Original Research Article

Correlation of iron deficiency anemia and events of febrile seizures among children aged 6 months to 5 years

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Abstract

Introduction: Simple febrile convulsion is the most common central nervous system disease seen in children. There are hypotheses that thresh hold of neuron excitation may be affected by iron deficiency anemia. Febrile seizures are convulsions that occur in a child who is between six months and five years of age and has a temperature greater than 100.4ºF (38ºC). The majority of febrile seizures occur in children between 6 months to 3 years of age.

The aim of the study: The purpose of this study was to determine the association between iron deficiency and febrile seizures in a large cohort of children who are admitted to the paediatric ward.

Materials and methods: The study was conducted in 100 children those concerned parents who are willing to participate in the study at Sree Balaji medical college and hospital, Chennai. Children were categorized into 2 groups. Group, I control group (n=50) admitted with febrile illness (fever duration < 3 days) including respiratory infections or acute gastroenteritis but without seizures and without iron supplements. Group II case group (n=50) admitted with febrile illness (fever duration < 3 days) including respiratory infections or acute gastroenteritis but with seizures and with iron supplements. Both the genders are in taken for the study. Parameters such as height, weight, BMI, body temperature, Hb, MCV, serum ferritin were analyzed using standard techniques and results were analyzed accordingly.

Results: The age group, height, and weight didn't show any specific variations which were found to less statically significant of p value<0.005. The mean hemoglobin level, MCV, MCH, serum ferritin level was found to be more in of Group I control group when compared to Group II case group of p-value <0.001**which was found to be more statically significant.

Conclusion: Children with febrile seizures are almost twice as likely to have iron deficiency anemia as compared to children with febrile illness without seizures. Iron deficiency anemia can be regarded as a modifiable risk factor that predisposes to febrile seizures in children between 6 months to 5 years. Early detection and timely correction of iron deficiency may help in preventing simple febrile seizures in children of this age group.

Key words

Febrile Seizures, Iron Deficiency Anemia, Hyperthermia, Neurological Defects.

Introduction

Seizures are a common event, and 4% of people will experience one in their lifetime. The potential to have a seizure depends on the threshold of the brain to withstand excess electrical activity [1]. In infants and children, high fevers can cause this threshold to lower, resulting in febrile seizures. A blow to the head can cause an electrical spike causing a seizure, and sometimes seizures just happen. A febrile seizure is a seizure accompanied by fever (temperature ≥ 100.4°F or 38°C by any method), without central nervous system infection, that occurs in infants and children 6 through 60 months of age. Febrile seizures occur in 2% to 5% of all children and, as such, make up the most common convulsive event in children younger than 60 months. In 1976, Nelson and Ellenberg, using data from the National Collaborative Perinatal Project, further defined febrile seizures as being either simple or complex [2]. Simple febrile seizures were defined as primary generalized seizures that lasted for less than 15 minutes and did not recur within 24 hours. Complex febrile seizures were defined as focal, prolonged (≥15 minutes), and/or recurrent within 24 hours [3]. Children who had simple febrile seizures had no evidence of increased mortality, hemiplegia, or mental retardation. During follow-up evaluation, the risk of epilepsy after a simple febrile seizure was shown to be only slightly higher than that of the general population, whereas the chief risk associated with simple febrile seizures was recurrence in one-third of the children. However, children who have had multiple simple febrile seizures, are younger than 12 months at the time of their first febrile seizure, and have a family history of epilepsy are at higher risk, with generalized afebrile seizures developing by 25 years of age in 2.4%. Despite this fact, no study has demonstrated that successful treatment of simple febrile seizures can prevent this later development of epilepsy, and there currently is no evidence that simple febrile seizures cause structural damage to the brain. Indeed, it is most likely that the increased risk of epilepsy in this population is the result of genetic predisposition. In contrast to the slightly increased risk of developing epilepsy, children with simple febrile seizures have a high rate of recurrence [4]. The risk varies with age. Children younger than 12 months at the time of their first simple febrile seizure have an approximately 50% probability of having recurrent febrile seizures [5]. Children older than 12 months at the time of their first event have an approximately 30% probability of a second febrile seizure; of those who do have a second febrile seizure, 50% have a chance of having at least 1 additional recurrence [6]. Finally, there is a theoretical risk of a child died during a simple febrile seizure as a result of documented injury, aspiration, or cardiac arrhythmia, but to the committee's knowledge, it has never been reported [7]. Iron has been found to act as a cofactor in a number of enzymatic reactions at the cellular level, and it effects neurotransmitter production and function, hormone function, and DNA replication. Deficiency of iron, therefore, results in disruption of normal cell and organ function [8]. The most clinically obvious consequence of ID is anemia, but virtually every organ system is affected, resulting in changes in cognitive and behavioral performance, impaired physical growth, and impairment of immune function.ID

