

# Assessing Iron Deficiency as a Risk Factor for Febrile Seizures in Children Aged 6 Months to 5 Years in a Tertiary Care Hospital Wayanad

Dr Abhirami Harisankar<sup>1</sup>, Dr Mohan Kumar MK<sup>2</sup>, Dr Cherian NC<sup>3</sup>

<sup>1</sup>MD Pediatrics Junior Resident, Dr Moopens Medical College, Meppady, Wayanad, Kerala

<sup>2</sup>Professor, Department of Pediatrics, Dr Moopens Medical College, Meppady, Wayanad, Kerala

<sup>3</sup>Professor & HOD, Department of Pediatrics, Dr Moopens Medical College, Meppady, Wayanad, Kerala

**Abstract:** *Febrile seizure is one of the common problems in pediatric population, typically occurring between the ages of 6 months and 5 years. This study was conducted in the Department of Paediatrics, Dr Moopen's Medical College, a tertiary care hospital in Wayanad, to determine the risk of developing febrile seizure in children with iron deficiency. Based on NFHS-5 survey 2019-21, 67.1% of children between age 6 month to 59 months are affected by anemia in India. However, in Kerala, 39.4% of children aged 6-59 months have anemia, which is significantly lower than the national average. Iron significantly influences neurological processes through alterations in neurotransmitter level, specifically it reduces inhibitory neurotransmitter production while elevating excitatory neurotransmitters, thus fostering an environment prone to seizures. Case control study was conducted to know the association of iron deficiency anemia and febrile seizure.*

**Keywords:** Febrile seizure, Iron deficiency anemia, Hemoglobin, Serum ferritin

## 1. Introduction

After obtaining approval from institutional research committee and the institutional ethics committee, case control study was conducted at pediatric ward of Dr Moopens Medical College Wayanad Kerala between June 2023 to December 2024 for evaluating the association between iron deficiency anemia & febrile seizure. There hasn't been much research done in Kerala, particularly in the Wayanad population, specifically examining the association between febrile seizures and iron deficiency anemia.

Febrile seizures commonly affect children between six months to five years of age with a temperature of 100.4 °F (38 °C) or higher. These seizures are not caused by central nervous system infections (CNS). There is no universal threshold for fever to develop febrile seizures, as each child has a unique temperature threshold at which seizures may happen. [1,3,4]. The primary risk factors linked to the occurrence of febrile seizures include family history of febrile seizure, preexisting neurological disorders, developmental delays, family history of epilepsy, and maternal smoking or stress during pregnancy [2]. Generally febrile seizures resolve on their own without lasting complications. But some children with febrile seizures may have a greater likelihood of subsequently developing epilepsy if there is family history of epilepsy, focal seizure occur during febrile seizures, or the child has developmental delay [2].

Based on NFHS-5 survey 2019-21, 67.1% of children within the 6 to 59-month age group in India are affected by anemia representing a significant rise compared to the previous NFHS-4(2015-16) survey. India currently has the highest global burden of anemia. However, in Kerala,

39.4% of children aged 6-59 months have anemia, which is significantly lower than the national average.

Iron significantly influences neurological processes through alterations in neurotransmitter level specifically, it reduces inhibitory neurotransmitter production while elevating excitatory neurotransmitters, thus fostering an environment prone to seizures.[12] Increased brain excitability linked to iron deficiency has been noted, across various neurological conditions such as restless leg syndrome, breath-holding episodes, and ADHD.[13]

## 2. Materials and Methods

Case Control study design was opted & study conducted at inpatient Department of Pediatrics, Dr Moopens medical college, Wayanad, Kerala. Children aged between six months to five years presenting with acute febrile seizure were taken as cases, and children in the same age group presenting with acute febrile illness, but without seizure episodes were taken as controls. The study was conducted between June 2023 to December 2024. Based on the prevalence of febrile seizure (67.1%) and fever but no seizure (32.9%) in iron deficiency as seen in a earlier publication by Sharif MR, Kheirkhah D, Madani M, (75) (2016 Feb;) with 80% power and 95% confidence interval, total sample size estimated as 110 & the minimum. required sample size for each group-55.

The inclusion criteria were children with febrile seizure - both 1st and recurrent episode, both simple & complex febrile seizures. Children on iron supplements, chronic illness, neurodevelopment delay, CNS infection, preterm babies & history of previous afebrile seizure were excluded from study. Cases and control groups were matched for age and sex. After getting consent from the parents, clinical data collected and entered in the

proforma. After history taking and clinical examination, blood samples collected from the patients for Hb, MCV, MCHC, RDW & Serum Iron. Iron deficiency anemia was diagnosed when hemoglobin <11 g/dl, mean corpuscular volume < 70 fL, MCHC < 33 g/dL, RDW > 15% & Serum iron < 30µg/dL.

