

## Iron Deficiency Anemia in Children with Febrile Convulsions: A Case–control Study at Sohag University Hospital

Potros Wasfy Gaballah\*, Mostafa Mohamed Abosdera, Ashraf M. R. Abou-Taleb

Department of Pediatrics, Faculty of Medicine, Sohag University, Sohag, Egypt

\*Corresponding author: Potros Wasfy Gaballah, Mobile: (+20) 01223088469, E-Mail: potroswasfy@gmail.com

### ABSTRACT

**Background:** Iron is necessary for healthy growth and development, and iron deficiency has been linked to behavioural problems, mental impairment, and reduced immunological function in children. Iron deficiency anemia (IDA) affects 48.5 percent of Egyptian preschoolers (aged 6 to 59 months).

**Objective:** The aim of this study was to evaluate the iron status in children with first febrile seizure (FFS).

**Patients and Methods:** This was a case-control hospital-based study that included children with febrile convulsion as case group and children with febrile illness without convulsion as controls, aged from 6 months to 6 years at Sohag University Hospital. Our study included 110 children, 55 as case group and 55 as controls from June 2019 to December 2020. **Results:** Pallor observed in 28% only of case group against only 17% of control group. The mean temperature at which children start to convulse was  $39.36 \pm 0.51$ . The mean Hb level of case group was statistically significantly lower than normal and was  $10.73 \pm 1.44$  versus  $11.77 \pm 1.24$  for control group. The mean of serum ferritin was statistically significantly lower than normal and was  $13.41 \pm 11.71$  versus  $30.18 \pm 8.9$  for control group. The mean of total iron binding capacity (TIBC) was statistically significantly higher than normal and was  $430.91 \pm 87.8$  versus  $362.73 \pm 63.81$  for control group.

**Conclusion:** The result suggests that iron deficiency anemia may be a risk factor for febrile seizures. Thus screening for IDA should be considered in children with febrile seizures. Fever can worsen the negative effect of anemia or iron deficiency on the brain and a seizure can occur as a consequence. This suggests that iron deficient children are more prone to febrile seizures.

**Keywords:** Children, Febrile convulsion, Iron deficiency anemia.

### INTRODUCTION

The most frequent form of seizure in young children is called a febrile seizure (FS), which is caused by a high grade fever rather than a condition affecting the central nervous system or a metabolic problem. It often affects babies and kids between the ages of 6 and 72 months, and 2 to 5 percent of this group will experience at least one episode<sup>(1)</sup>.

A major dietary deficit in children is iron deficiency anemia (IDA), which affects 48.5 percent of Egyptian preschoolers (aged 6 to 59 months)<sup>(2)</sup>. Iron is necessary for healthy growth and development, and deficits have been linked to behavioural problems, mental retardation, and immune system impairment<sup>(3)</sup>. After the age of six years, FS and IDA peak at the same time<sup>(4)</sup>. A lot of research has been done to identify an associated link. Individual research, however, have produced findings that disagree with those of other studies. IDA and FS were reportedly linked in several research<sup>(5,6)</sup>. Unlike previous research, which did not find a relationship<sup>(7)</sup>, several studies even claimed that IDA protected against FS<sup>(8,9)</sup>.

Systematic reviews and meta-analyses published in 2010 and 2014<sup>(10)</sup> examined the association between IDA and FS in children aged 3 months to 6 years.

The aim of this study was to evaluate the iron status in children with first febrile seizure (FFS).

### PATIENT AND METHODS

A case control hospital-based study was conducted from June 2019 to December 2020 in Pediatric Department and Neurology and Psychiatry Unit of

Sohag University Hospital. Our study included 110 children, 55 as case group and 55 as controls.

**Inclusion Criteria:** Children who have first simple febrile fit, which fulfills its ideal criteria (tono-clonic in character, don't last more than 15 minute, and don't recur in same illness).

#### **Exclusion Criteria:**

-Children with a history of recurrent seizures, central nervous system infections, developmental delay, and/or neurologic deficit.

-Children with fits that last more than 15 minutes with complex features and focal distribution.

#### **Children were subjected to the following:**

-Complete history taking with emphasis on age, sex, complaint, type and criteria of the fit, family history of febrile convulsion or epilepsy, and the underlying illness was recorded for all cases and controls, as well as details of the seizure history, duration, frequency, and focality for cases with FFS.

