WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.074
Volume 7, Issue 18, 142-153. Research Article ISSN 2277– 7105

PREVALENCE OF IRON DEFICIENCY IN CHILDREAN WITH FEBRILE SEIZURE

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Article Received on
30 August 2018,

Revised on 20 Sept. 2018,
Accepted on 10 October 2018

DOI: 10.20959/wjpr201818-13537

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ABSTRACT

Objective: Febrile seizures are one of the most common neurologic problems during infancy and childhood periods, occurring in 3-4% of the children with a recurrence rate of 30 to 40%. They occur rarely before 6 months and after 5 years of age, with a peak incidence between 14-18 months of age which overlaps with that of iron deficiency anemia which is from 6 to 24 months. General objective of this study is to determine prevalence of iron deficiency in children with febrile seizure. **Methods**: The study was conducted in the Department of Pediatric Medicine, Institute of child health & Shishu Sasthya Foundation, Mirpur, Dhaka over a period of 6 months from August 2016 to January 2017. A structured data collection form was developed containing all the variables of interest which was finalized following pretesting. Data were collected by interview, observation, clinical and laboratory testing. **Results:** In the study it has been found that over half (51.3%) of the simple febrile patients had a history of iron deficiency compared to 45% of the complex febrile seizure patients. The comparison was not statistically significant between groups with respect to iron deficiency ($p = 0.648$). Over 28% of simple febrile seizure patients had a history of recurrence of febrile seizures compared to 20% of complex febrile seizures. The comparison did not turn to significant with respect to recurrence of febrile seizure as evident by $p = 0.493$. Laboratory investigations shows that mean hemoglobin, PCV, mean corpuscular volume, mean corpuscular hemoglobin, serum iron concentration, serum ferritin level and total iron binding capacity were 9.7 ± 1.4 gm/dl (range:6.8 – 14.2), 30.7 ± 4.6% (range:22 – 44), 67.9 ± 7.1 fl (range:53 – 88), 24.7 ± 4.7 pg (range:15.5 – 33.0), 22.1 ± 0.9 µg/dl (range:14.3 – 38.0), 5.6 ± 1.3 µg/L (range:2.3 – 32.4) and 566 ± 25 µg/dl (range:290 – 963) respectively. Thirty nine

percent of patients had hemoglobin level less than 9 gm/dl, 35.6% mean corpuscular volume less than 65 femtoliter, 64.4% mean corpuscular hemoglobin less than 28 picograms per cell and 49.2% serum ferritin level less than 12 µg/L. **Conclusion:** The prevalence of iron deficiency in febrile seizures among hospitalized children is high compared to that in developed countries and is mainly attributed to low and middle socioeconomic status. The simple febrile seizure is the most frequent type of febrile seizure and patients with iron deficiency and risk of recurrence of febrile seizures are higher in simple febrile seizure than complex febrile seizure.

KEYWORDS: Febrile Seizure, Iron Deficiency in Children.

INTRODUCTION

According to International League Against Epilepsy (ILAE), a febrile seizure is defined as a seizure attack associated with a febrile illness unrelated to brain infection or acute electrolyte imbalance in children older than one month without any previous history of a febrile seizure. Febrile seizures are one of the most common neurologic problems during infancy and childhood periods, occurring in 3-4% of the children with a recurrence rate of 30 to 40%. They occur rarely before 6 months and after 5 years of age, with a peak incidence between 14-18 months of age which overlaps with that of iron deficiency anemia which is from 6 to 24 months.[1][2]

Febrile seizures are classified as either simple or complex. Simple febrile seizures consist of a brief (lasting less than 10 minutes) tonic clonic seizure which occurs only once within a 24-hour period. There are no focal features and it resolves spontaneously. Conversely, complex febrile seizures are prolonged (greater than 10-15 minutes), focal, or multiple (recurrent within the same febrile illness over a 24-hour period). While the majority of febrile seizures are simple (70-75%), 9-35% of febrile seizures are complex.[1]

