CASE-CONTROL STUDY OF IRON DEFICIENCY ANAEMIA IN FEBRILE SEIZURES

Shailaja Potdar¹, Sunil Junagade², Jayesh Panot³, Vandana Kumavat⁴, Mohit V Rojekar⁵, Aniruddha Malgaonkar⁶, Madhuri Bhusare⁷

¹Associate Professor, Department of Paediatrics, Rajiv Gandhi Medical College, Thane.

²Associate Professor, Department of Paediatrics, Rajiv Gandhi Medical College, Thane.

³Assistant Professor, Department of Paediatrics, Rajiv Gandhi Medical College, Thane.

⁴Professor and HOD, Department of Paediatrics, Rajiv Gandhi Medical College, Thane.

⁵Assistant Professor, Department of Biochemistry, Rajiv Gandhi Medical College, Thane.

⁶Assistant Professor, Department of P.S.M., Rajiv Gandhi Medical College, Thane.

⁷Registrar, Department of Paediatrics, Rajiv Gandhi Medical College, Thane.

ABSTRACT

BACKGROUND

Febrile Seizure (FS) is the most common type of childhood seizure, which occurs in 2-5% of neurologically-healthy children between 6 months to 5 years. The exact cause for febrile convulsion is not known, but genetic and environmental factors have influence on its occurrence. Iron deficiency is postulated as a risk factor for febrile seizures in children and it is an easily correctable condition. We therefore studied the association between iron deficiencies in simple febrile seizures.

MATERIALS AND METHODS

This case-control study was done in the Department of Paediatrics of a tertiary care hospital and medical college. Ethical clearance was obtained for the study from the institutional ethical committee.

RESULTS

Hb, Red Cell Width (RDW) and serum ferritin are significantly among cases and controls. Analysis shows there were 9 cases of recurrent febrile seizures among all cases of seizures. Among these, 2 were having onset earlier than 12 months while remaining 7 had onset between 12-18 months.

CONCLUSION

We report iron deficiency as a modifiable risk factor for febrile seizures in Indian children of age group 6 months to 5 years. Early detection and timely correction of iron deficiency maybe helpful for prevention of simple febrile seizures in children of this age group.

KEYWORDS

Iron Deficiency Anaemia, Febrile Seizures, Risk.

HOW TO CITE THIS ARTICLE: Potdar S, Junagade S, Panot J, et al. Case-control study of iron deficiency anaemia in febrile seizures. J. Evolution Med. Dent. Sci. 2017;6(65):4717-4719, DOI: 10.14260/Jemds/2017/1021

BACKGROUND

Febrile Seizure (FS) is the most common type of childhood seizure, which occurs in 2-5% of neurologically-healthy children between 6 months to 5 years.^[1] The exact cause for febrile convulsion is not known, but genetic and environmental factors have influence on its occurrence. Age for peak incidence of febrile seizure is 14-18 months, which overlaps with that of iron deficiency anaemia, which is from 6 to 24 months. Iron deficiency is the commonest micronutrient deficiency worldwide and is a preventable and treatable condition.^[2] Iron is needed for brain energy metabolism for metabolism of neurotransmitters and for myelination. Thus, iron deficiency may alter the seizure threshold of a child.^[3,4]

The pathogenesis of this condition is still unknown. Several potential hypotheses such as genetic basis,

immunologic disorders, low serum iron, as well as reduction of serum and Cerebrospinal Fluid (CSF), zinc, calcium and magnesium levels and low gamma-amino butyric acid have all been proposed to explain the pathophysiology of this condition.^[5] Iron deficiency is postulated as a risk factor for febrile seizures in children and it is an easily correctable condition.^[6] We therefore studied the association between iron deficiencies in simple febrile seizures.

MATERIALS AND METHODS

This case-control study was done in the Department of Paediatrics of a tertiary care hospital and medical college in Thane during June 2015 to May 2016. Ethical clearance was obtained for the study from the institutional ethical committee. Cases were children of age group 6 months to 5 years presenting with simple febrile seizures to the Paediatrics Emergency Department and wards of the hospital during the study period. Cases were included based on diagnostic criteria for simple febrile seizures (based on AAP Clinical Practice Guidelines) included seizures associated with fever and the seizures were generalised short duration (less than 15 minutes). 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.^[7] Consecutive cases were selected for the study and concurrent controls were selected from the same

Financial or Other, Competing Interest: None.

