22	3.23
White blood cell count (thousand/mm3)	8.99	6.13
Red blood cell count (million/mm3)	4.16	1.22
Reticulocyte count	0.733	0.66
Mean corpuscular volume (MCV) (fl)	73.3	5.1
Mean Corpuscular Haemoglobin (MCH) (pg)	24.3	4.5
Mean corpuscular haemoglobin concentration (MCHC) (pg)	26.1	3.6
Red cell distribution width (RDW) (%)	16.8	1.3
Serum ferritin (ng/ml)	29.5	21.3
Serum iron levels (µg/dl)	48.91	22.96
Total iron-binding capacity (TIBC)	433.85	125.18
Serum transferrin	248.64	64.43
Total leukocyte counts	13.82	7.11
Neutrophils	55.77	15.32
Lymphocytes	37.65	16.04
C-reactive proteins	18.40	17.85
Neutrophil-lymphocyte ratio	2.08	1.55

The prevalence of iron deficiency anemia was 58.3% as depicted in figure 2.

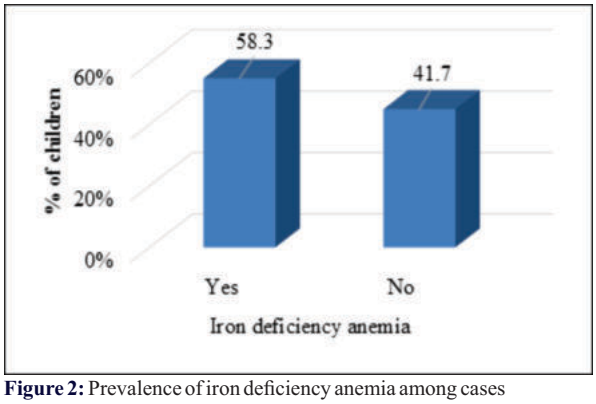

Figure 2: Prevalence of iron deficiency anemia among cases

Table 4 shows the type of febrile seizure and the duration of seizure in children with or without iron deficiency. This indicates that in children with iron deficiency, recurrent episodes febrile seizure was more frequent and the duration of seizure was longer (7.55±3.56 min).

Table 4: No. Of Episodes Of FS And Seizure Duration In Children With Iron Deficiency

Parameters		With iron deficiency	Without iron deficiency	P value
Febrile seizure	1st episode	24 (38.09%)	28 (62.22%)	0.038
	Recurrent episode	39 (61.90%)	17 (37.77%)	
	Total	63 (100.0%)	45 (100.0%)	
Duration of seizure	Mean	7.55 ± 3.56 min	5.17 ± 2.95 min	0.01

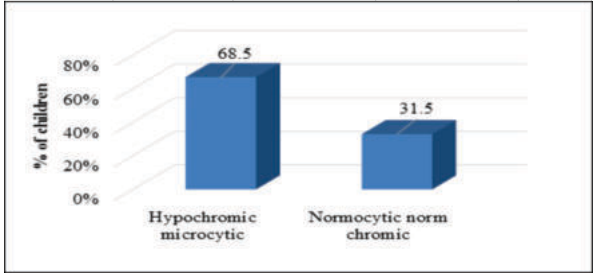

Figure 3: Peripheral blood smear examination

Among 108 cases, maximum 74 (68.5%) patients had hypochromic microcytic peripheral smears, while 34 (31.5%) patients had normocytic normochromic peripheral smears, (Figure 3).

DISCUSSION

Generally, it is noted that the most common age in which the febrile seizure and the first febrile seizure occur is second year of life. In the present study the mean age of onset of febrile seizure was 24 months, with early onset between 6 months to 1 year (35.2%). The male predominance was observed with male to female ratio of 1.56:1. These findings are comparable to the other studies [18,19]. Most of the children (64.76%) had weight <10 kgs whereas 37.03% of children had weight >10 kgs. The mean weight of children was 9.78±2.33 kgs which is comparable with the study conducted by Fallah R et al [20]. Being a rural hospital, maximum 46(42.6%) of children belongs to upper-lower class followed by lower-middle class 42 (38.9%) which is similar to the previous studies [21,22].

Recurrent episodes of febrile seizures were more common (61.9%) in patients with iron deficiency anaemia which is comparable with the study done by Ling et al [23]. Shorter the duration of recognized fever, the higher the chances of recurrence. In the present study, most of the children i.e., in 69.4% of children seizures lasted for <5 min, in 20.3% of children seizures lasted for 5 to 10 min and in 10.2% children the seizures lasted for more than 10 min. The mean length of seizures was 6.42±2.54 min. Among 108 children, 19 children (17.6%) had presented with family history of FS and 89 (82.4%) children were not having the family history of FS. Family history of epilepsy was present in 7 children with FS. According to literatures family history of FS is associated with an increased risk of recurrence [24, 25].