The occurrence of a child's first febrile seizures has been associated with: first or second-degree relative with history of febrile and afebrile seizures, day care attendance, developmental delay, Influenza A viral infection, Human herpes virus- 6 infection, Human Metapneumovirus, and iron deficiency anemia. Other exogenous circumstances that have been identified as predicting an increased risk of initial febrile seizures include difficult birth, neonatal asphyxia, and coiling of the umbilical cord. The risk of initial febrile seizures has also been studied after receipt of pediatric vaccinations such as diphtheria-tetanus-whole cell pertussis and Measles, Mumps and Rubella (MMR). Febrile seizures frequently recur. Although febrile seizure usually occurs as single, isolated incidents, the reoccurrence rate is 30% overall, and increases to 50% if the initial febrile seizure

occurs in a child under one year of age.[1]

Iron deficiency anemia is one of the most prevalent micronutrient deficiencies in young children and it is strongly associated with persistent cognitive and motor delays even after the anemia and iron deficit have been repaired.[3] Though anemia is common manifestation of iron deficiency, other effects of iron deficiency on various tissues, organs and systems are usually under recognized.

Impaired brain development and cognitive, behavioral and psychomotor impairment are most worrisome manifestations of iron deficiency. Studies have demonstrated that some of these changes occurring during period of brain growth spurt (<2 years' age) may be irreversible. Association of iron deficiency with febrile seizures, pica, breath holding spells, restless leg syndrome and thrombosis is increasingly being recognized.[4]

The World Health Organization estimates that anemia, largely caused by iron deficiency, affects between 500 million to two billion people worldwide. In some developing countries, up to 50 percent of preschool children have anemia that principally is caused by iron deficiency. It is the most common nutritional deficiency and hematological disease of infancy and childhood. Iron is a nutritional element not only needed for the synthesis of hemoglobin, but is also essential for enzymes involved in neurochemical reactions. Neurological symptoms like poor attention span, learning deficits, weak memory, delayed motor development and behavioral disturbances caused by iron deficiency are well known. Thus it is possible that iron deficiency may predispose to neurological disturbances like febrile.[2]

OBJECTIVE

General objective

To determine prevalence of iron deficiency in children with febrile seizure.

Specific objectives

- To find out the demographic characteristics of patients
- To assess the clinical features and peripheral blood film findings of patients.
- To assess the laboratory investigations (Hb, erythrocyte PCV, MCV, MCH, serum iron concentration, serum ferritin level and total iron binding capacity) of patients
- To see the association between recurrent FS and type of febrile seizures.

MATERIALS AND METHOD

The study was conducted with following methods and materials.

Study design

A cross sectional observational design was considered suitable for the study.

Place and period of Study

The study was conducted in the Department of Pediatric Medicine, Dr. M R Khan Shishu Hospital & Institute of child health, Mirpur, Dhaka over a period of 6 months from August 2016 to January 2017.

Study sample

Children with a diagnosis of febrile seizures admitted in the above mentioned place were the study population.

Enrollment criteria

Inclusion Criteria

Patients with following characteristics were included in the study.

- Children with any type of febrile seizure
- Aged from 6 months to 6 years
- Children of either gender

Exclusion criteria

Patients with following characteristics were excluded from the study

- Co-morbid conditions like epilepsy
- Patients already on iron therapy
- Patients with delayed development
- Patients known for other causes of anemia
- CNS infection with seizure
- Parents refusing to give written consent.

Sample size

The sample size was determined using following formula.

$$n = \frac{Z^2 pq}{e^2}$$

Where, z=1.96 (where 5% error is acceptable)

P = prevalence of the disease 4%=0.04 (Akbar et al., 2010; Jones & Jacobsen 2007)

q = 1-p = 1-0.04 = 0.96

e = acceptable error 5% =o.o5

$$n = \frac{Z^2 pq}{e^2}$$

$$= \frac{(1.96)^2 \text{ X } 0.04\text{x}0.96}{0.05^2}$$

$$= \frac{3.84 \text{ x } 0.384}{.0025}$$

$$= \frac{0.147456}{0.0025}$$

= 58.9

= 59

Therefore, a total of 59 subjects were included in the study.

