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Relationship between Febrile Seizures and Iron Deficiency Anemia in Children

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Abstract

BACKGROUND: The febrile seizure is the most common type of seizures occur in children under 5 years old and the peak age is 18 months, the temperature of body 38°C or more with no neurological infection or metabolic disorder.

AIM: The aim of the present study is to found the association between iron deficiency anemia (IDA) and febrile seizure.

METHODS: A case–control study has been carried out to determine the association between febrile convulsion and IDA. One hundred and twenty-two children with febrile seizure and 130 healthy babies include in study, period of study from May 2019 to December 2019 in Bunt Al Huda teaching hospital Nasiriyah, Dhi Qar, Iraq. The sociodemographic data are age of babies, weight, and gender. Diagnosis of febrile seizure done after details history and examination. Children aged 6 months–5 years presenting with febrile convulsion for cases and controls group of same age with fever but no convulsion. Both first and recurrent episodes of FC were included for cases.

RESULTS: A case–control study of 122 children with seizures and 130 children without seizures, seizures babies have more weight than non-seizures, convulsion babies have low mean corpuscle volume than non-seizures, and seizures babies have low serum ferritin than non-seizures. There is a significant difference between mean serum ferritin of seizures and non-seizures babies, seizures babies have low serum ferritin than non-seizures.

CONCLUSION: Serum ferritin also decreases more in babies with febrile seizure so IDA is occurring more in febrile seizure, and there is an association between iron supplements deficiency and febrile seizure.

Introduction

The febrile seizure is the most common type of seizures occur in children under 5 years old and the peak age is 18 months, the temperature of body 38°C or more with no neurological infection or metabolic disorder [1], [2]. There are two types of febrile seizures (FS); simple febrile seizures (SFS): The duration of SFS 15 min or less it is called "generalized tonic clonic," complex febrile seizures (CFSs), the fever duration also 15 min or less but return within 24 h later and have focal location signs [3], [4]. Status epilepticus defines as long duration of seizure attack last for more than 30 min [5]. In Europe, the incidence of FS is 2–5% in 6 months–5 years' children and in Asia (5–10%) [6], [7]. The complications of the febrile seizure are aspiration and psychological upset to both parent and child [8]. Numerous independent danger factors "genetic factors, age, gender, fever, type and duration of seizure, family and developmental history, multiple seizures, etc." may lead to later epilepsy [9]. Iron deficiency anemia (IDA) is defined as most common illness occur due to lack of sufficient body's iron. There is prevalence of IDA in 50% of all preschool children [10], [11]. Treatment of IDA is very easy by iron supplements that need for hemoglobin (Hb) production as well as for enzymes contributing in neurochemical responses [12]. The symptoms of children with IDA are attention debit, reduced memory, leaning debility, underdeveloped motor activity, and behavioral inequity [13]. Many studies show that there is an association between IDA and FS in 5 years children and less [14]. IDA is related with social abnormalities and reduced mental function. It has permanent brain damage if it happens during the brain growth in early childhood [15]. Due to the iron status and prevalence of IDA are very associated with socioeconomic status, undernourishment, and weaning, which is very reliant on social and geographical alterations, the relationship between FS and IDA may differ country to country [16]. The aim of the present study is to found the association between IDA and febrile seizure.

Methods

A case–control study has been carried out to determine association between febrile convulsion and IDA. A case–control study has been carried out to determine the association between febrile convulsion and IDA. One hundred and twenty-two children with