is associated with neurological problems in young children, including developmental delay, stroke, breath-holding spells, and pseudotumor cerebri. [9, 10].

Materials and methods

The study was conducted between the year 2016-2017 in 100 children who are willing to participate in the study at Sree Balaji medical college and hospital, Chennai. Group, I control group (n=50) admitted with febrile illness (fever duration < 3 days) including respiratory infections or acute gastroenteritis but without seizures and without iron supplements. Group II case group (n=50) admitted with febrile illness (fever duration < 3 days) including respiratory infections or acute gastroenteritis but with seizures and with iron supplements. All the 100 children were age, and sex-matched. Both the gender is taken for the study. Parameters such as height, weight, BMI, body temperature, Hb, serum ferritin were analyzed using standard techniques and results were analyzed accordingly. Oral consent got from the parents of study for collecting the blood sample. The need and purpose of the study were explained in detail. The anthropometric assessment included weight, height, body temperature are measured. Simultaneously, IV blood sample was obtained from cubital vein to measure Hb, serum Ferritin, Results are analyzed accordingly. Blood investigations are done to diagnose iron deficiency include hemoglobin estimation using an automated hematology analyzer (Sysmex Kx-21) and serum ferritin estimation using ELISA method (Acubind ELISA). Iron deficiency was diagnosed by hematologic investigations of hemoglobin value <11g%, serum ferritin value <12 ng/mL and RDW >15% (WHO) [10]. SPSS-17 was used for statistical analysis of this data.

Statistical Analysis

The data were entered into the SPSS version -19 and Chi-square and t-test were performed to compare the parameters and P values less than 0.05 were considered statistically significant.

Results

Group, I control group (n=50) admitted with febrile illness (fever duration < 3 days) including respiratory infections or acute gastroenteritis but without seizures and without iron supplements. Group II case group (n=50) admitted with febrile illness (fever duration < 3 days) including respiratory infections or acute gastroenteritis but with seizures and with iron supplements. Both the gender were in taken for the study. Parameters such as height, weight, BMI, body temperature, Hb, MCV, MCH serum ferritin are analyzed using standard techniques.The age group of Group I control group was around (18.83±4.93) and in Group II case group was around (23.89±6.45) of p-value 0.45 which is found to be statically insignificant. The height of Group I control group was around (73.95±8.2) and in Group II case group was around (72.95±8.2) of p-value 0.56 which was found to be statically insignificant. The weight of Group I control group was around (12.03±7.6) and in Group II case group was around (14.94±2.9) of p-value 0.33 which was found to be statically insignificant. The mean hemoglobin level of Group I control group was around (11.98±5.7) and in Group II case group was around (9.76±3.4) of p-value <0.001**which was found to be more statically significant. The MCV level of Group I control group was around (68.54±0.3) and in Group II case group was around (67.98±0.8) of p-value <0.001**which was found to be statically more significant. The MCH level of Group I control group was around (21.11±3.8) and in Group II case group was around (19.63±2.8) of p-value <0.001**which was found to be statically more significant. The serum ferritin level of Group I control group was around (49.67±9.0) and in Group II case group was around (26±0.56) of p-value <0.001**which was found to be statically more significant (**Table – 1**).