Sampling procedure

The required number of children were consecutively included in the study.

Variable studied

The demographic and anthropometric variables were age, sex, body mass index, monthly family income, sanitation facility, source of drinking water and food habit. The clinical features of febrile seizures were fever, duration of fever, cough & cold, duration of cough & cold, loose motion, vomiting, anemia, temperature at admission and temperature at seizure episode. The hematological and biochemical parameters were hemoglobin, findings of peripheral blood film, erythrocyte PCV, MCV, MCH, serum iron concentration, serum ferritin and total binding capacity also recorded.

Institutional approval

Prior permission was taken from Ethical Review Committee, Dr. M R Khan Shishu Hospital& Institute of child health, Mirpur, Dhaka, Bangladesh to conduct this study.

Addressing ethical issues

Keeping compliance with Helsinki Declaration for Medical Research Involving Human Subjects 1964,

parents of the study subjects were informed verbally about the study design, the purpose of the study and right for withdrawing their children from the project at any time, for any reason, what so ever. Parents who gave informed consent to allow their children to participate in the study were included as study sample.

Data collection

A structured data collection form was developed containing all the variables of interest which was finalized following pretesting. Data were collected by interview, observation, clinical and laboratory testing.

Operational definition: Febrile seizure

Febrile seizure was defined as a convulsion associated with an elevated temperature greater than 38 ºC in a child between 6 months to 6 years of age without central nervous system infection or inflammation, acute systemic metabolic abnormality that may produce convulsions and history of previous afebrile seizures.[2]

Iron deficiency: Measurement of serum ferritin is a laboratory test for diagnosing iron deficiency and a ferritin value <12 µg/L is generally acknowledged to be a specific indicator of iron deficiency.[5]

Iron deficiency anemia

Iron deficiency anemia was defined as a hemoglobin value less than 10.5g% and the serum iron to TIBC ratio less than 12% and MCV less than 70fl.[6][7]

Clinical manifestation observed

Fever accompanied by seizure, pallor, angular stomatitis, weakness having no sign of meningeal irritation.

Procedures of preparing and organizing materials

Children were examined for body temperature and presence of seizure. 4 cc venous blood collected from children with febrile illness admitted in the Pediatric medicine wards of Institute of Child Health, Mirpur and sent to Pathology Departments of same hospitals for measurements of hemoglobin, peripheral blood film, PCV, estimate MCV and MCH, serum iron level, serum ferritin level, serum total iron binding capacity.

Data processing and statistical analysis

Data were processed and analyzed using software SPSS (Statistical Package for Social Sciences) version 11.5. The test statistics used to analyze the data were descriptive statistics and Chi-square (χ^2) test. For analytical test the level of significance was set at 0.05 and $p < 0.05$ was considered.

RESULTS

The present study was conducted on 59 children admitted in Pediatric Medicine Department of Dr. M R Khan Shishu Hospital & Institute of child health, Mirpur, Dhaka to assess the prevalence of iron deficiency in febrile seizure patients. The findings of the study derived from data analysis are presented below.

Demographic characteristics

Over one-quarter (25.4%) of patients was below 12 months of age, 39% between 12 – 24 months, 22% between 24 – 36 months and rest 13.6% ≥36 months. The mean age was 19.5 ± 10.6 months and the lowest and highest ages were 6 and 48 months respectively. About 60% was male and 42% female giving a male to female ratio of 1.4:1. A higher proportion of patient's parent or guardians had monthly incomes between Taka 10000 – 15000 and mean monthly income was Taka 11898 ± 3955. 95% of patients used sanitary latrine and rest 5% used kancha latrine or used open spaces.