Data collected were statistically analyzed using IBM SPSS version 22. Mann-Whitney U test was used to compare non-normally distributed continuous variables between the febrile seizure and control groups, whereas the Chi-square test or Fisher's exact test was applied to compare categorical variables. Crude odds ratios (COR) with 95% confidence intervals (CI) were calculated

using binary logistic regression to assess the relationship between iron deficiency anemia and febrile seizures. A p-value of less than 0.05 was considered statistically significant.

**3.Results**

110 participants were equally divided into two groups. The study group [cases] consisted 55 children aged 6 months to 5 years who presented with febrile seizures and 55 children of the same age group with fever but no seizures in the control group.

**Table 1:** Distribution of Age and Sex among Study Participants (n=110)

Variable	Category	Frequency	Percentage
Age Group	6months-1yr	20	18.20%
	1 – 2 years	52	47.30%
	2 – 3 years	21	19.10%
	3 – 5 years	17	15.50%
Sex	Female	48	43.60%
	Male	62	56.40%

**Table 2:** Distribution of Hematological Parameters (n=110)

Variable	Median [Q1, Q3]
Haemoglobin (Hb) (g/dL)	11.9 [9, 12.6]
Mean Corpuscular Volume (MCV) (fL)	72.9 [67.67, 78]
Mean Corpuscular Hemoglobin (MCHC) (g/dL)	25.6 [23, 27]
Red Cell Distribution Width (RDW) (%)	15 [13.72, 17.8]
Serum Iron (µg/dL)	56.9 [23, 79]

Participants in the study had a median hemoglobin level of 11.9 g/dL, with an interquartile range of 9 to 12.6 g/dL. There was a median of 72.9 fL for the mean corpuscular volume and 25.6 g/dL for the mean corpuscular hemoglobin concentration. The median

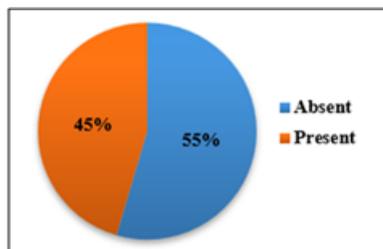
value of the red cell distribution width which measures the diversity in red blood cell size, was 15%. With an interquartile range of 23 to 79 µg/dL, the median serum iron level was 56.9 µg/dL.

**Table 3:** Iron deficiency anemia among study participants (n=110)

Iron Deficiency Anaemia	Frequency	Percentage	95% C.I
Absent	60	54.50%	45.2% to 63.5%
Present	50	45.50%	36.5% to 54.8%

Iron deficiency anemia (IDA) among the study participants was 45.5% (95% CI: 36.5% to 54.8%),

while 54.5% (95% CI: 45.2% to 63.5%) of study participants did not have IDA.



**Figure 1:** Iron deficiency anemia among study participants (n=110)

**Table 4:** Association between Febrile Seizures and Iron deficiency anemia Among Study Participants (n=110)

Variable	category	Febrile seizure n (%)	Fever, no seizure n (%)	ODDS ratio	95% CI	p Value
Iron deficiency anemia	Absent	17 (28.3%)	43 (71.7%)	8.01	(3.45 - 18.61)	<0.001
Iron deficiency anemia	Present	38 (76.0%)	12 (24.0%)			

Out of 110 children, 38 children with febrile seizure had iron deficiency anemia & 12 without seizure had iron

deficiency anemia. 17 children with febrile seizure had no anemia & 43 children with no seizure had no anemia.

Iron deficiency anemia (IDA) among the study participants was 45.5% (95% CI: 36.5% to 54.8%),

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**Table 5:** Association between febrile seizure & other factors among study participants (n=110)

