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RELATIONSHIP OF FEBRILE CONVULSION WITH SERUM SODIUM AND HEMOGLOBIN LEVEL

A Thesis

Submitted to the Council of the College of Medicine / University of Diyala in Partial Fulfillment of the Requirements for the Degree of Master in Pediatrics

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بسم الله الرحمن الرحيم

﴿وَتَوَكَّلْ عَلَى اللَّهِ وَكَفَى بِاللَّهِ وَكِيلًا﴾

صدق الله العظيم

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*We certify that this thesis entitled (**RELATIONSHIP OF FEBRILE CONVULSION WITH SERUM SODIUM AND HEMOGLOBIN LEVEL**) prepared by **Suadad Mustafa Abd Alameer** in the College of Medicine / University of Diyala was done under our supervision as a partial fulfillment of the requirements for the Degree of Master of Medicine in Pediatrics Department*

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Dedication

To whom

Who have encouraged and

inspired me all the way

To my parents, To my husband and lovely

children

To my friends who have helped me

my teachers in the past,

at present and in the future

SUMMARY

Febrile convulsions are the most common form of childhood convulsions, affecting 2% to 5% of children. It usually occurs in children below five years of age, associated with fever (temperature ≥ 100.4 °F or 38 °C) but without evidence of intracranial infection or defined cause. Although the prognosis is usually benign however, many factors increase convulsion risk have been identified. After an initial febrile convulsion, there is a 15 - 70% risk of recurrence in the first two years and the risk is increased in patients younger than 18 months and those with a lower fever, short duration of fever before convulsion onset, or a family history of febrile convulsions.

Since studies on febrile convulsions are rare, this case-control study was conducted in Diyala province to investigate the changes in the complete blood count indices and certain biochemical parameters; namely, serum iron, ferritin, total iron binding capacity and serum sodium in patients with febrile convulsions compared to age_and sex _matched healthy children. Furthermore, the study aimed to explore the association of febrile convulsions with patient's and mother's characteristics.

A total of 200 children aged six months to six years were included. One hundred were patients with febrile convulsion (patient group) and the other one hundred were apparently healthy (control group). A questionnaire form was specially designed and filled by each subject incluing all required information. Three milliliters of venous blood were drawn from each participant. One milliliter was placed in EDTA tube for determination of CBC as quick as possible. The two milliliters were placed in plane tubes. These were left to clot for 15 minutes at room temperature. Sera were separated by centrifugation at 5000 RPM for five minutes. Sera were used for determination of biochemical parameters. Human privacy was respected by taking the parent's consent. Statistical analysis was done using the SPSS Version 25, and P-value was considered significant wherever it is < 0.05.

The results showed that 99% of fit were a generalized type and 95% of them lasted for < 15 minutes and occurred irrespective of day or night (51% *versus* 49%). Furthermore, 90% of patients have no febrile convulsion attack during hospital stay and 78% have no previous fit at all. Moreover, the cause of fever in patients was found due to respiratory cause in 84%

and non-respiratory cause in 16% of patients. The fever duration before fit lasted for 12 hours or less in 82% of patients compared to 18% of patients who had fever duration more than 12 hours. Furthermore, 82% of patients had a temperature of 39 or more Celsius at the time of admission while 18% had a temperature of < 39 Celsius at the time of admission.

Regarding the CBC, the results showed that there was a statistically significant increase in the means ± SD of total red blood corpuscles in the controls compared to patient (4.76 ± 0.43 *versus* 4.61 ± 0.51, **P= 0.032**). Likewise, there was a statistically significant increase in the hemoglobin concentration in controls versus patients (11.85 ± 0.9 *versus* 11.38 ± 1.22, **P= 0.003**). The packed cell volume was also found to be significantly higher among controls versus patients (37.67 ± 5.7 *versus* 34.07 ± 3.18, **P= 0.001**). However, the mean corpuscles volume was significantly higher in controls compared to patients (78.01 ± 5.42 *versus* 74.06 ± 8.19, **P= 0.001**). The red distribution width was significantly higher in patients compared to controls (14.73 ± 1.85 *versus* 13.51 ± 1.08, **P= 0.001**). while, the difference in the mean corpuscles hemoglobin was insignificantly higher among patients compared to controls (25.58 ± 5.62 *versus* 25.06 ± 2.35, **P= 0.396**).

