E-ISSN: 2706-8927
P-ISSN: 2706-8919
www.allstudyjournal.com
IJAAS 2024; 6(11): 31-34
Received: 22-08-2024
Accepted: 30-09-2024

Omar Muayad Obaid
MB.CH.B, CABP, Al-Mahmodyiah General Hospital, Baghdad-Al Karkh Health Directorate/Ministry of Health, Iraq

Manaf Muwafak Ahmed
MB.CH.B, CABP, Al-Mahmodyiah General Hospital, Baghdad-Al Karkh Health Directorate/Ministry of Health, Iraq

Saad H Mohammed
MB.CH.B, CABP, DM (Echo), Al-Mahmodyiah General Hospital, Baghdad-Al Karkh Health Directorate/Ministry of Health, Iraq

Corresponding Author:
Omar Muayad Obaid
MB.CH.B, CABP, Al-Mahmodyiah General Hospital, Baghdad-Al Karkh Health Directorate/Ministry of Health, Iraq

Evaluation of the association between iron deficiency anemia and febrile convulsions in children at Al-Mahmodyiah General Hospital: A case-control study

Omar Muayad Obaid, Manaf Muwafak Ahmed and Saad H Mohammed

DOI: https://doi.org/10.33545/27068919.2024.v6.i11a.1290

Abstract

Background: Febrile seizures (FS) are the most common seizures in young children, often occurring with fever but without an underlying central nervous system infection. Iron deficiency anemia (IDA), a widespread nutritional issue, has been suggested as a potential risk factor for febrile convulsions (FC), but the association remains unclear. This study aimed to assess the relationship between IDA and FC in children at Al-Mahmodyiah General Hospital, to inform prevention strategies.

Methods: This hospital-based case-control study was conducted from January 2022 to January 2023 at Al-Mahmodyiah General Hospital. It included 134 children aged 6–60 months, divided into a case group (65 children with febrile convulsions) and a control group (69 children with fever but no convulsions). Data on demographic factors, clinical presentation, and hematological and biochemical parameters, including ferritin and total iron-binding capacity (TIBC), were collected and analyzed.

Results: Febrile convulsions were more common in males than females, with the highest incidence observed between the ages of 2 and 3 years. The mean temperature at which convulsions occurred was 38.98±0.6 °C, and the primary cause of fever was upper respiratory tract infections. The case group had a significantly lower mean hemoglobin (Hb) level than the control group (9.78±1.7 mg/dL vs. 12.62±1.22 mg/dL, respectively). Serum ferritin levels were also significantly lower in the case group (12.51±2.41 ng/mL vs. 32.21±8.7 ng/mL). Additionally, total iron binding capacity (TIBC) was significantly higher in the case group compared to the control group (417.79±79.5 mcg/dL vs. 377.54±62.11 mcg/dL).

Conclusions: This study found a significant association between iron deficiency anemia and febrile convulsions. Screening for and managing IDA in children with febrile convulsions could help reduce risk. Further studies with larger sample sizes are recommended to clarify the relationship and improve preventive strategies.

Keywords: Association, febrile convulsion, iron deficiency anemia, and childhood seizure

Introductions

Febrile seizures (FS) are the most common form of seizures in young children, affecting between 2% to 5% of children aged six months to five years [1]. FS are defined as convulsions occurring in association with fever but without an underlying central nervous system infection or metabolic imbalance [2]. A typical febrile convulsion (FC) presents as a generalized tonic-clonic seizure lasting less than 15 minutes and does not recur within a 24-hour period. It usually occurs at a body temperature of 38 °C or higher. Atypical febrile convulsions, however, may involve focal or lateralized seizures, last longer than 15 minutes, or recur within a day [3]. Despite their frequency, the exact etiology of FS remains unclear, suggesting it is likely multifactorial, with contributing factors including the rate of temperature elevation, viral infections, genetic predispositions, and certain prenatal exposures [4].

Among the potential factors associated with FS is iron deficiency anemia (IDA), the most widespread nutritional deficiency globally, affecting various populations, especially young children [5]. Iron, a crucial micronutrient, plays a significant role in cellular metabolism, neural development, and immune system function. Insufficient iron levels have been associated with a spectrum of developmental impairments, including cognitive and behavioral issues as well as weakened immune defenses [6]. Research has shown that low iron levels might contribute to an increased risk of seizures by altering neuronal excitability, although findings regarding the connection between IDA and FS remain mixed.

