

Research paper

Iron deficiency anemia as a risk factor for simple febrile seizures: myth or reality?

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Abstract:

Background: Simple febrile seizure is a common childhood occurrence. It has been reported that there can be an association between underlying iron deficiency anemia (IDA) and simple febrile seizure. Iron deficiency anemia is a treatable micronutrient deficiency which can be easily overcome by simple management. This study therefore aims to investigate iron deficiency anemia as a risk factor for simple febrile seizure. **Methods:** This case control study is based on a sample size of 120 in total (60 cases and 60 controls). Quantitative and qualitative variables were same for both groups; except for the fact that the control group showed no febrile seizure. Fever was recorded and biochemical tests including hemoglobin and ferritin level, red blood cells distribution width (RDW) and red blood cell count (RBC) were performed. The lab results were then analyzed statistically using Statistical Package for Social Sciences (SPSS) version 19.0. **Results:** It was observed that iron deficiency anemia was more prevalent in cases as compared to control, having mean hemoglobin values as 8.16 ± 0.80 , and 11.53 ± 0.67 respectively. Statistically significant difference was measured in mean ferritin, RDW and RBC i.e. 6.25 ± 0.67 , 18.38 ± 0.53 , 3.5 ± 0.39 and 12.56 ± 0.83 , 13.61 ± 0.66 , 4.3 ± 0.84 in cases (Group B) and controls (Group A) respectively. Based on these values, group A has been categorized as non-anemic and group B as IDA. Simple febrile seizures were more prevalent in iron deficiency anemia group. Chi-square test and p-values for iron deficiency anemia and number of seizures revealed statically significant results. **Conclusion:** In the light of the study conducted it can be concluded that iron-deficiency anemia is a risk factor for triggering the onset of simple febrile seizure. Timely intervention and simple management of iron deficiency anemia can help to prevent frequent recur of simple febrile seizure.

Keywords: Anemia, Iron Deficiency anemia, Febrile Seizure, Fever.

Introduction:

A febrile seizure also known as convulsion is linked to elevated core temperature without any potentially serious reason/etiological agent (1). These are common in children between 6 months to 5 years of age without any central nervous system (CNS) infection or metabolic imbalance (3). Simple febrile seizures are defined as generalized convulsions that last for less than 15 minutes and do not recur within 24 hours. Most fits are under 5 minutes and may be as long as 60 minutes before the child returns to normal.

This condition occurs in 2-5% of neurologically healthy children. Febrile seizure is sometimes genetic caused by autosomal dominant genes and run in the families (3). These seizures usually occur with high fever caused due to otitis media, urinary tract infection (UTI) and acute respiratory infection (ARI). Diagnosis is based on making sure that no infection of the brain is present and that no seizure has ever been encountered without fever (1).

Among the many risk factor associated with simple febrile seizures, iron deficiency anemia has been reported to be

the most common factor. Iron deficiency anemia is defined as a common nutritional deficiency (30%) especially in developing countries (50%) and commonly found in the age group between 6 months to 5 years (2). Iron is a vital micronutrient and is used by all body cells specially those involved in neurotransmitter metabolism of neurotransmitters. Role of iron can also be seen in several processes including hormonal function, DNA duplication, brain functions, myelin formation and as cofactor for different human enzymes (3). This factor however is easily manageable; in Pakistan this micronutrient deficiency is increasing as a predisposed factor for simple febrile seizure. Therefore, current study was designed to check the association iron deficiency anemia with simple febrile seizure.

Materials and Methods

This was a case control study based on 120 (60 cases and 60 controls) samples in total. Sample were collected from KRL Hospital, Islamabad during July to December 2018. Prior permission was taken from the hospital ethical committee. Children between the ages of 6 months to 5 years were included in the study. Gender, duration and episode of seizure were recorded. Detailed information was collected from the parents/guardians with

informed consent. Control group of 60 febrile patients of same age and gender but no seizure was compared to the case group. Inclusion into the study was based on fever 101°F and above caused by UTI, ARI and otitis media. Seizures that lasted for less than 15 minutes and did not recur were considered to be simple febrile seizure. Cases with known history of CNS infection, electrolytes imbalance, cardiac problems and metabolic problems were excluded. Iron deficiency anemia was diagnosed based on physical examination and lab reports indicating hemoglobin levels <10.5 g/dl, ferritin levels <12 ng/ml, RDW value >14 and RBC <3.8. SPSS version 19.0 was used for statistical analysis and p value of <0.05 was considered to be statistically significant.

Results

Out of 120 sample size, 60 were cases and 60 were controls. Mean values for matching variables for both groups are shown in table 1. The chi-square test was performed for both groups to evaluate the relationship between iron deficiency anemia and simple febrile seizure (Table 3). The p-Value was found to be <0.05 indicating statistically significant difference.

Table 1: Matching variables; case & control group

Variable	Case (n=60)	Control (n=60)
Age	3.75±0.60	3.75±0.60
Gender	Male=24 Female=36	Male=36 Female=24
Fever	101.25±1.12	101.25±1.28
Weight	12.63±1.16	12.75±2.15

Table 2: Comparing variables; case & control group

Variable	Case (n=60)	Control (n=60)	p-Value (<0.05)
Hemoglobin Levels	8.16±0.80	11.53±0.67	0.001
Ferritin Levels	6.25±0.67	12.56±0.83	0.002
RDW Value	18.38±0.53	13.61±0.66	0.002
RBC	3.5±0.39	4.3±0.84	0.024
Episode of Seizure	1.70±0.78	0.20±0.48	0.004

Table 3: Chi-square test for association between Iron Deficiency Anemia and simple febrile seizure.