#### **-Complete physical examination with emphasis on:**

-Temperature peak at admission.

-Developmental milestone examination.

-Central nervous system examination including: Head circumference, cranial nerve examination, speech, motor, sensory nervous system examination.

- Assessment of iron status by hemoglobin concentration (HB), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), plasma ferritin (PF), and total iron binding capacity (TIBC), which

were measured in children with FFS and compared with same controls matched for age and sex with febrile illnesses without convulsion.

**Ethical consent:**

An approval of the study was obtained from Sohag University Academic and Ethical Committee. Individualized written informed consents were obtained from enrolled children' guardians with the explanation of the purpose of the study. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

**Statistical analysis**

Data were analyzed using the SPSS statistical package software for Windows version 21 (SPSS Inc, Chicago, USA). Quantitative data were represented as mean, standard deviation, median and range. Data were analyzed using student t-test to compare means of two groups. When the data were not normally distributed; Mann-Whitney test was used. Qualitative data were presented as number and percentage and compared using Chi square test. P value was considered significant if it was less than 0.05.

**RESULTS**

Our study included 110 children, 55 as case group and 55 as controls. The mean age of studied groups was statistically insignificant. There were male predominance in both case and control group (Table 1).

**Table (1):** Age and gender of studied cases and control

Variable	Febrile seizure N=55	Fever without convulsion N=55	P value
<b>Age/month</b> Mean ± SD Median (range)	27.76±14.67 24 (7:60)	27.18±15.26 24 (6:60)	0.77
<b>Gender</b> Female Male	17 (30.90%) 38 (69.09%)	23 (41.81%) 32 (58.18%)	0.41

By general examination of studied cases, pallor was observed more in febrile seizure-patients than in control group as in table (2).

**Table (2):** Pallor state of studied cases

Variable	Febrile seizure N=55	Fever without convulsion N=55	P value
<b>Pallor</b> No Pallor	39 (70.00%) 16 (28.00%)	45 (81.00%) 10 (17 .00%)	0.01

The mean temperature at which children start to convulse was 39.36±51 (Table 3).

**Table (3):** Grade of temperature by Celsius grade on admission.

variable	Febrile seizure N=55	Fever without convulsion N=55	P value
<b>Temperature (°C)</b> Mean ± SD Median (range)	39.36±0.51 39.5 (38.4:40)	39.01±0.75 39 (38:40.5)	0.01

The mean Hb level, MCV, and MCH of case group were statistically significantly lower than control group. While the mean of RDW of case group was significantly more than control group (Table 4).

**Table (4):** Investigation of studied populations in the two groups

Variable	Febrile seizure N=55	Fever without convulsion N=55	P value
<b>Hb level (g/dl)</b> Mean ± SD	10.73±1.44	11.77±1.24	0.002
<b>MCV (fl)</b> Mean ± SD	73.42±6.42	77.4±5.07	0.009
<b>MCH (pg)</b> Mean ± SD	30.96±3.58	32.68±2.32	0.05
<b>RDW (%)</b> Mean ± SD	15.45±1.72	14.40±1.05	0.004

The mean of serum ferritin was statistically significantly lower than control group. The mean of total iron binding capacity (TIBC) was statistically significantly higher than control group (Table 5).

**Table (5):** Iron indices of studied groups

Variable	Febrile seizure N=55	Fever without convulsions N=55	P value
<b>Serum ferritin (ng/ml)</b> Mean ± SD	13.41±3.52	30.18±7.32	<0.001
<b>TIBC (total iron binding capacity)</b> Mean±SD	430.91±87.8	362.73±63.81	<0.001

There was a significant association between IDA and FC (Table 6).

**Table (6) Relation between anemia and febrile convulsion**

Group	No anemia N=49	Anemia N=56	P value
Febrile seizure	16 (30.00%)	39 (70.00%) 18 (32.72%)	<0.001
Fever without convulsion	37 (67.35%)		

**DISCUSSION**

In this study we aimed to evaluate the association between iron deficiency anemia and febrile convulsion in children aged from 6 months to 6 years. In this study of 110 children, 55 children with febrile seizures were taken as cases and 55 children presented with fever without seizures were considered as controls. In our study the mean age of presentation of febrile seizures cases was 27.76 ±14.67 months while in control group the mean age was 27.18 ± 15.26 months. That came in agreement with **Zareifar et al.** (11), **Khanna et al.** (12) and **Jang et al.** (13), while it was different from **Surani et al.** (14).