febrile seizure and 130 healthy babies included in the study, period of study from May 2019 to December 2019 in Bunt Al Huda teaching hospital Nasiriyah, Dhi Qar, Iraq. The sociodemographic data are age of babies, weight, and gender. Diagnosis of febrile seizure done after details history and examination. Children aged 6 months–5 years presenting with febrile convulsion for cases and controls group of same age with fever but no convulsion. Both first and recurrent episodes of FC were included for cases. Exclusion criteria: Electrolyte disturbance, diagnosed organic cause of convulsion, delayed milestones, neurological defects, central nervous system infection – meningitis, encephalitis, and anemia resulting from other causes – hemolysis, bleeding, and refusal of consent. Data collection: A special questionnaire was designed for the purpose of the study including the following data: Age, sex, current weight, parent consanguinity, family history of febrile convulsion, family history of epilepsy, temperature, type of feeding, cause of fever, history of iron therapy, febrile seizure occurring among 6 months–5 years children at temperature 38°C or more without CNS infection or any metabolic difference, SFSs define as generalized, tonic-clonic with fever, for 15 min or less, and not recurrent within 24 h. Laboratory procedures: A 2 mL of venous blood sample were collected in to tubes with EDTA from all patients and controls then send to laboratory to find the Hb level, mean corpuscle volume (MCV), mean corpuscle hemoglobin (MCH), mean corpuscle hemoglobin concentration (MCHC), red blood cell (RBC), red blood cell distribution width (RDW), and platelet count by Sysmix KX 21N, Japan. Serum ferritin level checking done by miniVIDAS BIOMERIEUX SA FRANCE verbal consent was taken from the parents. Statistical analysis done by SPSS 22, frequency and percentage used for categorical data, mean, and SD for continuous data. Chi-square used for assessed association between variables. t-test used for evaluation differences between mean and median of continues variables. $p \leq 0.05$ is reflected significant. Ethical approval: Accepted by a committee conferring to the certificate no. 188 (date in May 10, 2019) to become approval.

Results

This is a case–control study of 122 children who have seizures and 130 children who do not have seizures, where the mean age of babies with seizures is (19.8 ± 15) months.

Distribution of babies with seizures according to Table 1 is as the following; 62% are male and 38% are female, 54.1% of babies are with parents consanguinity, 52.5% of babies have positive family history of febrile convulsion, 80.3% have simple febrile convulsion, only 12.3% of babies have a history of epilepsy, 51.6% have the same feeding with family, 40.2% of them have fever due to gastroenteritis infection, and 26.2% of children have fever due to upper respiratory infection. About 94.3% of babies have no previous of iron therapy, as shown in Table 1.

Table 1: Distribution of variables includes in the present study in seizures babies

Variables	Frequency	Percentage
Gender		
Female	46	37.7
Male	76	62.3
Parents consanguinity		
No	56	45.9
Yes	66	54.1
FH of febrile convulsion		
No	58	47.5
Yes	64	52.5
Types of febrile convulsion		
Complex	24	19.7
Simple	98	80.3
FH of epilepsy		
No	107	87.7
Yes	15	12.3
Types of feeding		
Bottle feeding	9	7.4
Breastfeeding	18	14.8
Complimentary diet	5	4.1
Mixed feeding	27	22.1
Same family diet	63	51.6
Causes of fever		
Gastroenteritis	49	40.2
LRTI	20	16.4
Other	3	2.5
URTI	32	26.2
UTI	16	13.1
Vaccine	2	1.6
History of iron therapy		
No	115	94.3
Yes	7	5.7

Table 2 shows that there is a significant difference between mean weight of seizures and non-seizures babies, seizures babies have more weight than non-seizures. Furthermore, there is a significant difference between mean MCV of seizures and non-seizures babies, convulsion babies have low MCV than non-seizures. There is a significant difference between mean serum ferritin of seizures and non-seizures babies, seizures babies have low serum ferritin than non-seizures.

Table 2: Differences in means of parameters includes in the present study according to seizures and non-seizures groups

Parameter	Type	N	Mean	SD	p-value
Age (M)	Control	130	20.23	16.5	0.8
	Case	122	19.85	14.9	
Weight	Control	130	10.15	3.5	0.0001
	Case	122	12.20	3.7	
Temperature	Control	130	38.99	0.9	0.2
	Case	122	38.77	1.6	
Hb	Control	130	10.22	1.5	0.5
	Case	122	9.87	5.9	
MCV	Control	130	68.96	11.0	0.9
	Case	122	68.82	9.1	
MCH	Control	130	27.19	20.1	**0.03**
	Case	122	23.29	2.8	
MCHC	Control	130	33.76	27.5	0.9
	Case	122	34.20	26.7	
RBC count	Control	130	5.05	3.4	0.1
	Case	122	4.45	2.7	
RDW	Control	130	17.02	10.4	0.6
	Case	122	16.59	2.9	
PLT	Control	130	278.41	82.2	0.16
	Case	122	295.89	116.3	
Serum ferritin	Control	130	75.66	53.5	**0.0001**
	Case	122	10.71	10.2	

$p \leq 0.05$ (significant).

