***THE RELATIONSHIP BETWEEN IRON DEFICIENCY ANEMIA AND***

***FEBRILE SEIZURES IN CHILDREN BETWEEN 6 MONTHS TO 60 MONTHS***

***IN AL-NASSIRIYA CITY***

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بِسْمِ اللَّهِ الرَّحْمَٰنِ الرَّحِيمِ

**((وَفَوْقَ كُلِّ ذِي عِلْمٍ عَلِيمٌ**))

صدق اللَّه العلي العظيم

**(يوسف(76**

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**Dedication**

**For those sharing the difficult time and offering continuous support, our family**

**We dedicate this work with our love.**

|  |  |
| --- | --- |
|  | List of Abbreviations |
| CBC | **Complete blood count** |
| CNS | **Central nervous system** |
| CSF | **Cerebrospinal fluid** |
| DNA | **Deoxyribonucleic acid** |
| DPT | **Diphtheria-pertussis-tetanus** |
| EDTA | **Ethylene diaminetetra acetic acid** |
| EEG | **Electroencephalography** |
| FC | **Febrile convulsion** |
| FS | **Febrile seizure** |
| GABA | **Gamma-amino butyric acid** |
| GABRG2 | **Gamma aminobutyric acid receptors subunit gene** |
| GEFS+ | **Generalized epilepsy with febrile seizuresplus,** |
| Hb | **Hemoglobin** |
| HHV | **Human herpes virus** |
| ID | **Iron deficiency** |
| IDA | **Iron deficiency anemia** |
| ILAE | **International league against epilepsy** |
|  |
| MCH | **Mean corpuscular hemoglobin** |
| MCHC | **Mean corpuscular hemoglobin concentration** |
| MCV | **Mean corpuscular Volume** |
| MMR | **Measles, mumps, rubella** |
| NIH | **National institutes of health** |
| RBC | **Red blood cell** |
| RDW | **Red cell distribution width** |
| SCN1A | **Sodium channel, neuronal alpha- subunit type 1** |
| SCN2A | **Sodium channel, neuronal alpha- subunit type 2** |
| SCN1B | **Sodium channel, neuronal beta- subunit type 1** |
| SD | **Standard deviation** |
| SI | **Serum iron** |
| SPSS | **Statistical Package for the Social Sciences** |
| TIBC | **Total iron binding capacity** |

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**Chapter One**

**-Introduction**

**-Aim of study**

* 1. **INTRODUCTION**

Febrile seizures (FS) are among the most common reasons that patients present with to pediatric emergencies(1). They are the most common causeof seizures in children less than five years of age and mostly benign, rarely caused brain damagewith a peak incidence in the second year of life(2).It can be emotionally traumatic and anxiety provoking when witnessed by parents(3). Most seizures are less than five minutes in duration and the child is completely back to normal within an hour of the event(4),and many factors that increase seizure risk have been identifiedinclude developmental delay, discharge from a neonatal unit after 28 days, day care attendance, viral infections, a family history of febrile seizures, certain vaccinations, and possibly iron and zinc deficiencies.FS may occur before or soon after the onset of fever, with the likelihood of seizure increasing with the child's temperature and not with the rate of temperature rise. The risk of a 1st febrile convulsion is greater if there is a family history of other relatives with febrile convulsion .The risk of younger sibling of affected child is around 10-20% and this is higher if a mother and father was also affected. Male are more likely to be affected than female. It a fantastic model of extraordinary network activity during development because they do not occur later in life. In addition, they provide biologically relevant examples of activity-dependent, enduring plasticity(4,5,6,7).

***1.2.* Criteria of febrile seizures include**

* **Age**

6 months to 5 years old

* **Convulsion**

Duration: usually no longer than 3-6 minutes; class as complex of prolonged more than 10-15 minutes

Pattern: usually generalized tonic-clonic; class as complex if focal

* **Recovery of level of consciousness**

 usually complete within an hour; class as complex if not fully recovered within an hour

* **Temperature**

 Fever around the time of the convulsion

* **History of previous febrile convulsion**

class as complex if convulsions recur in the same febrile illness

* **Recent immunization**

It is rare for a febrile convulsion to precipitate by an immunization

* **Electroencephalogram (EEG)**

done within a week after a febrile convulsion may be abnormal but after a week it usually shows no abnormality(8,89).

***1.3.* Definition**

**(FC) is defined** as convulsion which occurs in children aged 6 months to 60 months and is accompanied by fever higher than 38°C (100.4°F), and does not involve symptoms of central nervous system infections(9) .

**The (NIH) definition** is that febrile spasm is an event in infancy or childhood generally happen between(3monthsto 60 month's) of age associated with fever relationship but without evidence of intracranial infection or defined cause

**The (ILAE) definition** is that febrile seizure is seizure take place in kids after age1 month ,associated with afebrile illness not caused by an infection of CNS , without preceding neonatal seizure or preceding unprovoked seizure and notmeeting criteria for other acute symptomatic seizures(10) .

