Iron Deficiency Anemia among Children with Febrile Seizures Presenting at CMH Muzaffarabad

Naheem Ahmed¹, Kiran Ashfaq Ahmed², Munazza Nazir³, Zehra Batool⁴, Shanza Khan⁵, Rashada Bibi⁶

- 1 Associate Professor, Department of Pediatrics, Azad Jammu Kashmir Medical College, Muzaffarabad Pakistan Manuscript writing and guidelines-
- 2 Senior Registrar, Department of Pediatrics, Azad Jammu Kashmir Medical College, Muzaffarabad Pakistan Literature review and analysis
- 3 Associate Professor, Department of Pediatrics, Azad Jammu Kashmir Medical College, Muzaffarabad Pakistan Draft formatting and data analysis
- 4 Senior Registrar, Department of Pediatrics, The Children Hospital, PIMS, Islamabad Pakistan Data analysis and review literature
- 5 Post Graduate Resident, Department of Pediatric Medicine, CMH, Muzaffarabad Pakistan Data collection and paper writing
- 6 Radiology, Azad Jammu Kashmir Medical College, Muzaffarabad Pakistan Data analysis

How to Cite: Ahmed N, Ahmed KA, Nazir M, Batool Z, Khan S, Bibi R. Iron Deficiency Anemia among Children with Febrile Seizures Presenting at CMH Muzaffarabad. APMC 2022;16(1):17-20. DOI: 10.29054/APMC/2022.1022

ABSTRACT

APMC

Background: Febrile Convulsions (FC) are convulsions that occur in children aged 6 months to 5 years old with a 38°C or more body temperature that are not caused by a Central Nervous System (CNS) illness or any metabolic imbalance and are not preceded by afebrile seizures. This syndrome affects 2-5 percent of children who are otherwise healthy neurologically. Although the exact etiology of FC is unknown, various genetic and environmental variables have been linked to it. **Objective:** To find out the prevalence of iron deficiency anemia (IDA) is in children who have febrile seizures at CMH Muzaffarabad. Study Design: Descriptive, cross-sectional study. Settings: Department of Pediatrics, CMH Muzaffarabad. Duration: Study duration was six months from July 2020 to December 2020. Methods: A total of 200 children presenting with diagnosed febrile seizure (already diagnosed cases), aged between 6 months to 5 years and both genders were included. Detail history and laboratory investigations were done for the confirmation of febrile seizure in the included children. A 5cc blood sample was taken from the included each child and was sent to hospital laboratory for the diagnosis of Iron deficiency anemia. All the laboratory investigation were performed by an expert pathologist having at least 3 years of experience to avoid any bias. IDA was labeled as positive if the concentration of hemoglobin less than 10 gm/dl, MCV less than 70fl and the level of serum iron less than 22µg/dl. All the data were recorded in Performa and SPSS version 26 was used for the analysis. **Results:** Average age of the study subjects was 2.27 ± 1.24 years males were in majority 60.0% with ratio of male to female as 1.5:1. Overall hemoglobin average was 9.68±2.39 g/dl, serum ferritin average was 11.02±3.78 μ g/L and overall serum iron average was 4.76±1.09 μ mole/L. Among children having febrile seizure, the iron deficiency anemia was found in 59.50%. Conclusion: The frequency of Iron deficiency anemia was observed to highly frequent among children who were presented with febrile seizure.

Keywords: Febrile seizures, Iron deficiency, Anemia.

INTRODUCTION

Febrile seizures are the seizures that begin in childhood aged 6 months to 5 years old and are associated with the temperature (fever) of more than 100.4°F (38°C).¹ People have questioned whether these youngsters would benefit from daily anticonvulsant medication since the early twentieth century. Simple, complex and symptomatic febrile seizures are the three types of febrile seizures identified by epidemiological investigations. Even while febrile seizures are often safe for children, they can be alarming for caregivers, so it's critical to handle parental worry in the most compassionate way possible. Feverish seizures have an unclear pathogenesis. The event is thought to be triggered by a mix of genetic susceptibility and environmental circumstances, including the fever and its cause.²

Several mutations in the gamma-aminobutyric acid (GABA) A receptor 2 subunit gene have also been linked

CORRESPONDING AUTHOR Dr. Naheem Ahmed Associate Professor, Department of Pediatrics, Azad Jammu Kashmir Medical College, Muzaffarabad Pakistan Email: drnaeem885@gmail.com

> Submitted for Publication: 13-07-2021 Accepted for Publication 09-03-2022

to febrile seizures as previous studies.³ Delay in the development, discharge after 28 days from the neonatal unit of the hospital, viral infection, day care attendance, febrile seizures related family history, specific immunizations, and probably the deficiencies of the zinc and iron are all the febrile seizures' risk factors.⁴⁻⁶

