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EARLY MARKERS FOR PREDICTING FEBRILE SEIZURES IN INFANTS AND CHILDREN AT MOSUL CITY

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ABSTRACT

Background: Febrile seizure is among the most prevalent neurological findings in children. While the exact mechanism of Febrile seizure remains unclear, genetic and environmental variables are thought to play a significant influence. Objectives: Is to assess the role of vitamin D, calcium, and iron in early detection of febrile seizures, as well as their relation with clinical behavior and potential predictors of future illness outcomes and consequences. Methods: A case-control study of recorded data from the department of pediatric medicine at Ibn Sena Teaching Hospital, from January 2024 to the end of December 2024. The study included 50 subjects aged 6 months to 6 years diagnosed with febrile seizure according to American Academy of pediatrics (cases), ⁽¹⁹⁾ which were matched according to the age and gender to another 50 subjects having fever but with no febrile seizure. The questionnaire was consisted from three parts. Part one for demographic information of the study patients. Part two for clinical manifestation of the study participants. Part three for the investigation done for each patient. Results: The study included 100 patients, divided into two groups, with 50 subjects for each group. The mean age \pm standard deviation of the study participants is 26.45 ± 19.35 months, with male to female ratio of 1.08:1. There are no statistically significant difference regarding age and sex of the study participants (P-value >0.05). There were statistically significant differences between cases and controls regarding their primary infection site (P-value = 0.042), their hemoglobin level, MCV, MCH, platelets and WBC counts (P- value <0.001) for each variable and their means of serum calcium level, means of serum iron levels, and means of Vitamin D3 levels (P-value <0.001) for each variable. Moreover; the study found no statistically significant difference in serum calcium, serum iron, or vitamin D3 levels between different subgroups of patients with febrile convulsions. Conclusion: Febrile seizure had been found in this study to be significantly related to serum 25-hydroxy vitamin D level insufficiency and deficiency, slightly lower calcium levels (< 9.9 mg/dL), lower serum iron levels, and hemoglobin levels below 10.5 gm/dl. The different types of febrile seizures did not significantly different with serum levels of vitamin D, calcium, and iron level.

KEYWORDS: Febrile convulsion, Pediatric, Predicting, Iraq, Mosul.

1. INTRODUCTION

Febrile seizure (FS) frequently occurred in children aged 6 months to 6 years due to fever in the absence of central nervous system infection.^[1] It is among the most prevalent neurological findings in children. Although simple febrile seizures do not result in mortality, the risk of recurrence and epilepsy is significant, causing significant trauma for parents and leading to frequent admissions to pediatric emergency departments.^[2-3] 2-4% of children have FS.^[1] While the exact mechanism of FC remains unclear, genetic and environmental variables are thought to play a significant influence.^[4-5] Seizures can

be caused by several stimuli to the central nervous system, such as fever, electrolyte imbalances, certain disorders, or head trauma.^[6] The physiological response of the immature brain to temperature in febrile seizures is age-dependent. As a child grows older, their brain excitability increases, making them more prone to febrile seizures.^[7] The most prevalent causes are upper respiratory tract infections, acute gastroenteritis, and urinary tract infections.^[8-9] It is important to highlight that while some kids have fever without seizures, others develop febrile seizure.^[4] Furthermore, some children who have experienced febrile seizures in the past may not experience seizures during other feverish illnesses, which gives support to the theory that there might be additional underlying reasons.^[10] Based on the duration and frequency of seizures, there are two types of febrile seizures: simple febrile seizures (SFS) and complex febrile seizures (CFS).^[11] The majority of febrile seizures are simple seizures, which last for approximately 15 minutes.^[12] Simple febrile seizures are benign, but complex febrile seizures (CFS) and status epilepticus (SE) can lead to more serious harms such temporal lobe epilepsy later in adulthood.^[13]

Vitamin D deficiency is a serious public health concern across the world, particularly in developing countries, which is most common during periods of rapid development, such as infancy and adolescence.^[14-15] Vitamin D receptors can be found throughout the central nervous system. It is essential for neurotransmission in growing brains.^[16] Moreover; fever can affect the ions in the cell microenvironment with abnormal levels of potassium, sodium, calcium, and iron ions are observed during the start of FS, indicating a high-risk condition.^[17] Certain neurotransmitters, such as monoamine oxidase and aldehydeoxidase, require iron to function effectively. As a result; iron deficiency anemia, might increase the risk of febrile seizures.^[18]

The study aimed to assess the role of vitamin D, calcium, and iron in early detection of febrile seizures, as well as their relation with clinical behavior and potential predictors of future illness outcomes and consequences.