Variable	Category	Febrile seizures n[%]	Control n[%]	ODDS ratio	95% CI	pValue
Age	6 months -1 year	13 (65.0%)	7 (35.0%)	13.93	(2.36 - 82.04)	<b>0.002†</b>
	1 - 2 years	31 (59.6%)	21 (40.4%)	11.07	(2.30 - 53.31)	
	2 - 3 years	9 (42.9%)	12 (57.1%)	5.63	(1.04 - 30.50)	
	3 - 5 years	2 (11.8%)	15 (88.2%)		1	
Sex	Female	22 (45.8%)	26 (54.2%)		1	0.442
	Male	33 (53.2%)	29 (46.8%)	1.34	(0.63 - 2.86)	
<b>Iron Deficiency Anaemia</b>	<b>Absent</b>	<b>17 (28.3%)</b>	<b>43 (71.7%)</b>	<b>8.01</b>	<b>1 (Reference)</b>	<b>&lt;0.001</b>
	<b>Present</b>	<b>38 (76.0%)</b>	<b>12 (24.0%)</b>		<b>8.01 (3.45 - 18.61)</b>	
Past History of Febrile Seizure	No	41 (43.6%)	53 (56.4%)	8.12	1 (Reference)	<b>0.002</b>
	Yes	14 (87.5%)	2 (12.5%)		(1.69 - 38.98)	
Family History of Febrile Seizure	No	46 (46.9%)	52 (53.1%)	3.35	1 (Reference)	0.124
	Yes	9 (75.0%)	3 (25.0%)		(0.81 - 13.88)	

Children aged 6 months to 1 year had 13.93 times higher odds (95% CI: 2.36 - 82.04) of experiencing febrile seizures compared to those aged 3–5 years without iron deficiency anemia, while those in the 1–2 year age group the odds was 11.07 times higher (95% CI: 2.30 - 53.31, (p = 0.002). Sex difference was not significantly associated with febrile seizures, with males having 1.34 times higher odds compared to females (p = 0.442). Notably, iron deficiency anemia emerged as a strong risk factor, with children who had iron deficiency anemia showing 8.01 times higher odds (95% CI: 3.45 - 18.61) of febrile seizures compared to those without it (p < 0.001). A past history of febrile seizures was another significant risk factor, with affected children having 8.12 times higher odds of experiencing another episode (p = 0.002). Family history of febrile seizures, although more common among cases (75.0%), was not statistically significant in this study. (p = 0.124).

#### 4. Discussion

Iron deficiency is one of the most common dietary issues in underdeveloped nations, particularly in infants between the ages of 6 and 24 months. Iron deficiency anemia accounts for half of anemia in underdeveloped nations, where 46–66% of all children under 4 are anemic. Iron's impact on development, cognition, behavior, and neurophysiology particularly on brain metabolism, neurotransmitter function, and myelination has been amply shown in several researches. Motor and cognitive skills may be impacted by iron-deficiency anemia, which is prevalent in the second and third years of life and has been inconsistently linked to behavioral and developmental abnormalities.

A total of 110 children were included for the study, 55 patients who experienced febrile seizures, aged between 6 months and 5 years as case group. The control group consisted of 55 children in the same age range who had fever but did not experience seizures. In our study the age group of 1–2 years included 47.3% of the study participants, followed by 2–3 years (19.1%), <1 year (18.2%), and 3–5 years (15.5%). In terms of sex distribution, there were more boys (56.4%) than girls (43.6%). In the study by Syed et al, out of 150 patients, 75 cases and 75 controls each, with a mean age of 3.41 ±

1.51 years. The reason of higher mean age group in his study was, he included the children up to 6 years of age. 83 (55.3%) of these patients were male. [63].

Hussain et al.'s study [69] revealed that out of the 60 children enrolled 28 (46.6%) were boys and 32 (53.4%) were girls, indicating a boy to girl ratio of 1:1. The mean age of the case group was 2.93 ± 1.23 years, while the control group's was 3.0 ± 1.31 years. 39 (65.0%) of the patients were between the ages of 1-3yrs. In our study 47.3% of the study participants were between the ages of 1 and 2 years, followed by those between the ages of 2 and 3 (19.1%).

The results in our study showed a significant association between age and the odds of experiencing febrile seizures, with children aged <1 year exhibiting 13.93 times higher odds and children aged 1-2 years showing 11.07 times higher odds compared to those aged 3-5 years.

In the study by Syed et al, the average TIBC was 412.59 ± 43.67 µg/dL, while the average serum iron level was 79.09 ± 41.86 µg/dL [63]. In our study serum iron levels had a median of 56.9 µg/dL with an interquartile range of 23 to 79µg/dL.

In our study Iron deficiency anemia emerged as a strong risk factor, with children who had iron deficiency anemia showing 8.01 times higher odds (95% CI: 3.45 - 18.61) of febrile seizures compared to those without it (p < 0.001). A past history of febrile seizures was another significant risk factor, with affected children having 8.12 times higher odds of experiencing another episode (p = 0.002). The study by Hussain et al showed 11(36.7%) children in the febrile seizure group had IDA, compared to four (13.33%) children in the control group (febrile illness without seizures). With a significant P value of 0.037 and an odds ratio of 3.76, there is a positive correlation between IDA and febrile seizures [69].

