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Review Article

**RELATIONSHIP OF FEBRILE SEIZURES WITH IRON
DEFICIENCY ANEMIA: CHILDREN OF 6 TO 36 MONTHS
(A CASE CONTROL STUDY)**¹Dr Hina Abbasi, ²Dr Hina Anwar, ³Dr Nuzhat Rasheed¹Azad Jammu and Kashmir Medical College., ²Azad Jammu and Kashmir Medical College.,³Azad Jammu and Kashmir Medical College.**Article Received:** November 2020 **Accepted:** December 2020 **Published:** January 2021**Abstract:**

Aim: The purpose of this study was to establish the association between febrile seizures and iron deficiency anemia in children 6 to 36 months of age.

Study design: A follow-up case study.

Place of study: In the Pediatric Department of Holy Family Hospital, Rawalpindi for one-year duration from November 2019 to November 2020.

Patients and Methods: 150 cases (75 for each group, cases and controls) meeting the inclusion criteria were selected for the study. Demographics such as age, gender and addresses were recorded, and blood samples were taken from all patients in the patient and control groups for hemoglobin (Hb), mean blood cell volume (MCV), red blood cell distribution width (RDW), and plasma ferritin (PF) to determine the incidence of iron deficiency anemia.

Results: The mean age of the patients in the group of cases was 21.2 ± 5.7 months, and in the control group it was 19.5 ± 6.8 months. In the group of cases there were 43 (57.3%) men and 32 (42.7%) women, and in the control group there were 39 (52%) men and 36 (48%) women. In the group of cases the mean level of hemoglobin in patients was 10.4 ± 1.4 mg / dl, and in the control group it was 11.1 ± 1.4 mg / dl. In the group of cases, the mean concentration of ferritin in the plasma of patients was 13.7 ± 4.7 ng / dl, and in the control group it was 15.7 ± 4.8 ng / dl. In the case group, 28 (37.3%) patients had iron deficiency anemia, while in the control group 13 (17.3%) patients had iron deficiency anemia. The odd coefficient was found to be 2.84 and was statistically significant.

Conclusion: This study shows that iron deficiency anemia is more common in the patient group than in the control group, and there is a strong association between febrile seizures and iron deficiency anemia.

Key words: febrile convulsions, iron deficiency anemia, hemoglobin, ferritin

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INTRODUCTION:

Febrile seizures, also known as febrile seizures, are the most common type of seizure in children, affecting 3% to 4% of children by their fifth birthday. It is defined as an epileptic seizure in a child aged 6 months to 5 years associated with a febrile illness in the absence of an intracranial infection or with a history of non-febrile seizures. Most fever attacks occur between 6 and 36 months of age, peaking at 18 months. When your baby has a first seizure, it is associated with iron deficiency anemia. Iron deficiency is one of the most common nutritional problems in the world, affecting an estimated 5 billion people (including human infants, especially between the ages of 6 and 24 months). In developing countries, 46-66% of children under the age of four are anemic, and half have iron deficiency anemia. Central nervous system abnormalities such as apathy, irritability and poor concentration have been linked to iron deficiency, possibly due to changes in iron-containing enzymes (monoamine oxidase) and cytochromes. Iron deficiency in infants may be associated with later cognitive deficits and poor school performance. A study by Hartfield et al. Found that children with febrile seizures were almost twice as likely to be iron deficient as children with febrile illness. In another study a total of 35 (31.2%) cases had iron deficiency anemia (IDA), compared with 14 (11.6%) controls, statistically significant, $p = 0.0032$, but in another study by Susan and et al. ferritin was found in 26.5% of febrile seizures, compared to 29.5% in the control group. In another study, iron deficiency was not associated with an increased risk of acute seizures in 45/133 cases of iron deficiency compared with 36/133 controls, $p = 0.230$, or with status epilepsy. In view of the differences in the results reported in the literature, the aim of this study was to re-evaluate this issue and see if there is an association between febrile seizures and iron deficiency anemia. This will increase the existing knowledge and can help prevent febrile seizures.

Purpose: The purpose of this study was:

To establish the relationship between febrile seizures and iron deficiency anemia in children 6 to 36 months of age.