Among 108, 56 (51.9%) children had URTI, 34 (31.5%) had LRTI and 18 (16.7%) children had acute gastroenteritis. Thus, URTI as the commonest triggering factor of FS which is comparable with Nelson and Ellenberg [8] and Millichap et al study [26] However, the etiology of febrile convulsion varies from country to country due to different infection profile. The initial axillary temperature at admission, before prescribing anti pyretics was recorded by standardized protocol. In the current study, it was observed that most of the children had temperature between 102 to 103 0F (40.7%) followed by 100 to 101 0F (27.8%) and 101 to 102 0F (25.9%). These findings are in accordance with the study done by Nigade RM et al [18]. In the literature, the higher the peak temperature, the lower the chance of recurrence suggested by Berg et al [25], what was not established in present study. It was seen that 67.5% of the children had No malnutrition whereas 23.1% of children had moderate acute malnutrition and 9.3% had severe acute malnutrition. These findings are correlated with the previous study done by Janjale et al [27].

The mean Hb and haematocrit of the study population was 9.4±1.2 g/dL and 34.22±3.23% respectively. The mean WBC count was found to be 8.99±6.13 thousand/mm^3. Mean of total red blood cell count and reticulocyte count was 4.16±1.22 million/mm^3 and 0.733±0.66 respectively. The mean corpuscular volume (fl) was 73.3±5.1, mean corpuscular haemoglobin concentration (pg) was 26.1±3.6 and red cell distribution width (%) was 16.8±1.3%. However, in the various studies, haematological parameters suggestive of IDA was more common in FS [18, 28].

The prevalence of iron deficiency anaemia was 58.3% which is correlated with the study done by Nigade RM et al (85.88%) [18] and Fallah R et al (22%) [20]. Possible explanations for these differences in prevalence are differences in age, nutritional habit, geographic area, sample size. Children with iron deficiency, recurrent episodes of febrile seizure were more frequent (61.90%), and duration of seizure was longer (7.55±3.56 min) which is comparable with the study conducted by Fallah R et al [20]. Among the 108 cases, maximum 74 (68.5%) patients had hypochromic microcytic peripheral smears, while 34 (31.5%) patients had normocytic normochromic peripheral smears. These findings are comparable with the study done by Nigade RM et al [18] and Neyazuddin and Nistane [29].

There are some limitations of the study which includes- It was a single center study conducted in those children admitted in our tertiary care hospital; hence it will not reflect the data from entire community. The prevalence of exposure and outcome variables may be different from a community setting. Other contributing factors for febrile seizures such as iron and zinc levels were not assessed.

CONCLUSION

Based on the results of present study, iron deficiency anemia was more frequent in children with febrile seizures, and which may be a risk factor for development of febrile seizures. Screening for iron deficiency anemia should be considered in children with febrile seizure. All the laboratory investigations carried out to evaluate iron deficiency anemia were significantly lower. This suggests that iron deficient children are more prone for febrile seizures. Early detection and iron supplementation in children who are at risk of developing iron deficiency might prevent febrile seizures.