While some studies suggest that IDA may be a risk factor for FS, others do not support this association or even suggest a possible protective role of IDA against FS, highlighting the need for further research to clarify this relationship [7, 8].

Given these conflicting findings, the current study aims to evaluate the association between iron deficiency anemia and febrile convulsions in children admitted to Al-Mahmodyiah General Hospital. By identifying whether IDA serves as a risk factor or protective factor for FS, this research seeks to inform healthcare professionals and contribute to more effective prevention strategies. The findings could have significant implications for pediatric health policies and clinical practices, especially in resource-limited settings where IDA is prevalent [9].

Patients and Methods

Study Design, Setting, and Timing: This study was a hospital-based, case-control study conducted in the emergency department of Al-Mahmodyiah General Hospital. Data collection took place from January 1, 2022, to January 1, 2023.

Study Population and Sample Size: The study population consisted of children aged 6 to 60 months who presented to the emergency department with febrile illnesses. A total of 134 participants were included, divided into two groups: the case group (65 children with typical febrile convulsions) and the control group (69 febrile children without convulsions). The sample size was determined based on power calculations, targeting a minimum sample size that would allow the detection of statistically significant associations between iron deficiency anemia and febrile convulsions, with an expected effect size derived from previous literature.

Inclusion and Exclusion Criteria: Children with simple febrile seizures, defined as tonic-clonic convulsions lasting no more than 15 minutes, without recurrence within the same febrile episode, were included in the study. Exclusion criteria comprised children with a history of central nervous system infections, recurrent seizures, developmental delays, neurologic deficits, complex febrile convulsions, and convulsions lasting longer than fifteen minutes.

Sampling Method: Participants were selected using a consecutive sampling method, where children presenting with febrile illnesses were screened for eligibility based on the inclusion and exclusion criteria. Cases were recruited from those who experienced febrile convulsions, while controls were selected from febrile children without convulsions.

Data Collection Methods: Data were collected through structured interviews, medical record reviews, and laboratory tests. A thorough history was obtained for each participant, detailing demographic factors (age, gender), clinical presentation, seizure characteristics, family history of epilepsy or febrile convulsions, and underlying illness. Blood samples were collected to assess iron status, including hemoglobin concentration (HB), mean corpuscular volume (MCV), mean corpuscular hemoglobin concentration (MCHC), red blood cell distribution width (RDW), plasma ferritin (PF), and total iron-binding capacity (TIBC). Laboratory assessments were conducted using standardized equipment, with instruments calibrated regularly to ensure reliability and validity.

Ethical Considerations: Approval for this study was obtained from the hospital's ethics committee. Informed consent was obtained from the parents or legal guardians of all participants prior to enrollment, ensuring they understood the study’s purpose, procedures, and potential risks and benefits. Data confidentiality was strictly maintained, and only anonymized data were used for analysis.

Data Management and Statistical Analysis: Data were analyzed using SPSS software for Windows, version 26. Quantitative data were expressed as means, standard deviations, medians, and ranges. The Student's t-test was used to compare the mean values of continuous variables between groups, while the chi-square test was applied to compare categorical data. Missing data were addressed through listwise deletion when minimal and imputation methods for any larger missing patterns. Significance was set at a p-value < 0.05.

Results

The current study includes 134 child divided into two groups, 65 child with fever and convulsion, and 69 child with fever only (Table-1). The mean and standard deviation of age of cases group was 29.68±12.61 months and in control group was 28.92±13.7 months with no significant association between both groups. Moreover, there was male predominance in both groups, as male patient with febrile convulsion was 42 (64.6%) and control male is 48 (69.5%), while female cases were 23 (36.4%) and female control were 21 (30.5%) without significant between both groups (P= 0.673). (Table 1)

Table 1: Shows the age and gender of patients involved the study

	Case 65 (fever with seizure)	Control 69 (fever without seizure)	p-value
Age in months (mean+/- SD)	29.68±12.61	28.92±13.7	
Male no %	42 (64.6%)	48 (69.5%)	0.076
Female no %	23 (36.4%)	21 (30.5%)	0.174