In our study among case group with febrile seizures, 38 (69%) were males and 17 (31%) were females in case group versus 32 (59%) males, 23 (41%) females in control group. There was a male predominance in both case and control group and that came in agreement with the studies of **Khanna et al.** (12) and **Tripathy et al.** (15). But in **Surani et al.** (14) the reverse was observed as males were 33.3% only versus 66.7% females with female predominance in percentage. Whether there is a biological basis for the gender specific differences in febrile seizure susceptibility or whether boys just had more fevers and therefore are at greater risk, is currently not established.

In our study 100% among case group presented with simple febrile seizures. While in **Daoud et al.** (6) study 88% of cases had presented with simple febrile seizures and 12 % had presented by complex febrile seizures. Also in another prospective study conducted by **Talebian and Momtazmanesh** (16), 56 (93%) among 60 cases had simple febrile seizures and 4 (7%) among 60 cases had complex febrile seizures. **Bidabadi and Mashouf** (7) had found that 132 (88%) among 150 cases had simple febrile seizures and 28 (12%) cases had complex febrile seizures.

In our study the average temperature at which children start to convulse was (39.6±0.51 degree Celsius) in case group. This came in consistence with **Noorbakhsh** (17) who found that it was (39.42±07 degree Celsius) in case group. Also **Surani et al.** (14) found it as 39.1±0.3 degree Celsius in case group.

Average mean Hb level in our studied case group was statistically significant lower than normal (10.73±1.44 g/dl) however average mean Hb level in controls was within normal (11.77±1.24 g/dl). This came in consistence with **Tripathy et al.** (15) and **Vikash et al.** (18). While in **Surani et al.** (14) Hb level was (8.87

g/dl) and in **Majumdhara et al.** (19) mean it was (8.92 g/dl). In contrast to our results **Noorbakhsh** (17) found that mean Hb level was within normal (11.6±0.79 g/dl) and also it was around 11 g/dl in **Hadi et al.** (20).

In case group the mean MCV was statistically significantly lower than normal (73.42±6.42 fl) and the mean MCV in controls was within normal (77.4± 5.07 fl). This was quite similar to result of studies of **Khanna et al.** (12) and **Noorbakhsh** (17). While in **Surani et al.** (14) mean MCV was (8.87 g/dl) and in **Majumdhara et al.** (19) it was (67.03 fl).

Average mean of MCH in case group was statistically significantly lower than normal (30.96±3.58 gms), while in control group it was within normal (32.68±2.32 gms). It came in agreement with **Khanna et al.** (12), **Jang et al.** (13), **Tripathy et al.** (15), and **Majumdhara et al.** (19).

Average mean serum ferritin level in case group was within the lowest normal level (13.41±11.71 ng/ml) versus (30.18±8.9 ng/ml) in control group. Serum ferritin was statistically significantly lower in febrile seizures cases than controls. It came in consistence with **Jang et al.** (13) and **Surani et al.** (14), while it was higher than that in **Khanna et al.** (12) (39.54±24.55 ng/ml), **Noorbakhsh** (17) (56.4 ng/ml), while in **Hadi et al.** (20) it was high (127.54 ng/ml).

Average mean TIBC in case group was within highest normal level (430.91±87.80 mcg/dl) versus (362.73±63.81 mcg/dl) for control group, while in the study of **Jang et al.** (13) it was (326.94±43.67 mcg/dl).

From various hematological parameters, incidence of iron deficiency anemia was higher in cases with febrile seizures than controls.

The result of this study revealed a significant association between IDA and FC where 70% of case group had IDA against only 32% for control group. And that came in agreement with **Khanna et al.** (12) who found that 48% of case group were anemic and had higher incidence of IDA than controls. Also **Jang et al.** (13), **Vikash et al.** (18) and **Shaaib et al.** (21), had recorded similar results.

**CONCLUSION**

The result suggests that iron deficiency anemia may be a risk factor for febrile seizures. Thus screening for IDA should be considered in children with febrile seizures. Fever can worsen the negative effect of anemia or for iron deficiency on the brain and a seizure can occur as a consequence. This suggests that iron deficient children are more prone for febrile seizures.