REFERENCES

1. Nelsons textbook of pediatrics:20 e: Mohamed A Mikati and Abeer J Hani; p 2829-2831.
2. Giuseppe Capovilla et al, Recommendations for the management of Febrile seizures Ad hoc Task Force of LICEGuidelines commission. Epilepsia Jan 2009:50 suppl 1:2-6.
3. Mikati MA, Hani AJ. Febrile seizures. In: Kleigman RM, Stanton BF, Geme JW, Schor NF, Behrman RE, editors. Nelson textbook of Pediatrics. 20th Ed. Philadelphia: Elsevier; 2016:2829-2831.
4. Banerjee TK, Hazra A, Biswas A, Ray J, Roy T, Raut DK, et al. Neurological disorders in children and adolescents. Indian J Pediatr. 2009; 76(2):139-46.
5. Graves RC, Oehler K, Tingle LE. Febrile seizures: risks, evaluation, and prognosis. Am Fam Physician. 2012; 85:149–53.
6. Laina I, Syriopoulou VP, Daikos GL, Roma ES, Papageorgiou F, Kakourou T, et al. Febrile seizures and primary human herpesvirus 6 infection. Pediatr Neurol. 2010; 42:28–31.
7. Madan N, Rusia U, Sikka M, Sharma S, Shankar N. Developmental and neurophysiologic deficits in iron deficiency in children. Indian Journal of Pediatrics 2011;78(1):58–64.
8. Nelson KB, Ellenberg JH. Prognosis in children with febrile seizures. Pediatrics 1978;61: 720.
9. Halliwell B. Oxidative stress and neurodegeneration: where are we now? J Neurochem. 2006 Jun 1;97(6):1634-58.
10. Idro R, Gwer S, Williams TN, Otieno T, Uyoga S, Fegan G, et al. Iron deficiency and acute seizures: results from children living in rural Kenya and a meta-analysis. PLoS One. 2010;5(11): e14001.
11. Shinnar S, Berg AT, Moshe SL, O'dell C, Alemany M, Newstein D, et al. The risk of seizure recurrence after a first unprovoked afebrile seizure in childhood: an extended follow-up. Pediatr. 1996 Aug 1;98(2):216-25.
12. Derakhshanfar H, Abaskhanian A, Alimohammadi H, ModanlooKordi M. Association between iron deficiency anaemia and febrile seizure in children. Med Glas (Zenica). 2012 Aug 1;9(2):239-42.
13. Papageorgiou V, Vargiami E, Kontopoulos E, Kardaras P, Economou M, Athanassiou-Mataxa M, et al. Association between iron deficiency and febrile seizures. Eur J Paediatr Neurol. 2015; 19:591–6.
14. Koksal AO, Ozdemir O, Buyukkaragoz B, Karaomerlioglu M, Bulus AD. The association between plasma ferritin level and simple febrile seizures in children. J Pediatr Hematol Oncol. 2016; 38:512–6.
15. Bidabadi E, Mashouf M. Association between iron deficiency anemia and first febrile convulsion: a case–control study. Seizure. 2009; 18:347–51.
16. Yousef CP, Eghbali A, Rafeie M, Sharafkhah M, Zolfi M, Firouzifar M. The relationship between iron deficiency anemia and simple febrile convulsion in children. J Pediatr Neurosci. 2014; 9:110.
17. Lanzkowsky's Manual of Pediatric Hematology and Oncology, 6th Edition: Philip Lanzkowsky, Jeffrey M. Lipton, Jonathan D. Fish: Chapter 6- Iron Deficiency Anemia: p69-83
18. Nigade RM, Khambalkar DV. Iron deficiency anaemia and its association with febrile seizures. Int J Contemp Pediatr 2018; 5:1120- 5.
19. Marol R, Marol R, Matti S, Marol R. Can we predict occurrence of febrile convulsions in children with fever by increased neutrophil-to-lymphocyte ratio and C- reactive protein? Indian J Child Health. 2020; 7(11):450-453
20. Fallah R, Tirandazi B, Akhavan Karbasi S, Golestan M. Iron deficiency and iron deficiency anemia in children with febrile seizure. Iran J Ped Hematol Oncol. 2013;3(1):200-3.
21. Majumdar R. "Iron Deficiency as a risk factor for first febrile seizure. Dissertation Submitted to the Rajiv Gandhi University of Health Sciences, Karnataka, Bangalore 2012.
22. Saha AK, Hassan MK, Kundu LC, Saha SK, Begum P, Lucky AS. Low Serum Ferritin is a Risk for Febrile Convulsion in Children; Faridpur Med. Coll. J. 2016;11(2):44-46.
23. Ling SG. Clinical characteristics and risk factors for a complex first febrile convulsion. Singapore Med J 2001; 42:264-7.
24. Verity CM, Butler NR, Golding J. Febrile convulsion in a National Cohort followed up from broth. Prevalence and recurrence in the first five years of life. BMJ 1985; 290:1307-10.
25. Berg AT. Febrile seizures and epilepsy: The contribution of epidemiology. Paediatr Perinat Epidemiol 1992; 6:145.
26. Millichap JG; Millichap JJ. Role of viral infections in the etiology of febrile seizures. Pediatr Neurol. 2006; 35(3):165-72.
27. Janjale A, Pande S, Sonawane R, Ahire N, Sonawane S. A Study of Severe Anemia in Children in a Tertiary Care Institute. MVP Journal of Medical Sciences 2018; 5(1):33-38.
28. Kumari PL, Nair MK, Nair SM, Kailas L, Geetha S. Iron deficiency as a risk factor for simple febrile seizures--a case control study. Indian Pediatr. 2012;49(1):17-9.
29. Neyazuddin and Nistane: Iron deficiency as risk factor for febrile convulsion and the association of iron deficiency anemia and febrile convulsion. Asian Journal of Medical Sciences 2022; 13(11):140-145.