Submission 21-07-2017, Peer Review 07-08-2017,

Acceptance 09-08-2017, Published 14-08-2017.

Corresponding Author:

Dr. Jayesh Panot,

Assistant Professor,

Department of Paediatrics,

Rajiv Gandhi Medical College, Thane.

E-mail: jayeshpanot@gmail.com

DOI: 10.14260/Jemds/2017/1021

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. Exclusion criteria were presentation with those having any signs of central nervous system infection, chronic neurodevelopment problems and diagnosed cases of other haematologic problems like haemolytic anaemia, bleeding or coagulation disorders, haematologic malignancy. Children who are on iron supplementation or have received blood transfusion before were also excluded.

Sample size is calculated using mean and SD from pilot study conducted. It was 9.89 ± 1.35 and 10.75 ± 1.16 for the cases and controls respectively for haemoglobin. Sample size comes out to be 27 with two-sided confidence interval is 90% and power of the study is 80%. Therefore, by considering 10% dropouts, we have taken 30 subjects in each. No matching was done. After written informed consent from parents or legal guardians, detailed history was elicited and physical examination was done. Hospital records were also examined for relevant data. Blood investigations done to diagnose iron deficiency included haemoglobin estimation and Red Cell Distribution Width (RDW) using an automated haematology analyser (Sysmex Kx-21) and serum ferritin estimation using ELISA method (AccuBind ELISA). Iron deficiency was diagnosed by haematologic investigations of haemoglobin value, serum ferritin value and RDW (WHO). Results were analysed using SPSS 20. It includes t-test, ROC curve analysis and Odds ratio calculation.

RESULTS

The average age of cases and controls was 18.9 ± 9.01 and 16.53 ± 8.34 months, respectively. Average age of onset of febrile seizures is 15.83 ± 7.41 . This is somewhat earlier in females (14.60 ± 4.27) than in males (16.45 ± 8.61).

Parameter	Cases	Controls	p-value
Age (months)	18.90 ± 9.01	16.53 ± 8.34	0.680
Convulsion onset age (months)	15.83 ± 7.41	-	-
Birth weight (g)	2816.00 ± 540.36	2929.17 ± 223.92	0.2892
Hb (g%)	10.04 ± 1.35	10.71 ± 1.16	0.039
RDW (%)	41.63 ± 5.41	37.41 ± 8.12	0.018
Serum iron (ug/dL)	29.83 ± 21.53	34.59 ± 30.48	0.484
Serum ferritin (ng/mL)	77.88 ± 95.83	37.92 ± 33.76	0.032
Transferrin sat (%)	8.27 ± 5.29	10.02 ± 8.11	0.322
TIBC (ug/dL)	386.82 ± 73.85	398.23 ± 83.20	0.575

Table 1. Study Parameters

Table 1 shows Hb, Red Cell Width (RDW) and serum ferritin are significantly different among cases and controls. Birth weights, serum iron, transferrin saturation, Total Iron-Binding Capacity (TIBC) are not statistically significant. Analysis shows there were 9 cases of recurrent febrile seizures among all cases of seizures. Among these, 2 were having onset earlier than 12 months, while remaining 7 had onset between 12-18 months. On ROC curve, Ferritin cut-off comes out to be 17 ng/mL. Odds ratio for iron deficiency anaemia being risk factor for febrile convulsion is 1.75.

Risk factor analysis for recurrent febrile seizure shows male gender (88.88%) as commonest risk factor seen. Other risk factors were age less than 1 year and complex febrile seizures were seen in 2 cases each (22.22%). Duration of fever less than 24 hours, fever 38-39°C, family history of epilepsy and low serum Na⁺ levels were seen in 1 case each (11.11%). Table 2 shows risk factor analysis in patients with recurrent febrile seizures. The risk factors are age less than 1 year, duration of fever less than 24 hours, fever 38-39°C (100.4-102.2 F), family history of febrile seizures, family history of epilepsy, complex febrile seizures, daycare, male gender, lower serum sodium at the time of presentation.^[6]

Risk Factor	Total Number Patients	Patients with Recurrence	%
0	4	0	0
1	13	3	23.08
2	9	5	55.56
3 or more	4	1	25
Total	30	9	

Table 2. Risk Factor Analysis in Patients with Recurrent Febrile Seizures

Anaemia parameters in febrile seizures are shown in table 3. There is no statistical difference among the patients with single episode and multiple episodes. Parameters studied were Hb, RDW, serum iron and serum ferritin. Serum iron and serum ferritin levels were found to be low in recurrent episode group as compared to single episode group.

