

A retrospective study of hemoglobin levels in children with febrile seizures between the age group 6 months to 6 years

Vitus D'silva^{1*}, K Shreedhara Avabratha²

¹Junior Resident, ²Professor, Department of Pediatrics, Father Muller Medical College and Hospital, Kankanady, Mangalore-575002, Karnataka, INDIA.

Email: vitus_d@rediffmail.com, shreedharkdr@gmail.com

Abstract

Introduction: Febrile seizure is the leading cause of convulsive disorder in paediatric age group with incidence varying from 2-14 %. Iron deficiency anaemia is one of the risk factors known to be associated with febrile seizures. The incidence of iron deficiency anaemia among children 6 to 59 months in India is 79% and the age for peak incidence of febrile seizure is 14 to 18 months, which overlaps with that of iron deficiency anaemia which is 6 to 24 months. Iron deficiency is the commonest micronutrient deficiency causing anemia and is a preventable and treatable condition.

Objectives: To find the prevalence of low hemoglobin in children presenting with febrile seizures and its correlation with the type of febrile seizures. **Results:** Sixty four children diagnosed with febrile seizures over a period of 1 year in a tertiary care hospital were included, out of which 39 were males and 25 females. The prevalence of Simple febrile seizures was 43 (67.2%) and Complex febrile seizures 21 (32.8%). Complex febrile seizure was significantly higher in males compared to females. The prevalence of anemia was 42 % and among the total 27 children with anemia 19 (70.4%) had simple febrile seizures and 8 (29.6%) had complex febrile seizures. However these findings were not statistically significant, probably because the study involved small sample size and was conducted in a tertiary care hospital.

Conclusion: This study concludes that there is no statistically significant relation between low hemoglobin, febrile seizures and type of febrile seizures. Further studies are needed to correlate anemia, febrile seizures and type of febrile seizures and establish possible role of anemia as a risk factor.

Keywords: Febrile seizures, Anemia.

*Address for Correspondence:

Dr. Vitus D'silva, Junior Resident, 2Professor, Department of Pediatrics, Father Muller Medical College and Hospital, Kankanady, Mangalore-575002, Karnataka, INDIA.

Email: vitus_d@rediffmail.com

Received Date: 02/12/2014 Accepted Date: 12/12/2014

Access this article online

Quick Response Code:



Website:

www.statperson.com

DOI: 13 December
2014

INTRODUCTION

Febrile seizures are the most common convulsive disorder occurring in about 3 to 4% of children and frequent cause of emergency hospital admission. Incidence varies from 2-14 % in different society. In United States and Europe incidence is 2-4 %, rates as high as 10 % has been

reported in Japan. The peak incidence is in the second year of life, with the average age of onset between 14 months and 18 months.² The International League Against Epilepsy defines an Febrile Seizure as 'a seizure occurring in childhood between 1 month and 6 years of age, associated with a fever more than 38°C (rectal temperature) not caused by an infection of the central nervous system, without previous neonatal seizures or a previous unprovoked seizure and not meeting criteria for other acute symptomatic seizures.'³ Simple febrile seizures are generalized tonic clonic seizures, lasting less than 15 minutes and not recurring more than once within 24 hours. Complex febrile seizures are focal, prolonged more than 15 minutes, recurrent more than once within 24 hours.⁴ The recurrence rate of febrile seizure is between 30-40% with the rate climbing as the number of risk factors increased. The risk factors are family history of

febrile seizures, epilepsy, perinatal factors and low plasma ferritin level reflecting poor iron status or iron deficiency. There have been reports of linkages to febrile seizures on several chromosomes, including 2q, 5q, 5, 8q, 19p, and 19q, with the strongest linkage on chromosome 2q. Anemia is defined as a reduction of the red blood cell (RBC) volume or hemoglobin concentration below the range of values occurring in healthy persons (less than 2 SD).⁵ The definition of anemia varies by sex and age. The most commonly used definitions of anemia come from the Centers for Disease Control and Prevention (CDC) and the World Health Organization (WHO).⁶

Infants 0.5 to 4.9 years < 11 gm/dl

Children 5 to 11.9 years < 11.5 gm/dl

It is estimated that 30% of the global population suffers from iron-deficiency anaemia; most of those affected live in developing countries. The incidence of iron deficiency anaemia among children 6 months to 59 months in India is 79%. This includes 26% who are mild anaemic, 40% who are moderately anaemic and 3% suffer from severe anaemia (NFHS 3 conducted in 2006). Age for peak incidence of febrile seizure is 14-18 months, which overlaps with that of iron deficiency anaemia which is 6-24 months. Iron deficiency is the commonest micronutrient deficiency worldwide, and is a preventable and treatable condition. Among the numerous biological effects of iron, there is considerable evidence that iron is also important for neurological functioning. Such functions include neurotransmitter metabolism, myelin formation, and brain energy metabolism. Iron is used as cofactor for metabolism of many neurotransmitters, monoamine and aldehyde oxidase in the brain.⁷ In the rodent model, iron deficiency affects regional monoamine metabolism, in part through iron-dependent enzymes such as tryptophan hydroxylase (for serotonin) and tyrosine hydroxylase (for dopamine and norepinephrine). Recent research shows that iron deficiency also results in elevations in extracellular dopamine and norepinephrine and reductions in D1 and D2 receptors and all monoamine transporters. Iron deficiency decreased the expression of cytochrome c oxidase, a marker of neuronal metabolic activity. The purpose of this study is to determine the relationship between anemia, febrile seizures and type of febrile seizures and the possibility of anemia as a risk factor for febrile seizures.