As the biochemical parameters are of concern, it was found that the serum iron was significantly reduced in patients compared to controls (4.02 ± 2.38 *versus* 4.74 ± 1.31, **P= 0.008)**. Similarly, the serum ferritin was significantly lowered in patients compared to controls (46 ± 24.61 *versus* 58.58 ± 15.28, **P= 0.001**). The total iron binding capacity was significantly increased in patients versus controls (80.84 ± 14.51 *versus* 66.12 ± 11.96, **P= 0.001**). while the serum sodium was also significantly reduced in patients compared to controls (131.11 ± 3.27 *versus* 139.89 ± 8.38, **P= 0.001**).

Regarding the duration of fit, the results revealed that none of CBC indices and the biochemical parameters significantly differed among patients with duration of fit of 15 minutes or less versus those with 15 minutes or more duration. Likewise, none of the CBC indices as well as biochemical parameters significantly differed in those patients who had secondary attack of fit during hospitalization compared to their negative counterparts.

The results also showed that none of the CBC indices was significantly changed among patients with a temperature less than 39 Celsius compared to those who had a temperature of 39 or more Celsius. However, regarding the biochemical parameters, it was found that the serum iron and serum ferritin were significantly lowered in patients with temperature of 39

Celsius or more compared to those with a temperature of less than 39 Celsius. (3.1 ± 2.47 *versus* 4.48 ± 1.86, t-test = 2.145, **P = 0.05**) and (32.34 ± 67.58 *versus* 64.9 ± 13.06, t-test = 3.954, **P= 0.001**) respectively. Besides, the duration of fever was found to have insignificant effect on CBC indices and biochemical parameters in patients who had less than 12 hours' duration of fever versus those who had 12 hours or more duration of fever.

In general, it was concluded that the laboratory determinations of complete blood counts, as well as, serum iron, ferritin, total iron binding capacity and serum sodium as biochemical parameters are of vital importance in the assessment and evaluation of children with febrile convulsion.

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List of Abbreviations

°C	Celsius
µg	Microgram
AAP	American Academy of Pediatrics
ADH	Anti-diuretic Hormone
CT	Computed Tomography
DTaP	Diphtheria, Tetanus, and a cellular Pertussis
ECLIA	Electrochemiluminescence immunoassay
EDTA	Ethylenediaminetetraacetic acid
EEG	Electroencephalography
°F	Fahrenheit degree
FC	Febrile Convulsion
FSE	Febrile Status Epilepticus
GABA	Gamma-Aminobutyric Acid
GEFC+	Generalized Epilepsy with Febrile Convulsions Plus
HHSV-6	Human Herpes Simplex Virus 6
HHV	Human Herpes Virus
Hib	Hemophilic influenza Type b
HWE	Hot Water Epilepsy
ILAE	International League Against Epilepsy
IQ	Intelligence Quotient
LP	Lumbar Puncture
MMR	Measles, Mumps, and Rubella
MRI	Magnetic Resonance Imaging
NIH	National Institutes of Health
SCN1A	Sodium Voltage-Gated Channel Alpha Subunit 1

SMEI	Severe Myoclonic Epilepsy of Infancy
SPSS	Statistical Package for Social Sciences
SUDEP	Sudden Unexpected Death in Epilepsy
UIBC	Unsaturated Iron Binding Capacity
WHO	World Health Organization

CHAPTER ONE
INTRODUCTION

INTRODUCTION

1-1 Background

Febrile convulsion is a most common form of childhood convulsion that occurs in 2-5% of them which represented the most common childhood convulsion disorder, exit only in association with an elevated temperature. Evidence suggests, however, that they have little connection cognitive function, so that prognosis for normal neurologic function is excellent with children with febrile convulsion (Swaiman KF, 2006). In the United States and Western Europe, they occur 2–4% of all children; In Japan, however, 9–10% of all children experience febrile convulsion, and rates as high as 14% have been reported from the Mariana Islands in Guam (Shinnar S, 2002). Febrile convulsions occur in young children at a time in their development when the convulsion threshold is low. This is a time when young children are susceptible to frequent childhood infections such as upper respiratory infection, otitis media, viral syndrome, and they respond with comparably higher temperatures (Landreau-Mascaro A, 2002). Animal studies suggest a possible role of endogenous pyrogens, such as interleukin 1beta, that, by increasing neuronal excitability, may link fever and convulsion activity (Matsuo M, 2006). Viral illnesses are the predominant cause of febrile convulsions. Recent literature documented the presence of human herpes simplex virus 6 (HHSV-6) as the etiologic agent in roseola in about 20% of a group of patients presenting with their first febrile convulsions.