Parameter	Single Episode	Recurrent Episode	p-value
Hb	10.10 ± 1.32	10.24 ± 1.49	0.927
RDW	40.81 ± 4.84	43.54 ± 6.10	0.205
Serum iron	33.50 ± 24.81	21.29 ± 4.69	0.283
Serum ferritin	88.21 ± 121.43	53.78 ± 77.31	0.441

Table 3. Anaemia Parameters in Febrile Seizures

DISCUSSION

Iron deficiency was found as a significant risk factor for febrile seizures in children of age group 6 months to 5 years in our study. In a recent study by Aly et al, it is shown that iron deficiency is a significant risk factor for febrile seizures in children less than 3 years of age.^[5] Similar picture emerges from the study by Leela Kumari et al. They found that serum iron, serum ferritin, TIBC and RDW are the parameters that are statistically and clinically different in cases of febrile seizures than in controls.^[8]

In the study done by Pisacane et al among children of the same age group, similar results were noted.^[9] Iron status was measured by haemoglobin, MCV and serum iron in that study. Dawn et al also found similar results with children with febrile seizures almost twice likely to have iron deficiency compared to controls.^[10]

In addition to the finding that iron deficiency is one of the risk factor for febrile seizures in the present study, we have tried to find out any difference exist between single episode and recurrent episodes of seizures. Here, we find that the anaemia parameters are statistically not significant among these two, but the levels were low in recurrent group compared to single episode group.

It is clear from the above study that iron deficiency is an important parameter many times overlooked. There is need

for the large-scale study, which maybe one of the lacunae of our study. The present study reports that no significant statistical difference exists among recurrent and single episode febrile seizures for iron deficiency. One of the possible reasons for this maybe limited sample size. It could have been significant if studied with larger sample size. The strength of our study included standardised criteria for diagnosing febrile seizures and iron deficiency, elimination of incidence prevalence bias, concurrent enrolment of controls and cases and no recall bias regarding exposure. The study does have some limitations. As it was a hospital-based study, the prevalence of exposure and outcome variables maybe 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 enrolment.

CONCLUSION

We report iron deficiency as a modifiable risk factor for febrile seizures in Indian children of age group 6 months to 5 years. Early detection and timely correction of iron deficiency maybe helpful for prevention of simple febrile seizures in children of this age group.

REFERENCES

- [1] Fallah R, Tirandazi B, Karbasi SA, et al. Iron deficiency and iron deficiency anemia in children with febrile seizure. *Iran J Ped Hematol Oncol* 2013;3(1):200-3.
- [2] World Health Organization. Iron deficiency anemia. Assessment, Prevention and Control. A Guide for Program Managers. WHO/NHD/013; Geneva: 2001.
- [3] Beard J. Iron deficiency alters brain development and functioning. *J Nutr* 2003;133(5 Suppl 1):1468S-72S.
- [4] Jyoti B, Seth PK. Effect of iron deficiency on developing rat brain. *Indian J Clin Biochem* 2002;17(2):108-14.
- [5] Aly IAERM, Kmal HM, Soliman DR, et al. Iron profile parameters and serum zinc & copper levels in children with febrile convulsions in Banha. *J Am Sci* 2014;10(7):1-5.
- [6] Mikati MA, Hani AJ. Nelson textbook of pediatrics. Seizures in childhood. In: Kliegman RM, Stanton BF, Schor NF, et al. (eds). 20th edn. Canada: Elsevier, 2016.
- [7] Steering Committee on Quality Improvement and Management, Subcommittee on Febrile Seizures American Academy of Pediatrics. Febrile seizures: clinical practice guideline for the long-term management of the child with simple febrile seizures. *Pediatrics* 2008;121(6):1281-6.
- [8] Kumari PL, Nair MK, Nair SM, et al. Iron deficiency as a risk factor for simple febrile seizures-a case control study. *Indian Pediatr* 2012;49(1):17-9.
- [9] Pisacane A, Sansone R, Impagliazzo N, et al. Iron deficiency anaemia and febrile convulsions: a case control study in children under 2 years. *BMJ* 1996;313(7053):343.
- [10] Dawn SH, Jonatan T, Jerome Y, et al. The association between iron deficiency and febrile seizures in childhood. *Clin Pediatr* 2009;48(4):420-6.