As show in Table 3; there is a significant association between occurrence of seizures and FH of febrile convulsion, 52.5% of babies with seizures

have FH of febrile convulsion. There is a significant association between occurrence of seizures and FH of epilepsy, just 10.7% of babies with seizures have FH of epilepsy. There is a significant association between occurrence of seizures and types of feeding, just 51.6% of babies with seizures have the same diet with their families. There is a significant association between occurrence of seizures and cause of fever, 40.2% of babies with seizures have fever due to gastroenteritis infection. There is a significant association between occurrence of seizures and FH of epilepsy, 94.3% of babies with seizures have no iron supplement. There is no significant association between occurrence of seizures and (gender and parents consanguinity).

Table 3: Association between variables includes in the present study and occurrence of seizures

Variables	Groups		p-value
Gender	Control (%)	Case (%)	
Female	53 (40.8)	46 (37.7)	
Male	77 (59.2)	76 (62.3)	0.7
Total	130 (100.0)	122 (100.0)	
Parents consanguinity			
No	66 (50.8)	56 (45.9)	
Yes	64 (49.2)	66 (54.1)	0.45
Total	130 (100.0)	122 (100.0)	
FH of febrile convulsion			
No	130 (0.0)	58 (47.5)	
Yes	0 (0.0)	64 (52.5)	0.0001
Total	130 (100.0)	122 (100.0)	
FH of epilepsy			
No	130 (0.0)	109 (89.3)	
Yes	0 (0.0)	13 (10.7)	0.0001
Total	130 (100.0)	122 (100.0)	
Types of feeding			
Bottle feeding	24 (18.5)	9 (7.4)	
Breastfeeding	23 (17.7)	18 (14.8)	0.007
Complimentary diet	13 (10.0)	5 (4.1)	
Mixed feeding	26 (20.0)	27 (22.1)	
Same family diet	44 (33.8)	63 (51.6)	
Total	130 (100.0)	122 (100.0)	
Causes of fever			
GE	43 (33.1)	49 (40.2)	
LRTI	14 (10.8)	20 (16.4)	0.05
Other	6 (4.6)	3 (2.5)	
URTI	33 (25.4)	32 (26.2)	
UTI	21 (16.2)	16 (13.1)	
Vaccine	13 (10.0)	2 (1.6)	
Total	130 (100.0)	122 (100.0)	
History of iron therapy			
No	82 (63.1)	115 (94.3)	
Yes	48 (36.9)	7 (5.7)	0.0001
Total	130 (100.0)	122 (100.0)	

$p \leq 0.05$ (significant).

As show in Table 4; there is a significant association between types of seizures and FH of epilepsy, just 37.5% of babies with complex type of seizures have FH of epilepsy. Other variables have no significant association.

Table 5 shows that there is a significant difference between mean age of simple and complex type of seizures, complex seizures babies have low age than simple seizures. Furthermore, there is a significant difference between mean MCHC of simple and complex type of seizures, complex seizures babies have more MCHC than simple seizures. There is a significant difference between mean serum ferritin of simple and complex type of seizures, complex seizures babies have more serum ferritin than simple seizures.

Table 4: Association between variables includes in the present study and types of seizures

Variables	Seizers		p-value
	Simple (%)	Complex (%)	
Gender			
Female	33 (33.7)	13 (54.2)	
Males	65 (66.3)	11 (45.8)	0.9
Total	98 (100.0)	24 (100.0)	
Parents consanguinity			
No	44 (44.9)	12 (50.0)	
Yes	54 (55.1)	12 (50.0)	0.6
Total	98 (100.0)	24 (100.0)	
FH of febrile convulsion			
No	50 (51.0)	8 (33.3)	
Yes	48 (49.0)	16 (66.7)	0.17
Total	98 (100.0)	24 (100.0)	
FH of epilepsy			
No	94 (95.9)	15 (62.5)	
Yes	4 (4.1)	9 (37.5)	0.0001
Total	98 (100.0)	24 (100.0)	
Types of feeding			
Bottle feeding	6 (6.1%)	3 (12.5%)	
Breastfeeding	14 (14.3%)	4 (16.7%)	
Complimentary diet	1 (1.0%)	4 (16.7%)	0.007
Mixed feeding	23 (23.5%)	4 (16.7%)	
Same family diet	54 (55.1%)	9 (37.5%)	
Total	98 (100.0%)	24 (100.0%)	
GE	42 (42.9%)	7 (29.2%)	
Causes of fever			
LRTI	15 (15.3%)	5 (20.8%)	0.3
Other	2 (2.0%)	1 (4.2%)	
URTI	23 (23.5%)	9 (37.5%)	
UTI	15 (15.3%)	1 (4.2%)	
Vaccine	1 (1.0%)	1 (4.2%)	
Total	98 (100.0%)	24 (100.0%)	
History of iron therapy			
No	94 (95.9%)	21 (87.5%)	
Yes	4 (4.1%)	3 (12.5%)	0.14
Total	98 (100.0%)	24 (100.0%)	

$p \leq 0.05$ (significant).

