

Iron Deficiency as a Risk Factor for Simple Febrile Seizures– A Case Control Study

Dr. Gayatri Bezboruah, Dr Amit Kumar*, Dr Sivaraman

Department of Paediatrics, Gauhati Medical College & Hospital

*Corresponding Author: Dr.Amit Kumar

Abstract: Background: Febrile seizures are the most common seizures in children. Incidence is around 2-5% among children of age group 5-60 months. There is variable association between febrile convulsions and hematological parameters associated with iron deficiency anemia in children. Iron deficiency is also associated with many of the behavioural disorders in children.

Objective: To study the role of iron deficiency as a risk factor for simple febrile seizures.

Design: Prospective Case control study.

Setting: Pediatric department of a tertiary care teaching hospital.

Participants: 60 cases and 60 controls were included in the study. Consecutive cases and concurrent controls were selected. Cases were children of age group 6 months to 60 months presenting with 1st episode simple febrile seizures. Controls were children of same age group presenting with short febrile illness but without any seizures.

Methods: This is a case control study conducted over a period of one year in a tertiary care hospital. Consecutive sixty children with first prospective episode of febrile seizure in the age group of 5 months-60 months admitted in the institution were taken as cases and sixty children with fever due to other causes without seizures were taken as controls. Various blood parameters were compared among these two groups and statistically analysed for the outcome.

Results: Highly significant association was found between iron deficiency and simple febrile seizures in both univariate and multivariate analysis. Crude odds ratio was 3.27 ($P < 0.001$)

Conclusions: Iron deficiency is a significant risk factor for simple febrile seizures in children of age group 6 months to 60 months.

Date of Submission: 11-04-2018

Date of acceptance: 26-04-2018

I. Introduction

Febrile seizure is the most common neurologic disorder of children and the most frequent type of seizure in this age group. It occurs in 3%-4% of children under 5 years, most frequently from 14 to 18 months of age^{1,2}, although incidence rates as high as 14% have been reported.^{3,4} The recurrence rate of febrile seizure for the first time is 50% in children under 1 year of age and 28% for those older than 1.⁵ The simple febrile seizures are diffuse seizures lasting less than 15 minutes and occurring only once over 24 hours. If focal seizure or focal symptoms following the seizure are multiple or lasting more than 15 minutes, the seizure will be termed complex febrile seizure.⁶ Febrile seizure is more common in boys, usually manifesting as tonic-clonic convulsion.⁷ Febrile seizure episodes are agonizing to the parent and child and can cause psychological trauma to both.²⁰ Simple febrile seizure reflects a genetic predisposition to convulsion manifesting with abrupt elevation of body temperature.⁸ Otitis media, and upper respiratory tract infections (especially influenza) are among the most common clinical conditions resulting in febrile seizure in children.⁹ The pathophysiology of febrile seizure remains to be accurately described¹⁰; different studies have reported various risk factors, including iron deficiency as iron is needed for brain energy metabolism, for metabolism of neurotransmitters and for myelination.^{11,12} On the other hand, there are studies that fail to corroborate such an association, as well as those which demonstrate the opposite.^{13,14} Therefore, since iron deficiency anemia is a common disorder of pediatrics and preliminary data have failed to demonstrate a definitive association, we undertook the present study to investigate the association between iron deficiency anemia and febrile seizure in children.

II. Methods

This case control study was done in the Department of Pediatrics, Gauhati medical college, during August 2016 to February 2017. Ethical clearance was obtained for the study from the Ethical committee, Gauhati Medical College.

Cases were children of age group 6 months to 60 months presenting with 1st episode of simple febrile seizures to the Pediatrics Emergency Department and wards of the hospital during the study period.

Diagnostic criteria for simple febrile seizures (based on AAP Clinical Practice Guidelines) included seizures associated with fever and the seizures were generalized, short duration (less than 15 minutes), no recurrence of seizures within 24 hours, child is otherwise neurologically healthy and without any neurological abnormality before and after the episode of seizures, with age group between 6 months to 5 years.¹⁶ Consecutive cases were selected for the study and concurrent controls were selected from the same setting and included febrile children of age group 6 months to 5 years who presented with short duration fever (<3 days) but without seizures. Cases and controls were selected in 1:1 ratio. No matching was done.

Children presenting with atypical febrile seizures, afebrile seizures, h/o of neonatal or previous unprovoked seizures, h/o recent trauma or other causes of provoked seizure, those having any signs & lab findings suggestive of central nervous system infection or any metabolic cause of provoked seizure, those with any chronic neurodevelopment problems, readmission for febrile seizure, those who were previously diagnosed cases of other hematologic problems like hemolytic anemias, bleeding or coagulation disorders, haematologic malignancy, those who were on iron supplementation, and very sick children were excluded from the study.

After informed consent, detailed history was elicited and physical examination was done. Hospital records were also examined for relevant data. The diagnosis of anemia was made by a paediatrician who studied the results of tests without knowing the groups to which each of the test results belonged.