Over 93% reported that they used water that has been boiled for drinking, 5.1% tap water and remaining 1.7% from other different sources (tube well or river). Exclusive breast-feeding was practiced by 5.1% of mothers, 28.8% used formula feeding, 1.7% cow's milk, 30.5% rice-suji and 33.9% had family diet. Majority (86.4%) of patients was under weight, 11.9% normal and 1.7% overweight or obese. The mean body mass index was 16.8 ± 2.3 kg/m^2 (Table I).

Table I. Distribution of patients by demographic characteristics (n = 59)

Demographic characteristics	Frequency	Percentage
Age (months)		
< 12	15	25.4
12–24	23	39.0
24–36	13	22.0
≥ 36	08	13.6
Sex		
Male	34	57.6
Female	25	42.4
Monthly family income (Taka)		
<10000	13	22.0
10000 – 15000	38	64.4
>15000	08	13.6

Sanitation used	56	95.0
Source of drinking water		
Tap water	03	5.1
Boiled water	55	93.2
Others (Tubewell/river)	01	1.7
Food habit		
Exclusive breast-feeding	03	5.1
Formula feeding	17	28.8
Cow's milk	01	1.7
Rice-suji	18	30.5
Family diet	20	33.9
Body Mass Index (BMI)		
Under weight	51	86.4
Normal	07	11.9
Over-weight & obese	01	1.7

Clinical assessment

Clinical findings demonstrated that all of the patients were suffering from fever (74.6% for 1 day, 22% for 2 days and 3.4% for 3 days) and 28.8% had cough and cold (76.5% between 2 – 4 days and 23.5% between 5 – 7 days). The mean duration suffering from fever and cough & cold were 1.3 ± 0.5 days and 3.4 ± 1.7 days respectively. About 20% of patients experienced loose motion, 6.8% vomiting and 54.2% had anemia. The mean temperature at admission and seizure episode were 101 ± 2^0 F and 104 ± 1^0 F respectively (Table II).

Table II. Distribution of patients by clinical assessment (n = 59).

Clinical assessment	Frequency (%)	Mean ± SD
Fever	59(100.0)	-
Duration of fever		
day days days	44(74.6) 13(22.0) 2(3.4)	1.3 ± 0.5
Cough & cold	17(28.8)	-
Duration of cough & cold (n=17) 2 – 4 days 5 – 7 days	 13(76.5) 4(23.5)	3.4 ± 1.7
Loose motion	12(20.3)	-
Vomiting	4(6.8)	-
Anaemia	32(54.2)	-
Temperature at admission	-	101 ± 2
Temperature at seizure episode	-	104 ± 1

Findings of peripheral blood film

The commonest blood picture was microcytic hypochromic seen in 78% of the patients and normocytic normochromic in 22% (Table III).

Table III. Distribution of patients by peripheral blood film findings (n = 59).

Findings	Frequency	Percentage
Microcytic hypochromic	46	78.0
Normocytic-normochromic	13	22.0

Laboratory investigations

Laboratory investigations shows that mean hemoglobin, PCV, mean corpuscular volume, mean corpuscular hemoglobin, serum iron concentration, serum ferritin level and total iron binding capacity were 9.7 ± 1.4 gm/dl (range:6.8 – 14.2), 30.7 ± 4.6% (range:22 – 44), 67.9 ± 7.1 fl (range:53 – 88), 24.7 ± 4.7 pg (range:15.5 – 33.0), 22.1 ± 0.9 µg/dl (range:14.3 – 38.0), 5.6 ± 1.3 µg/L (range:2.3 – 32.4)and 566 ± 25 µg/dl (range:290 – 963) respectively (Table IV).

Table IV. Distribution of patients by laboratory investigations (n = 59).