Operational Definitions

Febrile seizures: A febrile seizure is defined as a generalized seizure that occurs with a rectal temperature of 38.3°C or more / an axillary temperature of 37.8°C as assessed by the history.

Iron deficiency anemia: Iron deficiency anemia is defined as:

1. Hemoglobin $<10\text{ mg / dL}$.
2. Mean blood cell volume $<70\text{ fl}$
3. Distribution width of red blood cells $> 14.5\%$
4. Plasma ferritin $<12\text{ng / dL}$

MATERIALS AND METHODS:

Setting: This study was conducted at the Pediatric Department of Holy Family Hospital, Rawalpindi for one-year duration from November 2019 to November 2020.

Study design: follow-up case study.

Sample size: sample size of 150 cases (75 in each group) was calculated with 80% test power, 5% significance level and assuming the expected percentage of iron deficiency anemia in both groups, i.e., 31.2% in cases and 11.6% in a control group in children aged 6 to 36 months.

Inclusion Criteria: for cases

1. Age from 6 to 36 months.
2. Gender: male and female.
3. First febrile seizures (assessed on the basis of medical history).

For control

1. Age from 6 to 36 months.
2. Gender: male and female.
3. Patients without seizures with febrile illness (assessed on the basis of medical history).

Exclusion Criteria: for cases and controls

1. Diagnosed patients with meningitis
2. Developmentally delayed history

Data collection procedure: 150 cases (75 per group, case and control) meeting the inclusion and exclusion criteria were enrolled with informed consent from parents of children from the Pediatric Department. Controls were taken from the same ward that was admitted for seizure-free febrile illness, such as upper or lower respiratory tract infections, gastroenteritis, and urinary tract infection. Their demographic data such as age, gender and addresses were recorded. Blood samples were collected from both case and control for hemoglobin (Hb), mean blood cell volume (MCV), red blood cell distribution width (RDW), and plasma ferritin (PF) to determine the incidence of iron deficiency anemia. All this information was recorded in a specially designed proforma.

Data analysis: Data collected was entered and analyzed with SPSS version 16. Descriptive analysis was used to describe the mean \pm standard deviation of quantitative data such as age and hemoglobin levels, while frequency and percentages were

calculated for qualitative data such as gender and anemia. The odd factor was calculated to see the relationship between febrile seizures and iron deficiency anemia. An odd ratio > 2 was considered statistically significant.

RESULTS:

The mean age of the patients in the group of patients was 21.2 ± 5.7 months, and in the control group 19.5 ± 6.8 months. In the group of cases there were 4

(5.3%) patients aged 6-12 months, 24 (32%) patients aged 13-18 months, and 27 (36%) patients aged 19 years. - 24 months, 15 (20%) patients aged 25-30 months and 5 (6.7%) patients aged 31-36 months. In the control group there were 10 (13.3%) patients in the age range of 6-12 months, 27 (36%) in the age range of 13-18 months, and 19 (25.3%) in the age range of 19 years. -24 months, 14 (18.7%) patients in the age range 25-30 months and 5 (6.7%) patients in the age range 31-36 months (Table 1).

TABLE 1: Distribution of patients according to age

Age (Months)	Cases group (n=75)		Controls group (n=75)	
	No.	Percentage	No.	Percentage
06-12	04	05.3	10	13.3
13-18	24	32.0	27	36.0
19-24	27	36.0	19	25.3
25-30	15	20.0	14	18.7
31-36	05	06.7	05	06.7
Mean \pm SD	21.2 \pm 5.7		19.5 \pm 6.8	

In the group of cases there were 43 (57.3%) men and 32 (42.7%) women, and in the control group 39 (52%) men and 36 (48%) women (Table 2).