For children aged 6 months to two years, IDA was defined as Hb < 10.5 g/dl, hematocrit (Hct) < 33%, MCV < 70 fL, MCH < 23 pg, MCHC < 30 g/dL, and RBC < 3.7 × 10⁶ cell/mm³. For 2-5-year-old children, IDA was defined as

Hb < 11.5 g/dL, Hct < 34%, MCV < 75 fL, MCH < 24 pg, MCHC < 31 g/dL and RBC < 3.9 × 10⁶ cell/mm³. MCHC, MCH, MCV, and peripheral blood smear were used to rule out other causes of anemia.

The normal level of serum iron was determined as Fe > 40 µg/dL for children younger than one year and Fe > 50 for children over one year of age. The normal range of ferritin was established as more than 12 ng/dL for healthy children and more than 30 ng/dL for children with infection. The normal range of TIBC was considered 210-430 µg/dL. The normal transferrin saturation percentage was considered higher than 15%.^{30,31}

Since this is a hospital based study, a critical sample size was deduced using the following formula:

Sample size = $4pq / l^2$.

P = previous prevalence (4%)

Q = 1 - p

l = absolute allowable error (5%)

The critical sample thus calculated was 30.

Data were entered in MS Excel, cleaned and completeness checked.

Analysis was done using SPSS Version 11. Analysis includes univariate analysis for crude odds ratio and confidence interval, bivariate analysis for confounding and interaction and multivariate analysis for adjusted odds ratio.

III. Results

60 cases and 60 controls were included in the study. Among the 60 cases 16 were diagnosed to have Iron Deficiency anemia. Among the 60 controls 6 were having iron deficiency.

Iron deficiency anemia was found to be a significant variable. Crude odds ratio was 3.27 ($P < 0.001$).

	CASES (30)	CONTROLS (30)	ODDS RATIO	P-VALUE
IRON DEFICIENCY	16 (26.6%)	6 (10%)	3.27	0.001

IV. Discussion

Iron deficiency was found as a significant risk factor for simple febrile seizures in children of age group 6 months to 5 years in our study. In the study done by Pisacane, *et al.*²⁶, among children of the same age group, similar results were noted and the odds ratio was 3.3 (95% CI of 1.7-6.5). Iron status was measured by hemoglobin,

MCV and serum iron in that study. Dawn, *et al.*²⁷ also found similar results with children with febrile seizures almost twice likely to have iron deficiency compared to controls.

In the study by Daoud, *et al.*²⁸, the significance of iron status as a possible risk factor was evaluated. The mean serum ferritin level in the cases was 29.5 mcg/L, much lower than the values in the controls (53.5 mcg/L).

Similar observations were made in a study done by Vaswani, *et al.*²⁹ from Mumbai. The mean serum ferritin level was significantly low in children with first febrile seizures (31.9±31.0 mcg/L) as compared to controls (53.9±56.5 mcg/L) ($P=0.003$). However, no significant difference was noted in the mean haemoglobin value of cases (9.4±1.2 g/dL) and controls (9.5±1.0 g/dL) ($P=0.7$), or in the mean value of blood indices.

Our study also adds & support the previous studies and prove that iron deficiency as a risk factor for febrile seizure.

The study does have some limitations. As the study involved only a small sample size and was a hospital-based study the prevalence of exposure and outcome variables may be different from a community setting. Serum ferritin, a nonspecific acute phase reactant can rise in any inflammatory conditions, although both cases and controls were having fever at the time of enrollment.

We report iron deficiency as a modifiable risk factor for simple febrile seizures in Indian children of age group 6 months to 60 months. Early detection and timely correction of iron deficiency may be helpful for prevention of simple febrile seizures in children of this age group.

Funding: None; *Competing Interest:* None stated.