Discussion

A febrile seizure, also known as a fever fit or febrile convulsion, is a seizure associated with a high body temperature but without any

serious underlying health issue [11]. The most commonly occur in children between the ages of 6 months and 5 years. Most seizures are less than five minutes in duration and the child is completely back to normal within sixty minutes of the even [12].

Table – 1: Anemic assessment between Group-I and Group-II.

PARAMETERS	GROUP –I CONTROL GROUP (n=50)	GROUP –II CASE (n=50)	P VALUE
1.AGE (months)	18.83±4.93	23.89±6.45	0.45
2. HEIGHT (cm)	73.95±8.2	72.08±3.8	0.56
3. WEIGHT (kg)	12.03±7.6	14.94±2.9	0.33
4. HB (gm/dl)	11.98±5.7	9.76±3.4	<0.001**
5.MCV (fl)	68.54±0.3	67.98±0.8	<0.001**
6. MCH (%)	21.11±3.8	19.63±2.8	<0.001**
7. SERUM FERRITIN (µg/L)	49.67±9.0	26±0.56	<0.001**

(P<0.05 considered being statistically significant, P value <0.001 was considered to be more significant)

The diagnosis is arrived at by eliminating more serious causes of seizure and fever: in particular, meningitis and encephalitis. However, in locales in which children are immunized for pneumococcal and Haemophilus influenzae, the prevalence of bacterial meningitis is low. If a child has recovered and is acting normally, bacterial meningitis is very unlikely. Long term outcomes are generally good with little risk of neurological problems or epilepsy [13]. Those who have one febrile seizure have an approximately 40% chance of having another one in the next two years, with the risk being greater in those who are younger [14]. Simple febrile seizures do not tend to recur frequently (children tend to outgrow them) and do not make the development of adult epilepsy significantly more likely (about 3–5%) compared with the general public (1%) [15]. Children with febrile convulsions are more likely to have a febrile seizure in the future if they were young at their first seizure (less than 18 months old), have a family history of a febrile convulsions in first-degree relatives (a parent or sibling), have a short time between the onset of fever and the seizure, had a low degree of fever before their seizure, or have a seizure history of abnormal neurological signs or developmental delay [16]. Similarly, the prognosis after a complex febrile seizure is excellent, although an increased risk of death has been shown for complex febrile seizures, partly related to underlying conditions. To explore if those with complex febrile seizures were more likely to have ID/IDA, we examined the association between seizure type (complex versus simple febrile seizure) and hemoglobin, MCV, and RDW. The mean hemoglobin of the 104 patients with complex seizures was 116 g/L compared with118 g/L in the 251 patients with simple febrile seizures (P = .012). Although this difference is statistically significant, both values are within the normal range of hemoglobin for age and are not clinically important. There was no significant difference found with MCV or RDW between those having complex and simple febrile seizures [17]. The most common clinical presentation of iron deficiency is anemia, but other systems may also be affected. Central system manifestations like behavioral impairments, Cognitive dysfunction, psychomotor retardation, are noticed. Other manifestations like pica, breath holding spells, restless leg syndrome may also be associated with iron deficiency [18]. Effect of iron deficiency in the developing brain and mechanism like the altered development of hippocampus neurons delayed maturation of myelin and alterations in synaptic

neurotransmitter systems which include Glutamate, Gamma – Amino Butyric Acid (GABA) Norepinephrine, Dopamine, and serotonin may be responsible for these symptoms [19]. Hence Iron deficiency reduces the metabolism of these neurotransmitters and may lead to the onset of a convulsion. In this study, 79.2 % of children in FC group and 20.8 % children in control group had anemia ($p<0.001$). Another study found that the incidence of FC in patients with thalassemia was much lower than among children in the general population. Thus, iron overload may be a major factor in the brain metabolism that prevents febrile seizures. Hemolytic anemias were excluded in this study [20].

Conclusion

Our study found that children with febrile seizures were almost twice as likely to be iron deficient when compared with controls. We would propose that ID is one of the risk factors for febrile seizure be included along with others such as family history, the rate of rising of fever, and specific viral illness. The chance of a child having a febrile seizure may increase as the number of risk factors in a given patient accumulates.

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