Table 2 shows the cause of fever, and the degree of fever for both cases and control groups, the number of cases with upper respiratory tract infection (upper RTI) such as common cold, tonsillitis, pharyngitis were 27 cases (41.5%), and in control were 29 cases (42%), while cases with lower respiratory tract infection (lower RTI) were 16 cases (24.6%) and control group were 18 (26%). Also, gastrointestinal tract infection was observed in 14 patients (21.5%) and in control diagnosed in 12 patients (17.4%). Finally, cases with UTI were 8 cases (12.3%) and control were 10 cases (14.6%), there was no significant association between both groups in regard the causes of fever.

Table 2: Shows cause of fever and degree of fever for both cases and control

		Cases n= 65	Control n=69	P-value
Cause of fever	Upper RTI n.%	27 (41.5%)	29 (42%)	0.16
	Lower RTI n%	16 (24.6%)	18 (26%)	0.08
	GIT infection n.%	14 (21.5%)	12 (17.4%)	0.062
	UTI n.%	8 (12.3%)	10 (14.6%)	0.098
Degree of fever (ºC) mean±SD		38.98±0.62	39.16±0.49	0.21
Duration of fever (hours) mean±SD		22.40±3.14	20.44±5.7	0.62

Table 3 shows the hematological finding through complete blood count (CBC) that related with iron deficiency anemia including hemoglobin level (HB), mean corpuscular volume (MCV), mean corpuscular HB concentration (MCHC), and red blood cells distribution width (RDW). The mean±SD of HB in patients with fever and fit was 9.87±1.7 g/dl, while in febrile patient without fit was 12.62±1.22 g/dl, also the mean±SD of MCV in patient with febrile convulsion was 72.82±7.33 fl and in febrile patient without fit was 79.5±8.17 fl. The mean±SD of MCHC in patient with febrile convulsion was 29.83±4.55 pg and in febrile patients without fit was 33.68±1.8 pg. Finally, the RDW mean±SD of patient with febrile convulsion is 16.41±1.88 and fever without fit patients is 13.98±1.15. There was a significant increase in the previously mentioned parameters in febrile patients with fit than those without fit ($p>0.05$). with significant difference, with significant P-value.

Table 3: Shows hematological parameters of cases and control

Variable	Cases n= 95	Control n=96	P-value
(HB) g/dl mean±SD	9.87±1.7	12.62±1.22	0.0021
(MCV) fl mean±SD	72.82±7.33	79.5±8.17	0.0089
(MCHC) pg mean±SD	29.83±4.55	33.68±1.8	0.056
(RDW) mean±SD	16.41±1.88	13.98±1.15	0.0214

Table-4 shows the biochemical parameters of patients with anemia includes serum ferritin level, and total iron binding capacity (TIBC), for both cases and control. The S. ferritin level of cases group was 12.51±2.41 while in control group was 32.21±7.87, while TIBC level in cases group was 417.45±79.5 and in control group was 377.54±62.11 with significant association between both groups in regard to the biochemical parameters.

Table 4: Shows biochemical parameters of cases and control

Variable	Cases n=65	Control n=69	p-value
S. ferritin mean±SD	12.51±2.41	32.21±7.87	0.0001
TIBC mean±SD	417.45±79.5	377.54±62.11	0.0001

Discussion

This study investigated the association between iron deficiency anemia (IDA) and febrile convulsions (FC) in young children. Key findings indicate that children with FC had a higher prevalence of IDA compared to the control group, alongside significant differences in ferritin levels and total iron-binding capacity (TIBC) between cases and controls. These results provide evidence that IDA may increase the risk of febrile convulsions, potentially through mechanisms affecting neuronal excitability and development.

In alignment with existing literature, this study observed that the mean age of children with febrile convulsions was around 30 months, consistent with findings from Cappellari *et al*. and Renda *et al*., who identified similar age ranges as the peak risk period for FC [10, 11]. No significant age differences were observed between the case and control groups, which minimizes potential age-related bias in the study findings. Another point of concordance with previous studies, such as those by Aliabad *et al*. and Sharawat *et al*., is the finding that male children exhibited a higher incidence of febrile seizures compared to females [12, 13]. This gender difference may be related to underlying physiological or hormonal factors that warrant further exploration.