On comparison of Hematological Parameters Between Febrile Seizure and Control Groups showed that Children with febrile seizures had significantly lower hemoglobin (10.0 [8.7, 12.0] g/dL vs. 12.5 [11.9, 13.0] g/dL, p < 0.001), mean corpuscular volume (68.0 [66.7,

75.0] fL vs. 76.0 [72.7, 78.0] fL,  $p < 0.001$ ), mean corpuscular hemoglobin concentration (23.1 [22.4, 27.0] pg vs. 26.5 [25.5, 27.0] g/dL,  $p = 0.004$ ), and serum iron levels (23.9 [19.9, 71.0]  $\mu\text{g/dL}$  vs. 76.0 [54.8, 85.8]  $\mu\text{g/dL}$ ,  $p < 0.001$ ). Additionally, the red cell distribution width (RDW) was significantly higher in the febrile seizure group (17.0 [15.0, 17.8] % vs. 13.8 [12.9, 14.8]%,  $p < 0.001$ ).

Our study results shed important light on the relationship between IDA and febrile seizures in children between the ages of six months to five years. IDA may be linked to a higher risk of febrile seizure in children, according to a 2017 meta-analysis by Kwak et al. [52]. A study conducted in 2021 by Chaudhury et al. [77] also showed a similar link, highlighting the significance of early detection and treatment of IDA in order to possibly lower the occurrence of febrile seizure.

## 5. Conclusion

Our study revealed that iron deficiency anemia is significantly associated with febrile seizures. Children with iron deficiency anemia had higher odds of having febrile seizure than children without iron deficiency anemia. As the prevalence of iron deficiency anemia is high in our country, preventing iron deficiency anemia may have an impact on the occurrence of febrile seizure. More research is needed to determine whether correcting iron deficiency is linked to lowering this risk. Regular checking for iron deficiency can be done and it will make the physician more alert to the occurrence of febrile seizures in patients with iron deficiency.

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Dr. Moopen's  
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## Institutional Ethics committee

Registered Under rules 8, 9, 10 and 14 of the New Drugs and Clinical Trials Rules 2019 and the Drugs and Cosmetics Act, 1940. Registration No. ECR/920/Inst/KL/2017/RR-20.

### Chairperson

Prof. Dr. Girish Menon Ramachandran  
MS, MCh, PDF

### Member Secretary

Dr. Joshima Janardhanan, MD

### Members

Dr. Ravindran.C.MD  
Dr. Jayadev B Betkerur, MD  
Dr. Aneesh Basheer, MD, ACME, FAIMER  
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Dr. Shanavas Palliyal, MDS  
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Dr. Cheriyan N.C, MD  
Dr. K.P Pradeep Kumar, MBBS  
Adv. P.Chathukutty, LLB  
Mr. Yahyakhhan Thalakkal  
Ms. Pushpa K  
Ms. T.Latha Kumar

Ref. No: IEC-SC/DMMC/May/ 2023 - 26

Date : 06/07/2023

### Communication of Decision of the Institutional Ethics Committee ( IEC )

This is to certify that the project, entitled "ASSESSING IRON DEFICIENCY AS A RISK FACTOR FOR FEBRILE SEIZURES IN CHILDREN AGED BETWEEN 6MONTHS TO 5YRS IN A TERTIARY CARE HOSPITAL IN WAYANAD: A CASE- CONTROL STUDY" submitted by Dr. Abhirami, Junior Resident ( MD 1<sup>st</sup> Year ) – Paediatrics of Dr.Moopen's Medical College has been approved by the Institute Ethics Committee (IEC) (Human Studies) held on 03<sup>rd</sup> June 2023.

### Guide Details:

1. Dr. Manoj Narayanan, Professor, Department of Paediatrics, Dr. Moopen's Medical College.

### Terms and conditions:

1. This certificate is valid for three years from the date of issue.
2. Patient informed consent need to be taken for enrolling in this study.

### Dr. Moopen's Medical College

Transforming Knowledge into Life: Wayanad Institute of Medical Sciences

Naseera Nagar, Meppadi (P.O), Wayanad, Kerala, India - 673577

medcollege@drmoopenismc.ac.in www.drmoopenismc.ac.in

+91 4936 287 200