TABLE 2: Distribution of patients according to sex

Sex	Cases group (n=75)		Controls group (n=75)	
	No.	Percentage	No.	Percentage
Male	43	57.3	39	52.0
Female	32	42.7	36	48.0
Total	75	100.0	75	100.0

In the group of cases the mean level of hemoglobin (Hb) in patients was 10.4 ± 1.4 mg / dl, and in the control group it was 11.1 ± 1.4 mg / dl. In the case group, 28 (37.3%) patients had Hb < 10.0 mg / dL, 36 (48.0%) patients had Hb in the range 10.0-12.0 mg / dL, and 11 (14.7%) of patients had an Hb range of 12.1-14.0 mg / dL. In the control group there were 13 (17.3%) patients with Hb < 10.0 mg / dL, 46 (61.3%) patients had Hb in the range 10.1-12.0 mg / dL, 12 (16%) patients had Hb in the range of 12.1-14.0 mg / dl and 4 (5.3%) patients had an Hb in the range of 14.1-16.0 mg / dl (Table 3).

TABLE 3: Distribution of patients according to hemoglobin level (Hb)

Hb (mg/dl)	Cases group (n=75)		Controls group (n=75)	
	No.	Percentage	No.	Percentage
< 10.0	28	37.3	13	17.3
10.0-12.0	36	48.0	46	61.3
12.1-14.0	11	14.7	12	16.0
14.1-16.0	0	0	04	05.3
Mean \pm SD	10.4 \pm 1.4		11.1 \pm 1.4	

In the case group, the mean blood cell volume (MCV) of the patients was 73.7 ± 8.3 fl, and the control group was 77.1 ± 7.2 fl. In the case group, 28 (37.3%) patients had MCV <70 fl, 30 (40%) patients had MCV in the range 70-80 fl, and 17 (22.7%) patients had MCV in the range 81-90 fl. In the control group, 13 (17.3%) patients had MCV in the range <70 fl, 37 (49.3%) patients had MCV in the range 70-80 fl, and 25 (33.3%) patients had MCV in the range 81-90 fl (Table 4).

TABLE 4: Distribution of patients according to mean corpuscular volume(MCV)

MCV (fl)	Cases group (n=75)		Controls group (n=75)	
	No.	Percentage	No.	Percentage
< 70	28	37.3	13	17.3
70-80	30	40.0	37	49.3
81-90	17	22.7	25	33.3
Mean \pm SD	73.7 ± 8.3		77.1 ± 7.2	

In the group of cases, the mean width of distribution of red blood cells (RDW) was $15.1 \pm 1.3\%$, and in the control group - $14.7 \pm 1.4\%$. In the case group, 32 (42.7%) patients had RDW $<14.5\%$, 29 (38.7%) patients had RDW ranging from 14.5-16.5%, and 14 (18.7%) patients had WFD in the range of 16.6-18.5%. In the control group, 41 (54.7%) patients had RDW $<14.5\%$, 26 (34.7%) patients had RDW ranging from 14.5-16.5%, and 8 (10.7%) patients had WFD in the range of 16.6-18.5%. % (Table 5).

TABLE 5: Distribution of patients according to red blood cell distribution width (RDW)

RDW (%)	Cases group (n=75)		Controls group (n=75)	
	No.	Percentage	No.	Percentage
< 14.5	32	42.7	41	54.7
14.6-16.5	29	38.7	26	34.7
16.6-18.5	14	18.7	08	10.7
Mean \pm SD	15.1 ± 1.3		14.7 ± 1.4	

In the group of cases, the mean concentration of ferritin in the plasma of patients was 13.7 ± 4.7 ng / dl, and in the control group it was 15.7 ± 4.8 ng / dl. In the group of cases, 28 (37.3%) patients had ferritin levels <12.0 ng / dL, 26 (34.7%) patients had ferritin levels in the range 12.0-18.0 ng / dL, and 21 (28 %) of patients had ferritin levels in the range of 18.1-24.0 ng / dL. In the control group, 19 (25.3%) patients had ferritin levels <12.0 ng / dL, 25 (33.3%) patients had ferritin levels in the range 12.0-18.0 ng / dL, and 31 (41 , 3%) of patients had ferritin levels in the range of 18.1-24.0 ng / dL (Table 6).