Discussion

This study showed that children with FS are highly association with iron deficient as low serum ferritin level it is may be increased the thershold of convulsion when there is IDA. There is disagreement concerning the role of iron in FSs, which are reflected a benign seizure syndrome separate from epilepsy [17]. The previous studies have described an association between IDA and convulsions in patients with malaria [18]. IDA leads to delay and behavioral disorders in early life [19]. Studies show that 44–66% of children

Table 5: Differences in means of parameters includes in the present study according to the types of seizures

parameter	Type	N	Mean	Std. deviation	p-value
Age (M)	Simple	98	20.949	15.5520	0.05
	Complex	24	15.375	11.5290	
Weight	Simple	98	12.255	3.9320	0.7
	Complex	24	12.017	2.8268	
Temperature	Simple	98	38.896	1.5419	0.11
	Complex	24	38.296	2.0836	
Hb	Simple	98	10.0384	6.59736	0.3
	Complex	24	9.2083	1.49751	
MCV	Simple	98	69.374	8.0543	0.3
	Complex	24	66.558	12.8079	
MCH	Simple	98	23.393	2.6139	0.4
	Complex	24	22.871	3.6095	
MCHC	Simple	98	31.901	2.6156	**0.05**
	Complex	24	43.625	60.2460	
RBC count	Simple	98	4.2472	0.53966	0.09
	Complex	24	5.3046	6.21242	
RDW	Simple	98	16.3669	3.03361	0.07
	Complex	24	17.5167	2.71320	
PLT	Simple	98	300.455	122.0366	0.16
	Complex	24	277.292	89.2158	
Serum ferritin	Simple	98	10.2588	10.60226	**0.0001**
	Complex	24	12.5875	8.48074	

$p \leq 0.05$ (significant).

below the age of 4 years have anemia, with half of these children suffer from IDA [14] due to in this age, there is increase in hypokalemia and hyponatremia, hypomagnesemia, and hypocalcemia related with Vitamin D deficiency, increase upper and lower respiratory infection. Many studies investigated the association between FS and IDA but these results still controversial, but other studies stated that IDA has significant association with febrile seizure like studied done in Iran and India [20], [21]. Canadian study presented that kids with FSs have double iron deficit (S. ferritin ≤ 30 ng/dL) than babies who have no febrile convulsion [22]. Papageorgiou *et al*. also identified that little serum ferritin or MCH related with FS [23]. Karimi *et al*. also prescribed that SFSs and CFSs increase with IDA [24]. Nasehi *et al*. also defined an increased danger of FS in kids with IDA [25]. In the present study, seizures babies have more weight than non-seizures this disagree with other study state that FSs increased with low birth weight babies this is due to small sample size [26]. Furthermore, in the present study, there is a significant association between occurrence of seizures and FH of febrile convulsion, this is similar to study done by Sang *et al*. that stated family history of febrile convulsion and family history of epilepsy highly associate with FSs [27]. In the present study, most of babies with seizures have fever due to gastroenteritis infection this is similar to another study state that most of patients in the FS group presented seizures at an early stage of gastroenteritis [28]. In the present study, there is no significant association between occurrence of seizures and gender. This means that gender is not a risk factor for increase of febrile seizure, and there is no significant association between occurrence of seizures and age. This means that age is not a risk factor for increase febrile seizure, which is similar to other studies that have similar outcomes and have stated that there is no significant association between iron deficit anemia and febrile seizure and age of children (p = 0.359) and gender (p = 0.598) [14], [20]. Even if this study suggested base data about the positive association of IDA and febrile seizure, but extra case–control studies must done with big samples size are required.

Conclusion

Hb is decrease in babies with febrile seizure more than babies with non-febrile seizure cause anemia, and serum ferritin also decreases more in babies with febrile seizure so IDA is occurring more in febrile seizure, and there is an association between iron supplements deficiency and febrile seizure.

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