	Mean	Standard deviation	p-Value (<0.05)
Simple febrile seizure	0.76	1.30	0.004
IDA	0.71	0.78	0.001

Discussion

Simple febrile convulsions commonly occur in 2-5 % in the age group 6 months to 5 years. Although this is a benign issue but highly frightening for the parents. Among many associated risk factors iron deficiency anemia is well known. This is widespread nutritional disorder particularly in kids and expecting women. In Pakistan, iron deficiency anemia is identified as a public health issue affecting 50% women of reproductive age leading to the birth of anemic children (4). According to an estimate 78% children below age of 5 years are anemic in Pakistan. Iron deficiency anemia is more frequently found in female kids as compared to males with a higher prevalence in rural areas relative to urban population (5). Deficiency of this micronutrient contributes to retarded growth, problems in learning and memory, physical lethargy, mortality and febrile seizures in children below the age of 5 years (5) (6).

Besides, febrile seizure are reported to be most common cause of childhood convulsions (7). Oral iron administration, however, improved the situation by increasing the hemoglobin levels. Several studies have reported the connection between iron deficiency anemia and febrile seizure (8). High prevalence of iron deficiency anemia has been reported from Karachi, semi urban Peshawar and Abbottabad (9-11). Dietary changes and deworming have been suggested as therapeutic measures leading to resumption of hemoglobin levels (4). Several studies from Iran have reported the association of febrile seizure with iron deficiency anemia. A report from 2012 studied the iron levels in cases with febrile seizure in children below 3 years. In this study researchers checked the hemoglobin, mean corpuscular volume (MCV), serum iron (SI), total iron binding capacity (TIBC) in children who had febrile seizures. Their results suggested that reduction of iron levels could be important

risk factor for febrile seizures (12). Another study assessed the hemoglobin, serum iron and ferritin levels from 45 girls and 55 boys and found a significant association of iron deficiency with febrile seizures (13).

Similarly, our results have revealed that iron deficiency anemia is higher in children suffering from febrile seizure when compared to age-matched controls with same degree of fever. In our study, hematological parameters like hemoglobin levels, serum ferritin levels, RBC count and RDW values which revealed iron deficiency anemia in children who suffered simple febrile seizures. However, few studies have reported that there is no link between iron deficiency anemia and simple febrile seizures.

Conclusion

The current results show that iron deficiency anemia is a risk factor for febrile fits. However, if anemia is treated by simple manageable therapy, incidences of simple febrile fits can be lowered.

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References

1. Gupta S, Agarwal N, Maheshwari M. Iron deficiency as a risk factor for febrile seizures—a case control study. *People*. 2015;8(2):37.
2. Razaq M, Digra SK, Sharma SD, Saini GS. The Relationship Between Iron Deficiency Anemia And First Febrile Convulsion In Children. *JK Science*. 2017;19(2):85-9.
3. Heydarian F, Vatankhah H. The role of anemia in first simple febrile seizure in children aged 6 months to 5 years old. *Neurosciences (Riyadh)*. 2012;17(3):226-9.
4. Akhtar S, Ahmed A, Ahmad A, Ali Z, Riaz M, Ismail T. Iron status of the Pakistani population—current issues and strategies. *Asia Pacific journal of clinical nutrition*. 2013;22(3):340.
5. Habib MA, Black K, Soofi SB, Hussain I, Bhatti Z, Bhutta ZA, et al. Prevalence and predictors of iron deficiency anemia in children under five years of age in Pakistan, a secondary analysis of national nutrition survey data 2011–2012. *PloS one*. 2016;11(5):e0155051.
6. Alzaheb RA, Alatawi N, Daoud KA, Altawil N. Assessment of the dietary intakes of 6-and 12-month-old infants in Saudi Arabia. *International journal for vitamin and nutrition research Internationale Zeitschrift für Vitamin-und Ernährungsforschung Journal international de vitaminologie et de nutrition*. 2017;87(1-2):37-48.
7. Karimi P, Badfar G, Soleymani A, Khorshidi A. Association of iron deficiency anemia and febrile seizure in Asia: A systematic review and meta-analysis. *Iranian Journal of Neonatology IJN*. 2018;9(1):42-52.
8. Ottman R, Hirose S, Jain S, Lerche H, Lopes-Cendes I, Noebels JL, et al. Genetic testing in the epilepsies—report of the ILAE Genetics Commission. *Epilepsia*. 2010;51(4):655-70.
9. Qureshi MIM, Khan SA, Farzana K, Murtaza G, Azhar S, Noreen S, et al. Prevalence of iron deficiency in adult population: A case study from Khyber Pakhtunkhwa (KPK), Pakistan. *International Journal of Physical Sciences*. 2012;7(11):1874-7.
10. Janjua NZ, Delzell E, Larson RR, Meleth S, Kabagambe EK, Kristensen S, et al. Maternal nutritional status during pregnancy and surma use determine cord lead levels in Karachi, Pakistan. *Environmental research*. 2008;108(1):69-79.
11. Paracha PI, Hameed A, Simon J, Jamil A, Nawab G. Prevalence of Anaemia in Semi-Urban Areas of Peshawar, Pakistan—A Challenge for Health Professionals and

Policy Makers. Journal-Pakistan medical association. 1997;47:49-53.

12. Sadeghzadeh M, ASL PK, Mahboubi E. Iron status and febrile seizure-a case control study in children less than 3 years. Iranian journal of child neurology. 2012;6(4):27.

13. Fallah R, Tirandazi B, Karbasi SA, Golestan M. Iron deficiency and iron deficiency anemia in children with febrile seizure. Iranian journal of pediatric hematology and oncology. 2013;3(1):200.