

Iron insufficiency predisposes febrile seizure in children

Research article

AKM Mamunur Rashid*, Tahera Nasrin and Luthfor Rahman

Department of Pediatrics, Khulna Medical College, Bangladesh

Received: Jan 30, 2020; **Accepted:** Feb 20, 2020; **Published:** Feb 26, 2020

***Corresponding author:** AKM Mamunur Rashid, Prof. and Head, Department of Pediatrics, Khulna Medical College, Khulna-9000, Bangladesh

Copyright: © 2020 AKM Mamunur Rashid. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Abstract

Objective: Iron deficiency is common in children of developing countries. Febrile seizure is also found between the ages of 6 months to 5 years. Iron has role in the metabolism of neurotransmitter (such as GABA and serotonin) and some enzymes (such as monoaminoxidase and aldehydeoxidase). So, might have the relationship between iron deficiency and febrile seizures. Thus objective of the study was to determine the association between serum ferritin status and febrile seizure in children aged 6 months to 5 years.

Method: This prospective case-control study was conducted among 29 children with febrile seizure (case) and 25 febrile children without seizure (control) from July 2017 to October 2018. Those who had seizure disorder and neurodevelopmental disease were excluded from the study. Age, sex, associated febrile illness and serum ferritin level of both the groups were recorded in preformed questionnaire. The data of both groups were compared and statistically analyzed.

Results: Among 29 children of the case group 03 had mild anemia clinically and others normal but in the control group 24 was not anemic, only one was mildly anemic. Majority, the number was 19 of the case group had acute respiratory infection. Serum ferritin level < 30 ng/ml was found in 11 children of the case group but none in the control group. This was statistically significant. P value was <.001.

Conclusion: Anemia might be clinically absent but low serum ferritin level was found in children of febrile seizure. Iron supplementation might be needed to prevent seizure to every child presenting with febrile seizure.

Keywords

Serum ferritin, febrile seizure

Introduction

Simple febrile seizures (SFSs) are the most common type of seizure that occur between the age of 6 and 60 months with a temperature of 38C (100.4 F) or higher that are not the result of central nervous system infection and that occur in the absence of prior febrile seizures [1,2]. The peak incidence is at the age of approximately 18

months, occurring 2-5% of all children with a recurrence rate of 30 to 40% [3,4] A simple febrile seizure is a primary generalized, tonic-clonic in nature lasts few seconds and to 15 minutes occurs only once in 24 hours [5,6]

Iron plays a critical role in the metabolism of several neurotransmitters and in low iron status aldehyde oxidases and monoamine are reduced. In addition, the

expression of cytochrome C oxidase, a marker of neuronal metabolic activity is decreased in iron deficiency [7]. In developing countries 46-60% of all children under 4 years of age are anemic, with half of the prevalence attributed to iron deficiency anemia. Many studies clearly demonstrated the effect of iron on development, cognition, behavior, and neurophysiology and especially on brain metabolism, neurotransmitter function and myelination, [8] because iron is important for the formation of various enzymes, and neurotransmitters in the central nervous system. Low serum levels of ferritin may lower the seizure threshold [9,10].

Iron deficiency anemia is one of the most prevalent micronutrient deficiencies in young children in Bangladesh and other parts of the developing countries. We compared the serum ferritin level with febrile seizure and a control group in order to determine the relation between iron status and febrile seizure in pediatric patients in pediatric department of a tertiary hospital of Bangladesh.

Patients and Method

A prospective case –control study was carried out in the pediatric department of a tertiary hospital in Bangladesh. Study period was one year 3 months, from July 2018 to October 2018. We enrolled 29 children of the age group 6 months to 6 years with a diagnosis of febrile seizure as case and 25 with fever without convulsion as control. Consent was obtained from the parents of all patients to include in this study, which was approved by the ethical committee of Khulna medical college, Bangladesh.

Cases were simple febrile seizure which were defined as seizures occurring between the ages of 6 months and 6 years, associated with a rectal temperature of at least 38.3°C or an axillary temperature of at least 37.8°C documented medical record, <15 minutes duration without evidence of central nervous system infection, focal neurological signs or history of seizures and occurring once in the previous 24 hours. The seizure was defined as complex if it lasted >15 minutes, occurred more than once in 24 hours or had focal features. Children with develop delay , definite neurological illness, or a history of proved iron deficiency anemia, regular blood transfusion or regular therapeutic dose of iron supplements were excluded from this study.

A control group was selected randomly from children admitted for febrile illness, such as gastroenteritis, otitis media, respiratory tract infection, viral fever without seizure, and also without previous history seizure or anticonvulsant therapy of same age group. Case and control group were comparable for age, sex, history of pica and associated illness.

Serum ferritin (SF) concentration was measured by ELISA. Serum ferritin concentration was compared in both the case and control group in this study. Serum ferritin level of <30.00 ng/ml was considered as low.

Statistical analysis

The data was analyzed with the SPSS version 16, windows 8.1, intelGfx. Chi-square test was used to calculate the differences in proportion. P value <.05 was considered significant.