References

- [1]. Kliegman RM, Stanton B, Geme J, Schor NF, Behrman RE. Nelson Textbook of Pediatrics. 19 edition, Philadelphia: Saunders company, 2011.
- [2]. Leung AK. Febrile seizures. J Pediatr Health Care. 2007; 21(4): 250-55.
- [3]. Jones T, Jacobsen SJ. Childhood febrile seizures: overview and implications. Int J Med Sci. 2007; 4(2): 110-14.
- [4]. Waruiru C, Appleton R. Febrile seizures: an update. Arch Dis Child. 2004; 89(8): 751-6.
- [5]. Abuexteish F, Daoud AS, Alsheyyab M, Non'man M. Demographic characteristics and risk factor of first febrile seizure: a Jordanian experience. J Trop Doct. 2000; 30(1) :25-7.
- [6]. Mikati MA. Seizures in Childhood. In: Menrman ER, ligman RM, Jenson M. Nelson text book of pediatrics. 19th ed. Philadelphia: Saunders company; 2011. P. 2017.
- [7]. Humite Haddad A, About-Khalid B. Epilepsy diagnosis and localization in patients with antecedent childhood febrile convulsions. Neurology, 1998; 50(4): 917-22.
- [8]. Nakayama J, Hamano K, Iwasaki N, Nakahara S, Horigome Y, Saitoh H, et al. Signification evidence for the linkage of febrile seizures to chromosome. Hum. Mol. Genet. (2000; 9(1): 87-91.
- [9]. Evans OB, Ingram JB. Top 10 facts you need to know about febrile seizures. J Miss State Med Assoc. 2011; 52(11): 346-7. Association between Iron Deficiency Anemia and Febrile Seizure... 18 J Pediatr Rev. 2013;1(2)
- [10]. Auvichayapat P, Auvichayapat N, Jedsrisuparp A, Thinkhamrop B, Sriroj S, Piyakulmala T, et al. Incidence of febrile seizures in thalassemic patients. J Med Assoc Thai. 2004; 87(8): 970-3.
- [11]. Daoud AS, Batieha A, Abu-Ekteish F, Gharaibeh N, Ajlouni S, Hijazi S. Iron status; a possible risk factor in first febrile seizure. Epilepsia, 2002; 43(7): 740-3.
- [12]. Kumari PL, Nair MK, Nair SM, Kailas L, Geetha S. Iron deficiency as a risk factor for simple febrile seizures--a case control study. Indian Pediatr. 2012; 49(1): 17-9.
- [13]. Abaskhanian A, VahidShahi K, Parvinnejad N. The Association between Iron Deficiency and the First Episode of Febrile Seizure. J Babol Univ Med Sci. 2009; 11(3): 32-36. [Persian]
- [14]. Hartfield DS, Tan J, Yager JY, Rosychuk RJ, Spady D, Haines C, et al. The association between iron deficiency and febrile seizures in childhood." Clinpediatr. 2009; 48(4): 420-6.
- [15]. Johnston MV. Seizures in childhood. In: Kliegman RM, Behrman RE, Jenson HB, Stanton BP. Nels Text Book of Pediatrics 18th Edition Philadelphia: Saunders Elsevier; 2007. p.2457-8.
- [16]. American Academy of Pediatrics. Febrile seizures. Pediatrics. 2008;121:1281-6.
- [17]. American Academy of Pediatrics, Steering Committee on Quality Improvement and Management. Classifying recommendations for clinical practice guidelines. Pediatrics. 2004;114:874-7.
- [18]. American Academy of Pediatrics. Committee on Quality improvement, Subcommittee on Febrile Seizures. The long-term management of a child with simple febrile seizures. Pediatrics. 1999; 103:1307-9
- [19]. Lynnet GS, Ingrid ES. Febrile seizures. BMJ. 2007;334:307-11.
- [20]. Waruiru C, Appleton R. Febrile seizures: an update. Arch Dis Child. 2004;89:751-6.
- [21]. World Health Organization. Iron Deficiency Anemia. Assessment, Prevention and Control. A Guide for Program Managers. WHO/NHD/013; Geneva: 2001.
- [22]. Beard JL. Iron deficiency alters brain development and functioning. J Nutr. 2003; 133:1468-72.
- [23]. Jyoti B, Seth PK. Effect of iron deficiency on developing rat brain. Indian J Clin Biochem. 2002;17:108-14.
- [24]. Wike WM, Kiser WR. Iron deficiency anemia and febrile convulsions. BMJ. 1996;313: 1205.
- [25]. Ansun N, Shasi S. Susceptibility to febrile Seizures: More than just a faulty thermostat. Canadian J Neurol Sci. 2009;36:277-9.
- [26]. Pisacane A, Roland P, Sansone R, Impagliazzo N, Coppola A, D' Appuzo A. Iron Deficiency anaemia and febrile convulsions: A case control study. BMJ. 1996;313:343.
- [27]. Dawn SH, Jonatan T, Jerome Y, Don S. The association between iron deficiency and febrile seizures in childhood. Clin Pediatr. 2009;48:420-6.
- [28]. Daud AS, Batieha A, Ekteish A, Gharaibeh N, Ajlouni S, Hijazi S. Iron status: a possible risk factor for first febrile seizures. Epilepsia. 2002;43:740-3.
- [29]. Rajwanti KV, Praveen GD, Swati K, Ghosh K. Iron deficiency as a risk factor for first febrile seizure. Indian Pediatr. 2010;47:437-9.
- [30]. Kliegman RM, Stanton BF, St Geme JW, Schor NF, Behrman RE. Nelson Textbook of Pediatrics. 19thed. Philadelphia (PA): WB Saunders Company; 2011. p.2017.

- [31]. Oski FA, Brugnara C, Nathan DG. A Diagnostic Approach to the Anemic Patients. In: Nathan DG, OrkinSH, editors. Nathan and Oski's Hematology of Infancy and Childhood. 7th ed. Philadelphia: WB SaundersCompany; 2008. Appendix 11.

Dr.Gayatribezboruah ." Iron Deficiency As A Risk Factor For Simple Febrile Seizures– A Case Control Study."IOSR Journal of Dental and Medical Sciences (IOSR-JDMS), vol. 17, no. 4, 2018, pp 63-65.