2. PATIENTS AND METHODS

After obtaining ethical approval from the ethical committee of Nineveh Health directorate. A case-control study of recorded data from the department of pediatric medicine at Ibn Sena Teaching Hospital, from January 2024 to the end of December 2024. Parents provided written consent for the gathering of blood samples and data.

The study included 50 subjects aged 6 months to 6 years diagnosed with febrile seizure according to American Academy of pediatrics (cases),^[19] which were matched according to the age and gender to another 50 subjects having fever but with no febrile seizure. Complete history and physical examination were taken from all the patients who had EEG and CT scans of the head showing

normal findings as well as radiological findings for every case were recorded and tabulated. In Addition to; laboratory investigations which include routine investigations together with assay of serum calcium, iron studies and Vitamin D3 (OH).

Pre-hospitalization intravenous fluid therapy was a disqualifying factor. The study excluded any brain issue or infections affecting the central nervous system. The study's case group was classified into three categories based on their seizure frequency: Those having simple febrile seizures (SFS) with generalized seizures lasting less than 15 minutes, not repeated within 24 hours or during the same illness, and no postictal neurological abnormalities, patients with complex febrile seizure (CFS) who exhibited neurological features such as focalonset seizures, protracted seizures lasting over 15 minutes, and recurring seizures on the same day. And lastly; status epilepticus (SE) subgroup who refers to a seizure lasting more than 30 minutes or recurring within 30 minutes without a break in open awareness. Serum from each case and control group was extracted by centrifugation at 3,500 rpm for 5 minutes and stored at -70°C. Blood samples from the FS group were collected within an hour of the seizure. Serum calcium and iron levels were measured using the Hitachi 7600-020 automatic biochemical analyzer.

Statistical analysis: Data from clinical examinations, lab investigations, and outcome measures were recorded, documented, and analyzed in Microsoft Excel. Data were entered into SPSS version 30.0, a statistical analysis tool for social sciences. A two-tailed test result with a P-value of less than 0.05 was considered statistically significant.

3. RESULTS

The study included two groups, with 50 subjects for each group. The mean age \pm standard deviation of the study participants is 26.45 \pm 19.35 months, with male to female ratio of 1.08:1. There are no statistically significant difference regarding age and sex of the study participants (P-value >0.05). As showed in table 3.1:

Table 3.1. Distribution	of the study natients	according to their age and sex
Table 5.1. Distribution	of the study patients a	according to their age and sex.

If of the study patients according to then age and sex.						
Variable	Case group=50	Control group=50	P-value			
Age (months): Mean	2.27 ± 19.78	22.62 ± 18.97				
± SD Median	18	19	0.728			
Range	6-56	7-49				
Sex:						
Male	26	26	1			
female	24	26	1			

Table 3.2 shows statistically significant difference between cases and controls regarding their primary infection site (P-value = 0.042).

Primary infection		Case group=50				Control	Develope
		SFS	CFS	SE	Total	group=50	P-value
-	Upper respiratory tract infection	19	3	1	23	16	
-	Lower respiratory tract infection	1	4		5	4	
-	Acute follicular tonsillitis	4			4	8	0.042
-	Acute suppurative otitis media	2			2	9	0.042
-	Gastroenteritis	8	3		8	6	
-	Urinary tract infection	3	1	1	8	7	

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Table 3.3 shows statically significant differences between cases and controls regarding their hemoglobin

level, MCV, MCH, platelets and WBC counts (P- value <0.001) for each variable.

Table 3.3: Comparison	n between th	ne cases and	l control acco	ding to their	hematological	variables.

Variable	Case group=50	Control group=50	P-value
Hemoglobin level:			
-Mean \pm SD	10.2 ± 0.69	11.21 ± 1.05	∠0 001
-Range	10-13	10.5-13.5	<0.001
MCV:			
-Mean \pm SD	72.5 ± 5.5	76.5 ± 5.5	-0.001
-Range	65-83	62-80	<0.001
MCH:			
-Mean \pm SD	23.9 ± 4.4	25.8 ± 3.4	-0.001
-Range	15-30	17-31	<0.001
Platelets:			
-Mean \pm SD	188368 ± 52977	2130200 ± 48900	∠0 001
-Range	115000-345000	121000-32200	<0.001
WBC counts:			
-Mean \pm SD	8.5 ± 2.8	8.8 ± 2.5	-0.001
-Range	5.2-13.8	4.5-12.1	<0.001

Table 3.4 shows statically significant differences between cases and controls regarding their means of serum calcium level, means of serum iron levels, and means of Vitamin D3 levels (P-value <0.001) for each variable.