Laboratory investigations	Mean ± SD	Range
Hemoglobin (gm/dl)	9.7 ± 1.4	6.8 – 14.2
PCV (%)	30.7 ± 4.6	22 – 44
Mean corpuscular volume (fl)	67.9 ± 7.1	53 – 88
Mean corpuscular hemoglobin (pg)	24.7 ± 4.7	15.5 – 33.0
Serum iron concentration (µg/dl)	22.1 ± 0.9	14.3 – 38.0
Serum ferritin level (µg/L)	5.6 ± 1.3	2.3 – 32.4

Hematological parameters

Table V shows the low level of iron markers. 39% percent of patients had hemoglobin level less than 9 gm/dl, 35.6% mean corpuscular volume less than 65 femtolitre, 64.4% mean corpuscular hemoglobin less than 28 picogram per cell and 49.2% serum ferritin level less than 12 µg/L.

Table V. Distribution of patients by hematological parameters (n = 59).

Hematological parameters	Frequency	Percentage
Hemoglobin (<9 gm/dl)	23	39.0
Mean corpuscular volume (<65 fl)	21	35.6
Mean corpuscular hemoglobin (<28 pg)	38	64.4
Serum ferritin level (<12 µg/L)	29	49.2

Type of febrile seizure

Of the 59 febrile seizures patients, 39(66%) patients suffered from simple seizure and 20(34%) had complex seizure (Figure 1).

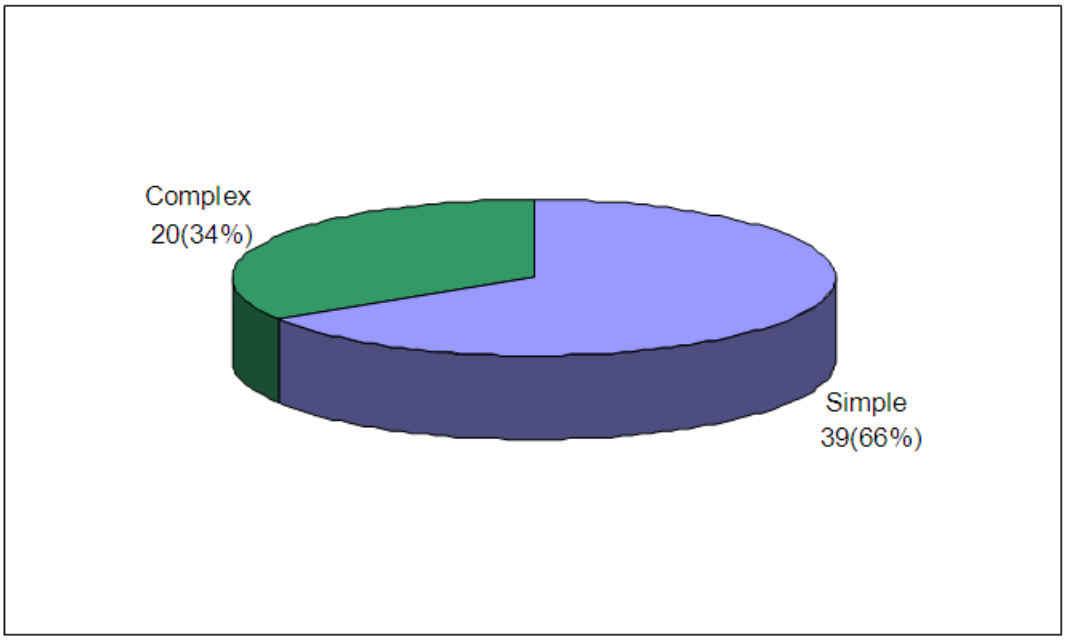

Fig. 1: Distribution of patients by type of febrile seizure (n = 59).

Recurrence of febrile seizure

Table VI compares the recurrence of febrile seizure between simple and complex febrile seizures. Over 28% of simple febrile seizure patients had a history of recurrence of febrile seizures compared to 20% of complex febrile seizures. The comparison did not turn to significant with respect to recurrence of febrile seizure as evident by p = 0.493.