Results

Total 54 children were included in this study. Among these 29 and 25 were cases and control respectively. 19 children were male and 10 female in case group. On the other hand 12 children were male 13 female in control group. Majority of the children in case group were between the ages 6-24 months. The number was 20, other 9 between the ages of 25- 48 months. In the control group it was between 49-60 months age. The number was 18 among 25 patients. 4 patients were between 25-48 and 3 in 6-24 months age. In the cases, about 16 out of 29 children, duration of convulsion was 1-4 minutes and other 10 had duration of 5-9 minutes. History of previous convulsion was found in 13 children. 23 children had convulsion within 24 hours. Associated diagnosis like acute respiratory infection (ARI) was found in 19 children but 21 of control group had diagnosis other than ARI. Table 1 depicts the associated diagnosis of both the groups. Positive family history of febrile seizure was found in 17 children. Only one patient in the case group had history of pica. Low serum ferritin level of less than 30 ng/ml was found in 11 children of cases group but all in the control group had normal level of >60 ng/ml. Table 2 represents the serum ferritin level in both the groups and its significance. 30-60 ng/ml of Serum ferritin was observed in 7 of the case and none in control group. Clinical anemia was found in 3 children of case and one in control group.

Table 1: Age, sex distribution and clinical scenario of this study.

Subject	ARI	UTI	Others	No	Age			Sex		Anemia			
					6-24m	25-48m	49-60m	M	F	No	Mild	Moderate	Severe
Case	19 (65.5)	01 (3.4)	08 (27.6)	01 (3.4)	20 (69)	09 (31)	00 (00)	19 (65.5)	10 (34.5)	26 (89.65)	03 (10.3)	00 (00)	00 (00)
Control	02 (8.0)	02 (8.0)	21 (84.0)	00 (00)	03 (12)	04 (16)	18 (17)	12 (48)	13 (52)	24 (96)	01 (04)	00 (00)	00 (00)

Figure within the parenthesis indicate percentage. ARI- Acute respiratory tract infection, UTI- Urinary tract infection. M-Male, F- Female, m-Month.

Table 2: Serum ferritin level in case/control group of the study.

Serum ferritin level		Subject		Total	P Value
		Case	Control		
Distribution of respondents by serum ferritin level	<30.00 ng/ml	11 100.0% 37.9%	0 0% 0%	11 100.0% 20.4%	.000
	30.00 – 60.00 ng/ml	7 100.0% 24.1%	0 0% 0%	7 100.0% 13.0%	.000
	>60.00 ng/ml	11 30.6%	25 69.4%	36 100.0%	.000

Discussion

In this study, majority of the febrile seizures (cases) found in male children and between the ages of 6-24 months which was similar to the study by AK Saha and et al., [11] ARI was found to be associated illness in majority of febrile seizures and 1-4 minutes was the duration of convulsion in most of the cases. Majority of the children of the case group in this study had low serum ferritin level as compared to the control that all had normal serum ferritin level. This observation of low serum ferritin associated with febrile seizure was similar to the other studies. There was controversy regarding the role of iron status in febrile convulsion, which is considered a benign seizure syndrome distinct from epilepsy.³ Like the other study fever was present in both the groups.¹ Iron is important for the function of various enzymes and neurotransmitter in the central nervous system, low serum levels of ferritin may lower the seizure threshold. None of the patients in

both the groups were treated for iron deficiency anemia on presentation. Response to iron therapy in children was not evaluated.

In this study significant number of patient with febrile seizure had low serum ferritin level in comparison to the control group. Low iron status might be a contributing factor for the febrile seizure in addition to other factors. Iron supplementation might be advised in patients with febrile seizure to prevent the recurrence of the febrile seizure.

References

1. Soheila Z, Hamid RH, Nader C. Association between iron status and febrile seizures in children. *Seizure* 21 (2012) 603-5.
2. Gowda ANBL, Praveen CS. *Inter J ContempPediatr.* 2018 Jul; 5(4):1300-1303.
3. Berg AT. Febrile seizures and epilepsy: the contribution of epidemiology. *Pediatric and Perinatal Epidemiology* 1992; 6:145-52.

4. Habib Z, Akram S, Ibrahim S, Hasan B. Febrile seizures: Factors affecting risk of recurrence in Pakistan children presenting at The Aga Khan University Hospital. J Pak Med Assoc; 53: 11-7.
5. Johnston MV. Febrile seizure. In: Behrman RE. Nelson textbook of Pediatrics, Philadelphia: Sunders; 2004: 1994-95.
6. Srinavasa S, Reddy SP. Iron deficiency anemia in children with simple febrile seizures – a cohort study. CurrPediater Res. 2014; 18(2): 95-8.
7. DeUnngria M. Rao R, Wobken JD, Luciana M, Nelson CA, Georgieff MK. Perinatal iron deficiency decreases cytochrome c oxidase (CytOx) activity in selected regions of neonatal rat brain. Pediatric Research 2000; 48: 169-76.
8. Madan N, Rusia U, Sikka M, Sharma S, Shankar N. Development and neurophysiologic deficits in iron deficiency in children. Indian Journal of Pediatrics 2011; 78(1): 58-64.
9. Daoud AS, Batieha A, Abu-Ekteish F, Gharaibeh N, Ajlouni S, Hijazi S. Iron status: a possible risk factor for the first febrile seizure. Epilepsia 2002; 43(7): 740-3.
10. Kobrinsky NL, Yager JY, Cheang MS, Yatscoff RW, Tenenbein M. Does iron deficiency raise the seizure threshold? Journal of Child Neurology 1995; 10(March 2): 105-9.
11. AK Saha, MK Hassan, LC Kundu, SK Saha, P Begum, AS Lucky. Low Serum Ferritin is a Risk for Febrile Convulsion in Children. Faridpur Med Coll J 2016; 11(2): 44-6.