Table 3.4: Comparis	son between tl	he cases and	l control	according t	to their l	biochemical	variables.

Variable	Case group=50	Control group=50	P-value
Serum calcium (mg/dl):			
-Mean \pm SD	9.2 ± 0.91	10.4 ± 0.94	<0.001
-Range	7.2-11.5	7.7-11.9	<0.001
S. iron (mg/dl):			
-Mean \pm SD	56.8 ± 21.3	75.9 ± 23.6	
-Median	50	83	< 0.001
-Range	27-81	27-111	
Vit D3 (mg/ml):			
-Mean \pm SD	20.6 ± 11.9	33.5 ± 11.3	
-Median	12.8	30.5	<0.001
-Range	8.1-63	11-50	

Table 3.5 compares between the cases subgroups regarding their biochemical variables, no statistically

significant found between the subgroups regarding this issue (P-value >0.05).

 Table 3.5: Comparison between the cases subgroups regarding their biochemical variables.

Drimony infaction	Con	D Voluo		
Filliary infection	SFS = 37	CFS = 11	SE = 2	r - value
Serum calcium (mg/dl):				
-Mean \pm SD	9.5 ± 0.91	9.1 ±0.89	8.9 ± 0.45	0561
-Range	7.0-11.5	8.5-10.3	8.7-10.7	0.304
S. iron (mg/dl):				

-Mean ± SD	53.6 ± 19.6	54 ± 23.2	62.8 ± 43.6	0.357
-Median	56	53	64	
-Range	21-87	32-85	33-93	
Vit D3 (mg/ml):				
-Mean \pm SD	$20.7 \pm 10.7 \pm 12.7$	19.2 ± 12.5	20.3 ± 3.8	
-Median	$20.7 \pm 18.7 11.3$ 9 1 79	9.2	20.8	0.829
-Range	0.1-/0	9.1-56	18-53	

4. DISCUSSION

The study that the median ages of onset of febrile convulsion was less than 2 years, with slight male predominance, which is closed to Kirstine J. et al^[20] and Hilal Aydın et al^[21] studies' findings. Moreover; the study found statistically significant link between certain types of primary infections and febrile seizures. Specifically, upper respiratory tract, lower respiratory tract, gastrointestinal, and urinary tract infections which were observed among children experiencing febrile seizures compared to those without seizures. This suggests that these types of infections may be more likely to trigger febrile seizures in susceptible children. This is consistent with Osama Y. Muthaffar et al^[22] and Dikshya Pan studies' findings.^[23]

The study showed that children experiencing febrile convulsions (cases) had significantly lower levels of several hematological parameters compared to a control group without seizures. Specifically, the study found lower levels of hemoglobin, Mean Corpuscular Volume (MCV), Mean Corpuscular Hemoglobin (MCH), platelets, and White Blood Cell (WBC) counts in the cases group. This finding is runs with Himanshu Gupta et al.^[24]

Furthermore; the current study found that patients with febrile convulsion had significantly lower serum calcium level, serum iron and Vitamin D level which is parallel to Mohamed El-Sayed Hamed et al study findings.^[25] On the other hand; the study found no statistically significant difference in serum calcium, serum iron, or vitamin D3 levels between different subgroups of patients with febrile convulsions. This suggests that these specific mineral and vitamin levels are not distinguishing factors in the various types or severity of febrile seizures. Comparable findings were obtained from Zafer Bağci^[26] and Mohamed El-Sayed Hamed et al study findings.^[25]

The current study's basic limitations include a small sample size, a short duration for data collection, a crosssectional design, and a single measurement of the variables.

5. CONCLUSION

Febrile seizure had been found in this study to be significantly related to serum 25-hydroxy vitamin D level insufficiency and deficiency, slightly lower calcium levels (< 9.9 mg/dL), lower serum iron levels, and hemoglobin levels below 10.5 gm/dl. The different types

of febrile seizures did not significantly different with serum levels of vitamin D, calcium, and iron level.

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Conflict of Intertest

About this study, the authors disclose no conflicts of interest.

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