Table VI. Comparison of recurrence of FS between simple and complex FS

Recurrence of FS	**Febrile seizures**		**p-value**
	Simple (n = 39)	Complex (n = 20)	
Yes	11(28.2)	4(20.0)	0.493
No	28(71.8)	16(80.0)	

#Data were analyzed using **Chi-square (χ^2)test.**

Prevalence of iron deficiency

The prevalence of iron deficiency is shown in Figure 2. The data regarding type of iron marker reveal that 49.2% of febrile seizure patients had iron deficiency.

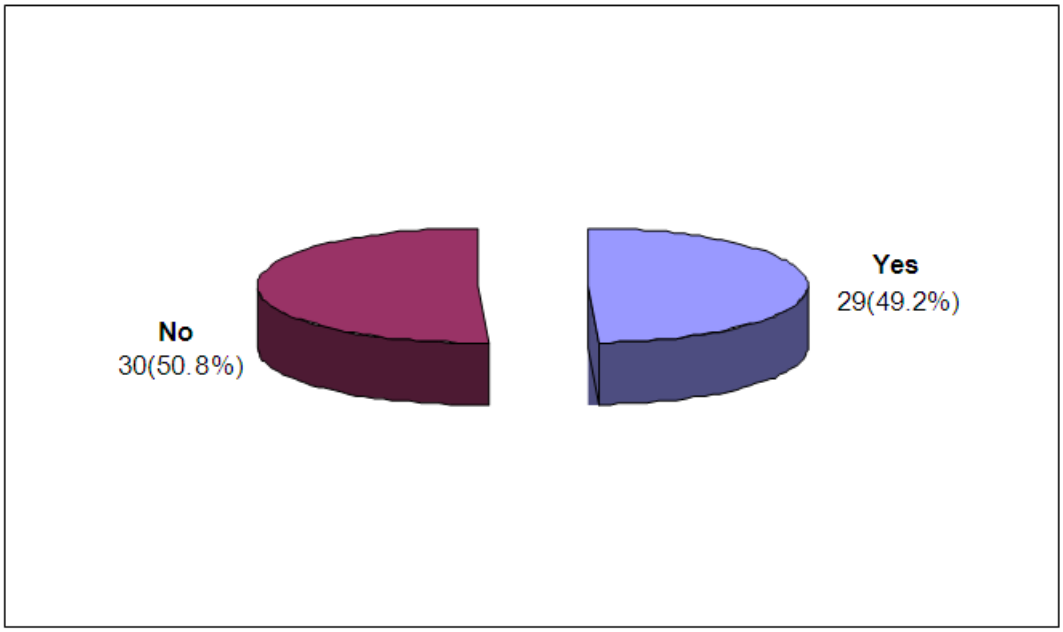

Fig. 2: Distribution of patients by prevalence of iron deficiency (n = 59).

Comparison of iron deficiency between FS

Over half (51.3%) of the simple febrile patients had a history of iron deficiency compared to 45% of the complex febrile seizure patients. The comparison was not statistically significant between groups with respect to iron deficiency (p = 0.648).

Table VII. Comparison of iron deficiency between simple and complex FS.

Iron deficiency	**Febrile seizures**		**p-value**
	Simple **(n = 39)**	Complex **(n = 20)**	
Yes	20(51.3)	9(45.0)	0.648
No	19(48.7)	11(55.0)	

#Data were analysed using **Chi-square (χ^2)Test.**

Figures in the parentheses denoted corresponding percentage.

CONCLUSION

The prevalence of iron deficiency in febrile seizures among hospitalized children is high compared to that in developed countries and is mainly attributed to low and middle socioeconomic status. The simple febrile seizure is the most frequent type of febrile seizure and patients with iron deficiency and risk of recurrence of febrile seizures are higher in simple febrile seizure than complex febrile seizure.

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