About half of all pre-school children in underdeveloped countries suffer from anemia, which is caused mostly by iron deficiency. The most frequent nutritional and hematological illness of infants and of early childhood is iron deficiency anaemia.^{7,8} One study of febrile seizures found zinc levels in the blood were found to be the significantly lower in cases with FS in contrast to controls (without febrile seizures),9 while in another study, Children having FS are about significantly more (twice) likely to have iron deficiency anemia as children having febrile illness contrast to those who did not have seizures.¹⁰ Anemia affects 293 million children globally, with a proportion of 47.4 percent in preschool-aged children.¹¹ Iron deficiency is the leading cause of anemia and according to an estimation 30% of worldwide population suffers from iron deficiency anemia (IDA), and most affected are living in developing nations.11 According to Pakistan National Nutrition survey, 65% children between age 760 months had iron deficiency anemia.12 Synthesis of hemoglobin and functions of various enzymes involved in neurochemical reactions require iron. As per above scenarios the iron deficiency can therefore lead to many neurological disturbances like febrile seizures. As the iron deficiency anemia is of great concern for development and growth of children, so it has been decided to conduct this study to find out how common iron deficiency anemia is in children who have a febrile seizure in the local population. As majority of our population belong to rural areas and poor socioeconomic status where proper nutritional needs of infants cannot be met, so there is a need of a local study to determine the magnitude of the problem. The results of this study not show the local status regarding the problem. Although previously it is established but locally, we are missing the statistics regarding this and also majority of our population belong to low socioeconomic status, so I am expecting higher percentage in our population. Then on the basis of the results, our public can be encouraged for proper nutrition to children and early screening and managing these particular patients in order to reduce the complications of anemia.

METHODS

This was Descriptive, Cross-sectional study conducted at Department of Pediatrics, CMH, Muzaffarabad Pakistan, during a period of (Six months) from July 2020 to December 2020.

Sample size was 200 keeping 52.5%¹⁴ prevalence of IDA in children having febrile seizures, confidence interval 95% and margin of error 7%. According to WHO formula for the calculation of sample size by using non-probability, consecutive sampling technique.

A All the children presenting with diagnosed febrile seizure (already diagnosed cases), aged between 6 months to 5 years and both gender (male/female) were included in the study.

All the children presenting with seizures due to proven CNS Infections, known hemoglobinopathies, personal or family history of any type of seizures i.e., epilepsy and children with neurological deficits and delay developmental were excluded from the study.

In the current study all the children fulfilling the inclusion criteria i.e., children presenting with febrile seizure were enrolled in the study through OPD and emergency department of CMH, Muzaffarabad. Permission from hospital ethics committee was taken and the parents of the children provided signed informed permission. Detail history and laboratory investigations were done for the confirmation of febrile seizure in the included children. A 5cc blood sample was taken from the included each child and was sent to hospital laboratory for the assessment of Iron deficiency anemia. All the laboratory investigation were performed by an expert pathologist having at least 3 years of experience to avoid any bias. If the concentration of Hemoglobin less than 10 gm/dl, MCV less than 70fl and the level of serum iron less than 22µg/dl, iron deficiency anemia was considered positive. All the data regarding gender, age, socio economic status, residence, family history of seizures and history of iron supplement intake were recorded in Performa. To eliminate bias in the study results, exclusion criteria were used. All the recorded information on Performa was entered in statistical software SPSS version 26.

RESULTS

The participants in this study ranged in age of six months to five years old, with the mean age of 2.27 1.24 years. The majority of the patients, 118 (59.0%), were between the ages of 6 months and two years. The male to female ratio was 1.5:1 among the 200 participants, with 60.0% males and 40.0% females. Mean hemoglobin levels were 9.68±2.39 g/dl. Mean serum ferritin levels were 11.02±3.78 μ g/L. Mean serum iron (μ mole/L) was 4.76±1.09. Distribution of patients according to residence and socioeconomic status and distribution of patients according to family history of seizures and history of iron supplement is shown in table 1.

Iron deficiency anemia affects 59.50 percent of children who have a febrile seizure as shown in Figure 1.

Table 1: Descriptive statistics of the demographicvariable (n = 150)

Variables		Statistics		
Age		2.27 ± 1.24 years		
Gender	Males	120 (60.0%)		
	Females	80 (40.0%)		
Residence	Rural	92 (46.0%)		
	Urban	108 (54.0%)		
Socioeconomic status	Poor	46 (23.0%)		
	Middle	100 (50.0%)		
	Upper	54 (27.0%)		
Family history of seizures	Yes	57 (28.5%)		
	No	143 (71.5%)		
History of iron supplement	Yes	33 (16.5%)		
	No	167 (83.5%)		

Figure 1: Iron deficiency anemia among children of febrile seizure (n = 150)



Stratification of iron deficiency with respect to age groups and gender, residence, socioeconomic status, family history of seizures and history of iron supplement. Table 2.