TABLE 6: Distribution of patients according to plasma ferritin level

Plasma ferritin level (ng/dl)	Cases group (n=75)		Controls group (n=75)	
	No.	Percentage	No.	Percentage
< 12.0	28	37.3	19	25.3
12.0-18.0	26	34.7	25	33.3
18.1-24.0	21	28.0	31	41.3
Mean \pm SD	13.7 ± 4.7		15.7 ± 4.8	

In the distribution of patients according to the frequency of iron deficiency anemia, 28 (37.3%) patients had iron deficiency anemia in 28 (37.3%) cases, while 47 (62.7%) patients did not have iron deficiency anemia. In the control

group, 13 (17.3%) patients had iron deficiency anemia, while 62 (82.7%) patients did not have iron deficiency anemia. The odd factor was calculated and found to be 2.84 (statistically significant) (Table 7).

TABLE 7: Distribution of patients according to frequency of iron deficiency anemia (IDA)

Iron deficiency anemia	Cases group (n=75)		Controls group (n=75)	
	No.	Percentage	No.	Percentage
Yes	28	37.3	13	17.3
No	47	62.7	62	82.7
Total	75	100.0	75	100.0

DISCUSSION:

The relationship between iron deficiency anemia and febrile seizures has been described in the last decade with conflicting results. Infants and young children under the age of five with iron deficiency anemia may be at particular risk of having fever attacks. We observed significantly low serum ferritin levels in children with first seizures than in the control group. Similar results were observed by Pisacane et al. And Daoud et al. In our study, iron deficiency anemia (IDA) was found in 37.3% in the group of patients and 17.3% in the control group, similar to the study by Khalid et al., IDA was more frequent in cases with febrile seizures than in the control group (31.2% vs.11.6%); these findings are in line with the results of previous studies. Daoud et al.¹² observed significantly lower plasma ferritin levels in the first group with febrile seizures than in the control group (49 out of 75 vs. 24 out of 75). Pisacane reported significantly higher IDA rates among children with febrile seizures than the control group (15% versus 9% and 30% versus 12%, respectively). Kobrinsky reported that iron deficiency raises the seizure threshold. Two large-scale studies, the third National Health and Nutrition Examination Survey (NHANES III) and the third report on nutrition monitoring in the United States, found the incidence of IDA by the age of 1-2 years to be 3%, and from one up to three years older than 15%. A more recent study, conducted in an urban setting with an equal mix of lower and middle socioeconomic groups, found that 10% of children between the ages of one and three had IDA¹⁶. In our study, the mean age of patients in the group of cases was 21.2 ± 5.7 months, and in the control group it was 19.5 ± 6.8 months. Compared to the Bidabadi and Mashout study, patients and controls had 22.86 ± 12.86 and 21.91 ± 13.58 months, respectively, which was comparable to our study. In our study, 57.3% of men and 42.7% of women were in the group of cases. The control group consisted of 52% of men and 48% of women. Compared to the study by Khalid et al. The study group comprised 59.8% of men and 40.2% of women, while the control group comprised 58.3%

of men and 41.7% of women, which is comparable to our study. In the group of cases, the mean hemoglobin concentration in patients was 10.4 ± 1.4 mg / dl, and in the control group it was 11.1 ± 1.4 mg / dl. Compared to the Bidabadi and Mashout study, the mean Hb of patients in the case group was 10.48 ± 1.16 mg / dl, and in the control group 10.29 ± 1.25 mg / dl, which is comparable to our study. In our study in the case group, the mean MCV of patients was 73.7 ± 8.3 fl, and in the control group it was 77.1 ± 7.2 fl. Compared to the Bidabadi and Mashout study, the mean MCV of patients in the group of cases was 77.54 ± 6.63 fl, and in the control group it was 77.36 ± 6.0 fl, which is comparable to our study. In our study, 37.3% of patients had iron deficiency anemia in our patient group and 17.3% of patients had iron deficiency anemia in the control group. Compared to the study by Khalid et al., Iron deficiency anemia was found in 31.2% in the patient group and 11.6% in the control group, which is comparable to our study. The study has some limitations. Serum ferritin, a nonspecific acute phase reagent, may increase in any inflammatory disease. Iron deficiency and seizures can be seen after lead poisoning, but levels could not be determined in subjects. More research is needed to confirm our findings.

CONCLUSION:

This study shows that iron deficiency anemia is more common in the patient group than in the control group, and there is a strong association between febrile seizures and iron deficiency anemia.

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