Shigella gastroenteritis also has been associated with febrile convulsions (Millichap JG, 2006). Febrile convulsions tend to occur in families. In a child with febrile convulsion, the risk of febrile convulsion is 10% for the sibling and almost 50% for the sibling if a parent has febrile convulsions as well. Although clear evidence exists for a genetic basis of febrile convulsions, the mode of inheritance is unclear (Audenaert D, 2006). Risk factors for febrile convulsions are as follows:

- Family history of febrile convulsions
- High temperature
- Parental report of developmental delay
- Neonatal discharge at an age greater than 28 days Daycare attendance
- Maternal alcohol intake and smoking during pregnancy (Two-fold).

Presence of two of these risk factors increases the probability of a first febrile convulsion to about 30% (Vestergaard M, 2002). There are two types of febrile convulsions:

- Simple febrile convulsions are usually over in a few minutes, but in rare cases they can last up to 15 minutes. During this type of convulsion, a child's whole body may convulse, shake, and twitch; their eyes may roll; and they may moan or become unconscious. Children can sometimes vomit or urinate (pee) on themselves during the convulsions.
- Complex febrile convulsions can last more than 15 minutes or happen more than once in 24 hours. They may also involve movement or twitching of just one part of the body (Gupta RC, 2016).During generalized febrile convulsions, the body will become stiff and the arms and legs will begin twitching. The child loses consciousness, although their eyes remain open. Breathing can be irregular. They may become incontinent (wetting or soiling themselves); they may also vomit or have increased secretions (foaming at the mouth). The convulsion normally lasts for less than five minutes. The child's temperature is usually greater than 38 °C (100.4 °F) (Symptoms of febrile convulsions, 2014).

Patients with active convulsions should be treated with airway management, high-flow oxygen, supportive care, and anticonvulsants as necessary. Acute treatment such as rectal diazepam (0.5 mg/kg) and buccal 0.4-0.5 mg/kg) or intranasal (0.2 mg/kg) are effective and can be given at home for a convulsion lasting longer than five minutes (Sadleir LG, 2007) Patients who are postictal should receive supportive care and antipyretics as appropriate, arrange for medical reevaluation of discharged patients and parental education in a follow-up appointment within 24-48 hours. Conditions requiring admission of the patient include:

- ✓ More than one convulsion within 24 hours
- ✓ Unstable clinical status
- ✓ Lethargy beyond the postictal period
- ✓ Uncertain home situation
- ✓ Unclear follow-up care (Hodgson ES, 2008).

Sodium is an electrolyte, and it helps regulate the amount of water that's in and around cells. Sodium plays a key role in our body. It helps maintain normal blood pressure, support the work of our nerves and muscles, and regulate our body's fluid balance. A normal sodium level is between 135-145 mill equivalents per liter (mEq/L) sodium, in hyponatremia, one or more factors ranging from an underlying medical condition to drinking too much water

during endurance sports causes the sodium in our body to become diluted. When this happens, our body water levels rise, and our cells begin to swell. This swelling can cause many health problems from mild to life-threatening. There is a relationship between low S. Na Level and risk of developing recurrent convulsion within the same febrile illness, Decrease in the level of S. Na or (relative hyponatremia) may play a role as a risk factor for recurrent febrile convulsion. There is a significant association between recurrent febrile convulsion and lower level of serum sodium, in which serum sodium concentration is lowest in those patients with recurrent febrile convulsion (Hashim JM, 2017).

Iron deficiency is more common in children under two years, and since febrile convulsion is more common in the same age group, some of the recent studies have reported that iron deficiency could be a risk factor for febrile convulsion (Østergaard JR, 2009). Among the numerous biological effects of iron, there is considerable evidence that iron is also important for neurological functioning such as neurotransmitter metabolism, myelin formation, and brain energy metabolism (Beard J, 2002). A basic principle of fetal/neonatal iron biology is that iron is prioritized to red cells at the expense of other tissues, including brain. When iron supply does not meet iron demand, the fetal brain may be at risk even if the infant is not anemic (Lozoff B, 2006). Iron deficiency reduces the metabolism of some neurotransmitters, which led to the hypothesis that iron deficiency can have a role in the onset of a convulsion (Beard J, 2006)

Recent studies suggest that a considerable percentage of children having febrile convulsion suffer from iron-deficiency anemia and low serum iron. This means the low serum iron and presence of anemia can serve as a reinforcing factor for the febrile convulsion in children (Sharif MR, 2016).

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The study aims to:

1- Determining the relationship between serum sodium level with occurrence of febrile convulsion in children between six months – six years old.

2- Determining the relationship between hemoglobin level with occurrence of febrile convulsion in children between six months – six years old.