Table 2: Stratification of iron deficiency anemia with respect to age groups (n = 150)

Variables		Iron Deficiency Anemia		P- value	
		Yes	No		
Age groups	6 months to 2 years	66	52	0.218	
	3-5 years	53	29		
Gender	Male	80	40	0.011	
	Female	39	41		
Residence	Rural	55	37	0.940	
	Urban	64	44		
	Poor	35	11		
Socioeconomic	Middle	48	52	0.003	
status	Upper	36	18	0.003	
Family history	Yes	38	19	0.192	
	No	81	62		
History of iron	Yes	15	18	0.072	
supplement	No	104	63	0.072	

DISCUSSION

More over a quarter of the world's population suffers from iron insufficiency, commonest nutritional deficiencies shortfall. Many physiological activities require iron, particularly oxygen binding and transport, gene control, growth of the cell its differentiation, reactions of the enzymes and the synthesis of the neurotransmitter.¹³ Iron deficiency promotes neuronal function and, as a result, raises the likelihood of convulsions also. This study has shown the Iron deficiency anemia affects 59.50 percent of children who have febrile seizures. Consistently El-Shafie AM et al14 reported that the prevalence of IDA higher significantly among the case study group 52.5% in contrast to the controls 20%. On other hand Sultan T et al10 also conducted the case control study and they reported that the children with iron deficiency anemia were found in 93 (46.5%) of cases and 56 (28%) of controls, and children having iron deficiency anemia had higher likelihood of the seizures than children lacking anemia, according to the odds ratio of 2.235. in the line of this study Hussain AW *et al*⁷ also reported that in the group suffering febrile seizures, 58% of the cases were anemic, with a hemoglobin concentration <10gm/dL, and 59% of the cases had lower concentration of the plasma ferritin <10ng/dL, while in 39% cases of the control group were anemic, with hemoglobin levels < 10 gm/dL, and 26% children had lower level of the plasma ferritin < 10ng/dL.7 On other hand in the study of Addil F et al15 demonstrated that the iron deficiency anemia affects more than half of the children who experience febrile seizures and the females had a higher rate of iron deficiency linked with febrile seizures (62.2%) than boys (56.6%), although the discrepancy was not significant statistically. In the first five years of life, febrile seizures are the most prevalent type of seizure, and numerous factors that enhance seizure risk have been reported. In this study mean age of the cases was 2.27 1.24 years and males were 60.0% of all study subjects. These findings were almost similar to the study of Sultan T et *al*¹⁰ as the average age of the cases was 2.081.07 years, whereas the average age of the controls was 3.21.69 years, followed by there were 130 males and 70 were female children in the cases, and there were 145 males and 55 females children in the controls. Similarly in the study of Hussain AW et al7 demonstrated that the participants of the febrile seizures group, average age was 30.73+ 20.69 months, with 71% cases under the age of 36 months, whereas the average age was 29.47 +20.99 months of the cases of control group, with 71% children under the age of 36 months, although in the group of febrile seizures, males were 74% and females were 26%, whereas in the group of controls males were 73% and females were 27%. In this study most of the cases had lower socioeconomic status, rural residency,

formal level education of the parents and lower rate of the iron supplement. Similarly in the study of maternal the iron supplementation during anemia, lack of gestation, and vegetarian mother all elevated the incidence of all types of anemia in offspring.¹⁶ ID may be linked to an increased risk of FSs in children, according to Kenyan case-control research and a meta-analysis of eight case-control studies that looked into the association of the febrile seizures or acute seizures with iron deficiency.¹⁷ Convulsions can occur when the effects of anemia or ID on the brain are exacerbated by fever. Furthermore, anemia is linked to the febrile illness severity, and individuals having symptoms more severe, may experience convulsions. However, febrile convulsions frequently occur during the start of a febrile illness, before Hb levels drop owing to infection.¹⁸ Furthermore, iron deficiency is linked to a variety of neurological problems, including restless leg syndrome, attention deficit hyperactivity disorder and the breath-holding spells, all of which are linked to increased brain excitability.⁵ In an animal study by Rudy et al19 recently observed that the mice exposed to shortage of iron postnatally had a lower seizure threshold and were more susceptible to specific seizures' types. Although the exact mechanism underlying the link in between deficiency of the iron and hyperexcitability of the brain has yet to be determined, the evidence demonstrates that the disruption of the activity of normal neurotransmitter and metabolism of brain could predispose the child having deficiency of iron to a higher risk of febrile seizures occurrence.5

CONCLUSION

According to the findings, the frequency of IDA among children having febrile seizures was observed extremely high. As a result, we urge that early detection and care of this illness be implemented in order to prevent child morbidity. Additionally, doctors might organize national and regional public awareness programs for early therapy of children having iron deficiency to minimize morbidity.