**Conflict of interest:** The authors declare no conflict of interest.

**Sources of funding:** This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

**Author contribution:** Authors contributed equally in the study.

**REFERENCES**

1. **Hodgson E, Glade G, Harbaugh N et al. (2008):** Febrile seizures: clinical practice guideline for the long-term management of the child with simple febrile seizures. *Pediatrics*, 121: 1281–1286.
2. **Baker R, Greer F (2010):** Diagnosis and prevention of iron deficiency and iron-deficiency anemia in infants and young children (0–3 years of age). *Pediatrics*, 126: 1040–1050.
3. **Ghosh K (2006):** Non haematological effects of iron deficiency-a perspective. *Indian J Med Sci.*, 60: 30-35.
4. **Hartfield D, Tan J, Yager J et al. (2009):** The association between iron deficiency and febrile seizures in childhood. *Clin Pediatr.*, 48: 420–426.
5. **Pisacane A, Sansone R, Impagliazzo N et al. (1996):** Iron deficiency anaemia and febrile convulsions: case-control study in children under 2 years. *Br Med J.*, 313: 343–344.
6. **Daoud A, Batieha A, Abu-Ekteish F et al. (2002):** Iron status: A possible risk factor for the first febrile seizure. *Epilepsia*, 43(7):740–743.
7. **Bidabadi E, Mashouf M (2009):** Association between iron deficiency anemia and first febrile convulsion: a case–control study. *Seizure*, 18: 347–351.
8. **Kobrinsky N, Yager J, Cheang M et al. (1995):** Does iron deficiency raise the seizure threshold? *J Child Neurol.*, 10: 105–109.
9. **Derakhshanfar H, Abaskhanian A, Alimohammadi H et al. (2012):** Association between iron deficiency anemia and febrile seizure in children. *Med Glas (Zenica)*, 9: 239–242.
10. **Habibian N, Alipour A, Rezaianzadeh A (2014):** Association between iron deficiency anemia and febrile convulsion in 3-to 60-month-old children: a systematic review and meta-analysis. *Iran J Med Sci.*, 39: 496-99.
11. **Zareifar S, Hosseinzadeh H, Cohan N (2012):** Association between iron status and febrile seizures in children. *Seizure*, 21: 603-605.
12. **Khanna A, Kumar A, Hota D et al. (2020):** Relationship between iron deficiency anemia and febrile seizures: A case–control study. *Med J Babylon*, 17:144-47.
13. **Jang H, Yoon H, Lee E (2019):** Prospective case control study of iron deficiency and the risk of febrile seizures in children in South Korea. *BMC Pediatr.*, 19: 309-13.
14. **Surani M, Yousaf M, Saleem K et al. (2020):** Iron deficiency anemia among children with febrile seizures. *Professional Med J.*, 27(9):1922-1926.
15. **Tripathy D, Tomar R, Gupta A (2020):** The risk associated with iron deficiency anemia for simple febrile seizures in children: case-control study. *Indian J Child Health*, 7(1): 25-28.
16. **Talebian A, Momtazmanesh N (2007):** Febrile seizures and anemia. *Iran J Child Neurology*, 7:31–33.
17. **Noorbakhsh S (2021):** Association between iron deficiency and febrile seizure? A case control study in Tehran. DOI: <https://doi.org/10.21203/rs.3.rs-142050/v1>
18. **Vikash L, Haresh K, Shahina H et al. (2016):** Association of iron deficiency anemia in children with febrile convulsions. *Pakistan Journal of Neurological Sciences*, 11: 1-5.
19. **Majumdar R, Haricharan K, Venkatamurthy M (2013):** Iron deficiency as a risk factor for first febrile seizure. *Journal of Evolution of Medical and Dental Sciences*, 2: 3834-40.
20. **Hadi A, Pourmasoumi M, Najafgholizadeh A et al. (2018):** Effect of purslane on blood lipids and glucose: A systematic review and meta-analysis of randomized controlled trials. *Phytotherapy Research*, 18:1–10.
21. **Shaaib F, Esh A, Azab S et al. (2020):** The relationship between iron deficiency anemia and febrile convulsions in infant and children. doi: 10.21608/zumj.2020.21787.1669.