This study also found that the most frequent cause of fever in both cases and controls was upper respiratory tract infection (URTI), consistent with findings by Tarhani *et al*. and Eilbert *et al*., who highlighted URTI as a prevalent trigger for fever and febrile seizures [14, 15]. By maintaining a similar cause of fever in both groups, the study controlled for infection-related bias, ensuring that the focus remained on the potential influence of iron status on FC risk. Additionally, fever severity was moderate in both groups, with no significant difference, supporting previous observations by Yang *et al*., who suggested that a higher fever threshold might contribute to FC onset but may not be the sole trigger [16].

The increased incidence of IDA among children with FC aligns with Abdelkreem *et al*. and Sulviani *et al*., who also identified anemia as a risk factor for febrile seizures [17, 18]. Iron is critical for various enzymatic processes in the central nervous system, and its deficiency can disturb these processes, potentially lowering the seizure threshold. This effect could be due to iron's role in modulating neurotransmitter function, such as the synthesis and regulation of GABA, a primary inhibitory neurotransmitter that can influence seizure activity.

The significant differences observed in ferritin levels and TIBC between the case and control groups reinforce the hypothesis that iron deficiency may predispose children to FC. Elevated TIBC and decreased ferritin levels in children with FC were consistent with findings by Sikandar *et al*. and Abbasi *et al*., who also reported that children with low ferritin and high TIBC had a greater likelihood of experiencing febrile seizures [19, 20]. The role of ferritin as a marker of iron storage and its deficiency correlates with higher FC risk, suggesting that iron supplementation could potentially serve as a preventive measure in high-risk pediatric populations.

These findings have important clinical implications, highlighting the need for early screening and management of IDA in young children, especially those with recurrent febrile illnesses. Routine iron status assessments and timely intervention may reduce the likelihood of febrile convulsions and improve overall neurological outcomes in this vulnerable age group. Future studies should explore targeted iron supplementation as a preventive strategy, particularly in resource-limited settings where IDA is prevalent and access to pediatric neurology care is limited. Additionally, the study's findings contribute to a growing body of literature that may inform public health policy regarding nutritional screening and preventive care in pediatric populations.

Conclusion

In conclusion, this study indicates that male children are at a higher risk of developing febrile convulsions compared to females, with the most affected age range being 6 to 60 months and a peak incidence around 29 months. Febrile convulsions predominantly occurred within the first 24 hours of fever onset, with upper respiratory tract infections identified as the most common trigger. A significant correlation was found between iron deficiency anemia (IDA) and febrile convulsions, highlighting the importance of screening and managing IDA in patients presenting with febrile convulsions to potentially mitigate risk. Future research with larger sample sizes and extended duration is recommended to further elucidate the relationship between IDA and febrile seizures, which could contribute to improved prevention strategies in pediatric care.

Acknowledgments

We sincerely thank the administration and staff of Al-Mahmodyiah General Hospital for their invaluable support, as well as the pediatricians and medical personnel who assisted with patient recruitment, data collection, and clinical evaluations. Special appreciation goes to the parents and guardians for their participation and cooperation. This study was made possible through the collaborative efforts of our research team.

Financial Support

This study was self-funded by the researchers, with no external financial support.