LIMITATIONS

Because the sample size was limited and the study was based on only one center, the results are only representative of that center and control cases were also not studied.

SUGGESTIONS / RECOMMENDATIONS

It is suggested that further large-scale case control studies be conducted.

CONFLICT OF INTEREST / DISCLOSURE

There was no conflict of interest.

ACKNOWLEDGEMENTS

Special thanks for seniors and departmental staff for their guidelines and help in the manuscript writing and data collection respectively.

REFERENCES

- 1. Leung AK, Hon KL, Leung TN. Febrile seizures: an overview. Drugs in context. 2018;7;2-12
- Sawires R, Buttery J, Fahey M. A Review of Febrile Seizures: Recent Advances in Understanding of Febrile Seizure Pathophysiology and Commonly Implicated Viral Triggers. Frontiers in Pediatrics. 2021;9.
- Mosili P, Maikoo S, Mabandla MV, Qulu L. The pathogenesis of fever-induced febrile seizures and its current state. Neuroscience Insights. 2020 Oct;15:2633105520956973.
- Kang JQ, Shen W, Macdonald RL. Why does fever trigger febrile seizures? GABAA receptor γ2 subunit mutations associated with idiopathic generalized epilepsies have temperature-dependent trafficking deficiencies. Journal of Neuroscience. 2006 Jan 1;26(9):2590-7.
- 5. Jang HN, Yoon HS, Lee EH. Prospective case control study of iron deficiency and the risk of febrile seizures in children in South Korea. BMC pediatrics. 2019 Dec;19(1):1-8.
- Sharawat IK, Singh J, Dawman L, Singh A. Evaluation of risk factors associated with first episode febrile seizure. Journal of clinical and diagnostic research: JCDR. 2016 May;10(5):SC10.
- Hussain AW, Haq AU, Shahzad S, Murtaza B, Nawaz U, Lodhi MA. Iron deficiency anemia-a risk factor for febrile seizures in children. PAFMJ. 2018 Oct 31;68(5):1300-05.
- Khan SHM, Sohail M, Ali A, Akhtar N, Khan H, Rasool F. Symptoms- Based Evaluation of Iron Deficiency Anemia in Students of Bahawalpur Correlated with their Eating Habits. Troop J Pharm Res 2014; 13(5): 769-72
- 9. Hosseini F, Nikkhah A, Goli MA. Serum zinc level in children with febrile seizure. Iranian journal of child neurology. 2020;14(1):43.
- Sultan T, Hanif AI, Ali S. Iron deficiency anemia as a risk factor for simple febrile seizures. Pakistan Journal of Neurological Sciences (PJNS). 2017;12(3):36-40.
- 11. Singh P, Mehta V. Is iron deficiency anaemia a risk factor for febrile seizure? a case control study. Int J Contemp Pediatr. 2016;3:1307-11.
- 12. Kamalammal R, Balaji MD. Association between iron deficiency anemia and various red cell parameters with febrile convulsions in children of age group 3 to 60 months. Int J Contemp Pediatr. 2016;3:559-62
- 13. Roganović J, Starinac K. Iron deficiency Anemia in children. Curr Topics Anemia. 2018 Feb 7;47:47-71.
- El-Shafie AM, Abou El-Nour ESS, El-Hawy MA, Barseem ZM. Study of iron deficiency anemia in children with febrile seizures. Menoufia Med J 2017;30:209-12
- 15. Addil F, Rehman A, Najeeb S, Imtiaz H, Khan S. Iron Deficiency Anemia in Children with Febrile Seizures. Systematic Reviews in Pharmacy. 2021;12(11):3463-5.
- Goswmai S, Das KK. Socio-economic and demographic determinants of childhood anemia. Jornal de pediatria. 2015 Sep;91:471-7.
- 17. Idro R, Gwer S, Williams TN, Otieno T, Uyoga S, Fegan G, et al. Iron Deficiency and Acute Seizures: Results from Children Living in Rural Kenya and a Metaanalysis. PLoS One. 2010;5(11):e14001.
- Pisacane A, Sansone R, Impagliazzo N, Coppola A, Rolando P, D'Apuzzo A, et al. Iron Deficiency Anemia and Febrile Convulsions: Casecontrol Study in Children under 2 Years. BMJ. 1996;313(7053).
- Rudy M, Mayer-Proschel M. Iron deficiency affects seizure susceptibility in a time-and sex-specific manner. ASN Neuro. 2017;9:1759091417746521.