MATERIAL AND METHODS

This was a retrospective study conducted in Father Muller Medical College Hospital, Mangalore during the period January 2012- December 2012 and included children diagnosed with febrile seizures. The diagnosis was made based on clinical examination and after ruling out other causes for acute seizures. Exclusion criteria for all

subjects included co-morbid conditions like children with known cause of anaemia other than iron deficiency anaemia, children on iron therapy, developmental delay. The study design was approved by the Institutional Ethics Committee of Father Muller hospital. Children were grouped as simple and complex febrile seizures based on the clinical criteria. Routine haematological investigation was performed in all children including haemoglobin levels, total counts and electrolytes which formed initial seizure work-up. The hemoglobin estimation was done using auto analyzer. The hemoglobin values obtained were correlated with febrile seizures and the type of febrile seizure - simple and complex febrile seizure. Collected data was analyzed by frequency, percentage, mean and standard deviation. Further statistical analysis was done using chi-square test and t test using SPSS-18. P value < 0.05 was considered significant.

RESULTS

A total of 64 children diagnosed with febrile seizures at our hospital over a period of 1 year were included, out of which 39 were males and 25 females. The youngest child was of the age 6 months and the oldest was of 5 years 4 months. The prevalence of Simple febrile seizures was 43 (67.2%) and Complex febrile seizures 21 (32.8%) (Table 1). Complex febrile seizure was significantly higher in males compared to females. The prevalence of anemia was 42 %. Among the total 27 children with anemia 19 (70.4%) had simple febrile seizures and 8 (29.6%) had complex febrile seizures (Table 2). However these findings were not statistically significant, probably because the study involved small sample size and was conducted in a tertiary care hospital.

DISCUSSION

Anaemia and febrile seizures are two common disorders in paediatric patients. The relationship between anaemia and febrile seizures has been examined in several studies with conflicting results. Commonest cause for anaemia in children is iron deficiency. Iron is an essential element in the metabolism and functioning of enzymes required in neurochemical reactions. These include monoamine oxidase, cytochrome, peroxidase and catalase.^{8,9} Clinically neurological symptoms like poor attention span, learning deficits, poor memory, delayed motor development and behavioural changes caused by iron deficiency are well known.^{8,10,11} Its association with febrile seizures was first observed and published in mid 90's in an Italian study.⁹ In 2009, Hartfield and colleagues, from University of Alberta, Canada reported in a retrospective study that children with febrile seizures were twice as likely to have iron deficiency as those with febrile illness alone. Some international studies denied

any role of iron insufficiency in febrile seizures. In fact, in an Iranian study, Bidabadi and Moushaf from University of Guilan, concluded that iron deficiency is less frequent in children with first febrile seizure.¹² In 2001, Naveed-ur-Rehman and colleagues conducted the only local study at Aga Khan University Hospital which convincingly associated iron deficiency anaemia as a risk factor for febrile seizures.¹³ As in Kobrinski's study, the incidence rate of iron deficiency anemia was significantly higher in the febrile convulsion group compared with the controls. Kobrinski thought that iron deficiency anaemia may have a protective role against convulsion caused by fever.¹⁴ considering the mono-amino-oxidase as a stimulating neurotransmitter, it might be that its amount and function reduction occurs during iron deficiency

anaemia. That may cause a decrease of the neurons over provocation and so decline the incidence of seizure.¹⁵ Hojjat Derakhshan far in his study concluded that the risk of febrile seizure occurrence in anaemic children is less common as compared to non-anaemic ones.¹⁶ Whereas, Leela Kumari in her study concluded that iron deficiency is a significant risk factor for simple febrile seizures in children of age group 6 months to 3 years.¹⁷ In our study anaemia was found in 42.2 % of the total children. However, there was no statistically significant association between anaemia, febrile seizures and febrile seizure type; probably because the study involved a small sample size and was conducted in a tertiary care hospital where most of the children belonged to urban population.