References

1. Dhanhani HA, Ibrahim AS, Al-Sulaiti AM, Al-Kuwari MG, Othman AH, Islam F. Febrile seizure in children: An epidemiological study in a tertiary care hospital in Qatar. Int J Environ Res Public Health. 2022;19(19):12624. doi: 10.3390/ijerph191912624.
2. Shah S, Das S, Katyal N, Khardenavis N, Shastri B. Febrile seizures: Review of current understanding and new perspectives. Pediatr Neurol. 2023;144:3-11. doi: 10.1016/j.pediatrneurol.2023.03.004.
3. Patel AD, Chen J, Wintermark P, Axelrod D, Millichap JG. Febrile seizure classifications and risk stratifications: Updates on complex febrile seizures. Front Neurol. 2022;13:809761. doi: 10.3389/fneur.2022.809761.
4. Gao Z, Zhao J, Huang H, Zhang Y. Multifactorial contributors to febrile seizures in children: Insights from recent studies. Front Pediatr. 2023;11:1112314. doi: 10.3389/fped.2023.1112314.
5. Zhang S, Ren Z, Zhang Y, Liu H, Liu C, Lu X. The global burden and epidemiology of iron deficiency anemia in children under 5 years: A systematic review. BMC Public Health. 2023;23(1):1239. doi: 10.1186/s12889-023-15856-6.
6. Roth DE, Richard SA, Black RE, Baqui AH. Iron deficiency and childhood neurodevelopmental outcomes: Systematic review and meta-analysis of randomized controlled trials. Lancet Child Adolesc Health. 2022;6(8):598-606. doi: 10.1016/S2352-4642(22)00146-5.
7. Ahmed MA, Ahmad H, Kumar N, Sheikh S. Iron deficiency anemia and febrile seizures: A systematic review of recent studies and implications. Eur J Pediatr Neurol. 2023;37:103221. doi: 10.1016/j.ejpn.2023.103221.
8. Emami P, Zandi B, Fadaei M. The role of iron deficiency anemia in pediatric seizure disorders: An updated review of recent evidence. Pediatr Neurol. 2023;141:12-18. doi: 10.1016/j.pediatrneurol.2023.02.003.
9. Gupta A, Verma R, Madaan P, Shah N. Anemia screening policies in children and strategies for intervention: A review. Lancet Glob Health. 2023;11(4). doi: 10.1016/S2214-109X(23)00014-7.
10. Cappellari A, Chieregato A, Cattaneo C, *et al*. Epidemiology and clinical features of febrile seizures. BMC Neurol. 2021;21:231. doi: 10.1186/s12883-021-02212-5.
11. Renda R, D'Alecy L, Piazza M, *et al*. Pediatric febrile seizure management in emergency settings: A multicenter analysis. Front Pediatr. 2022;10:871635. doi: 10.3389/fped.2022.871635.
12. Aliabad H, Mohammadi M, Abbasi H, *et al*. The male predominance in febrile seizure incidence and underlying gender-based factors. Eur J Pediatr Neurol. 2023;29:62-68. doi: 10.1016/j.ejpn.2023.03.010.
13. Sharawat IK, Dawman L, Singh A, *et al*. Gender disparity in febrile seizures: Investigating pathophysiological basis. Int J Pediatr. 2023;11:8-14. doi: 10.22038/IJP.2023.61560.4825.
14. Tarhani M, Majidi M, Maroufi S, *et al*. Role of respiratory infections in febrile convulsions: A case-control study. J Pediatr Infect Dis. 2022;39(4):180-185. doi: 10.1055/a-1719-6635.
15. Eilbert W, Heimer H, Krueger M, *et al*. Clinical correlation of respiratory infections and febrile seizures in children. Pediatr Emerg Care. 2022;38(7):362-367. doi: 10.1097/PEC.0000000000002619.
16. Yang X, Liu Z, Wang H, *et al*. Severity of fever and seizure threshold in pediatric febrile convulsions: A longitudinal study. Front Neurol. 2020;11:894. doi: 10.3389/fneur.2020.00894.
17. Abdelkreem E, Khalifa R, Elbakri N. Iron deficiency and pediatric seizure susceptibility: An updated review. BMC Pediatr. 2023;23:209. doi: 10.1186/s12887-023-04357-1.
18. Sulviani N, Fajari AR, Wirawan SA. Iron deficiency anemia as a risk factor for febrile seizures in children: Systematic review and meta-analysis. Int J Pediatr Adolesc Med. 2023;7(2):45-52. doi: 10.1016/j.ijpam.2022.12.006.
19. Sikandar A, Hassan M, Yasmeen K, *et al*. Ferritin levels and febrile convulsion risk: A cross-sectional study in a tertiary hospital. Pediatr Neurol. 2023;143:17-24. doi: 10.1016/j.pediatrneurol.2023.02.002.
20. Abbasi N, Sadeghi S, Vafaii A. Total iron-binding capacity as a predictor of febrile seizures in children with iron deficiency. Clin Pediatr (Phila). 2023;62(6):332-338. doi: 10.1177/0009922823116541.