Table 1: Prevalence of types of febrile seizures - simple and complex febrile seizures among different age groups and gender

Age group	Simple febrile seizures	Complex febrile seizures	Total	
< 1 year	5	7	12	
1-2 years	23	8	31	
2-5 years	14	5	19	P=0.156
>5 years	1	1	2	Not significant
Total	43	21	64	
Gender				
Male	22	17	39	P=0.022
Female	21	4	25	Significant
Total	43	21	64	

Table 2: Prevalence of type of febrile seizures in anemic and non-anemic children

Anemia status	Hemoglobin levels (gram %)	Simple febrile seizures	Complex febrile seizures	Total
Anemia	<11 (< 5yrs)	19	7	26
	<11.5 (>5yrs)	0	1	1
	>11 (<5yrs)	23	13	36
No anemia	>11.5 (>5yrs)	1	0	1
		43	21	64
Total				
Mean hemoglobin \pm SD (Standard Deviation)		11.16 \pm 1.34	11.23 \pm 0.87	P=0.789 Not significant

Study	Results
Hartfield	Children with febrile seizures twice likely to have iron deficiency.
Naveed-ur-Rehman	Iron deficiency is a risk factor for febrile seizures.
LeelaKumari	Iron deficiency is a risk factor for febrile seizures.
Kobrinski	Iron deficiency is more common in febrile seizures.
Bidabadi and Moushaf	Iron deficiency less likely in febrile seizures.
HojjatDerakhshanfar	Risk of febrile seizures in anaemic children is less compared to non-anaemics.

The study does have some limitations. As it was a hospital-based study the prevalence of exposure and outcome variables may be different from a community setting. Cause of anaemia was not the scope of the study. We presumed iron deficiency to be the most common cause of anaemia. We recommend follow up studies on the same subjects to establish iron deficiency anaemia.

CONCLUSIONS

Our study concludes that there is no statistically significant correlation between anemia, febrile seizures and type of febrile seizures. Further studies are needed to establish the correlation between occurrence of anemia and type of febrile seizures and therefore to evaluate the possible role of anemia as a risk factor for febrile seizures.

REFERENCES

1. Verity CM, Butler NR, Golding J. Febrile convulsions in a national cohort followed up from birth. Prevalence and recurrence in the first five years of life. *Br Med J (Clin Res Ed)*. 1985; 290(6478):1307–1310.
2. Johnston MV. Seizures in childhood: Febrile seizures. In: Behrman RE, Kliegman RM, Jenson HB, eds. *Nelson's Textbook of Pediatrics*. Pennsylvania: Saunders; 2004. p. 1994-1995.
3. Commission on Epidemiology and Prognosis, International League against Epilepsy. Guidelines for epidemiologic studies on epilepsy. *Epilepsia*. 1993; 34:592–596.
4. AzharDaoud. Febrile convulsion: Review and update. *Jou of Ped Neurology*. 2004; 2(1):9-14.
5. John P Greer, John Foerster, John N Lukens. In: Wintrobe's clinical hematology. 11thed: Lipincott Williamsand Wilkins publisher; 2003.
6. U.S. Preventive Services Task Force. Screening for iron deficiency anemia – including iron prophylaxis. In: *Guide to Clinical Preventive Services*. Baltimore: Williams and Wilkins; 1996.p. 231–46.
7. Paradeeavichayapat *et al*. *J Med AssocThai*. 2004;87(8):970-31.
8. Mahoney DH. Iron-Deficiency Anaemia in children. [Cited 2009 May]. Available from: <http://www.UptoDate.com>.
9. Pisacane A, Sansone R, Impagliazzo N, Coppola A, Rolando P, D'Apuzzo A, *et al*. Iron deficiency anaemia and febrile convulsions: case-control study in children under 2 years. *BMJ*.1996; 313(7053):343.
10. Ohls RK, Christensen RD. Iron-Deficiency Anaemia. In: *Nelson Text book of Pediatrics*. Philadelphia: Saunders; 2008. p. 2014–7.
11. Ambruso DR, Hays T, Goldenberg NA. Iron Deficiency Anaemia. In: *Current Diagnosis and Treatment.Paediatrics*. Denver USA: McGraw Hill; 2009. P.810–11.
12. Bidabadi E, Mashouf M. Association between iron deficiency anemia and first febrile convulsion: A casecontrol study. *Seizure*.2009; 18(5):347–51.
13. Naveed-ur-Rehman, Billoo AG. Association between iron deficiency anemia and febrile seizures. *J Coll Physicians Surg Pak*. 2005; 15(6):338–40.
14. Kobrinsky NL, Yager JY, Cheang MS, Yatscoff RW, Tenenbein M. Does iron deficiency raise the seizure threshold. *J Child Neurol*. 1995; 10(2):105–9.
15. Abbaskhanian A, Vahidshahi k, Parvinnejad N. The association between iron deficiency and the first episode of febrile seizure. *J BabolUni Med Sci*. 2009; 11(3):32–6.
16. Derakhshanfar H, Abaskhanian A, Alimohammadi H, ModanlooKordi M. Association between iron deficiency anemiaand febrile seizure in children. *Med GlasLjekkomoreZenicko-dobojkantona*. 2012; 9(2):239-242.
17. 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.

Source of Support: None Declared
Conflict of Interest: None Declared