**The American Academy of Pediatrics (2008)** has announced a popular definitionof febrile seizures as a seizure take place in febrile kids between the an age of sixmonths to sixteen months who don't have an intracranial infection, metabolic disturbance, or history of afebrile convulsions(11) .

***1.4.* Simple versus complex febrile seizure**

FS are subdivided into 2 categories: **simple and complex(12)**.

**Simple FS**are common accounting for more than 70%, its generalized, tonic clonic associated with fever,lasting not more than 15 minutes and not recurring within 24 hours, Peak age is 18 months(13)

**Complex FS** account for the balance 30%, are prolonged (>15 minutes), and/or focal, and/or occur more than once in a single febrile illness(14)

Complex FS sometimes may also have evidence of post seizure neuronal dysfunction such as Todd paresis which may last minutes to hours to even a few 7days(15) **.**

***1.5.* The risk of subsequent epilepsy**

is rare but increase with each of the following risk factors

* Neurological abnormalities or development delay before the onset of febrile convulsion
* Atypical seizure
* Family history of epilepsy
* Early age
* Short duration and low grade fever at presenting time
* Frequent numbers and high fever of subsequent febrile illnesses.

Complex seizure In the absence of these risk factors only 1% of children go on to develop epilepsy(compared with 0.4% if childrenwithout a history of onset epilepsy with and without preceding febrile seizures)(16,90). A kid with at least two risk factors or more has greater than 30% recurrence of risk at 2 years of age, and that risk of recurrence will be double with three risk factors. Higher recurrence risk also has been found to associated with seizure that occur at lower-Peake temperatures or within hour of fever onset(17) .

***1.6.* Historical Background**

FS has been recognized as a separate disease entity for mother types of seizures since the early mid-nineteenth century. This was emphasized more after the invention of the thermometer in the late 19th century(18).

Initial studies did not exclude seizures associated with underlying neurological disturbance(2).A few years later, the first community-based study was published, reviewing all convulsive disorders in young children and concluding that FS are probably benign and common and have good outcomes, but with a rare yet strong link to future epilepsy(19) .Pediatricians then started to recognize prolonged and recurrent FS as medical emergencies requiring more medical attention and urgent interventions; otherwise, future neurodevelopmental outcomes might be jeopardized(20).

***1.7.* Epidemiology**

FS have a prevalence of 2%–5% in children in Western Europe and the United States, and the peak age of onset is 18 months, 90% of seizures occur during first 3 years of life, 4% before 6 months and 6% after age 3 years(21). Children aged 12–30 months represent 50% of all children with FS, while the proportion of children who experience a ﬁrst episode of FS after four years of age is low (6%–15%)(22)Theincidence rate varies among other parts of the world,and all ethnic groups may present with FS, but there is a higher prevalence in some ethnic groups, in particular Guamanians (14%), Japanese (6%–9%), and Indians (5%–10%)(21,23).

FS are prevalent in up to 5% of children,with the overall incidence estimated to be 460/100,000 in the age group.The prevalence of febrile seizures between 3% and 8% in kids up to 7 years of age. febrile convulsion mostly simple, and at least one complicated feature was observed in approximately 35%of cases, including feature of focality(16.1%), multiple seizures (13.8%), prolonged period (>15 minutes, 9.3%) and recurrent febrile convulsion within 24 hours (16.2%), 6.5% confirmed two complex feature, and 0.7% confirmed three complex feature . Prevalence and incidence rates of FSs may be higher in regions of Asia and Africa, but epidemiological studies of low-income countries are scarce. Complex FSs have been reported to be more frequent in children in sub-Saharan Africa (11).The most prevalent age for affected children are 10 to 18 months and in 75%,it occurs in children younger than 3 years old(24) .Males bear consistently arisen as having a greater frequency of F.S (male to female ratio, 1.1:1 to 2:1). However Partial study show no significant gender difference. Febrile status epilepticus, that is, seizures that last more than 30 minutes, represent only 5% of FS (25). .Different in prevalence relates to change of case definitions, ascertainment methods, geographical , and cultural factors(26). about one third of kids will developed recurrent convulsions if have first febrile seizure before(27)  .Therefore considering the importance of prevalence, early diagnosis and treatment of febrile seizures in children, reducing the costs of hospitalization and treatment(28) .

***1.8.* Etiology and Pathophysiology**

Febrile seizures tend to occur in families, although the exact mode of inheritance is not known, children who have febrile seizure more often tend to have a history of febrile convulsions in close relatives(3). It has long been recognized that there is a significant genetic component for susceptibility to this type of seizure. In the past, the most prevalent theory attributed a direct effect of hyperthermia on compensatory hyperventilation. This was assumed to cause mild brain alkalosis, resulting in increased neuronal excitability and the subsequent development of clinical seizures(29).

This theory, however, has not explained why some children are more prone to develop such phenomena than others(30).

The exact role of fever in the etiology of febrile convulsion is not clear but there is a positive family history in 7-31% of cases(3).The definitive degree of fever is uncertain. In one series it was shown that at the time of convulsions, 75% of patients had a temperature over 39oC. Viruses are the most common cause of illnesses in children admitted to the Hospital with a first febrile seizure(31). Seizuresthat occur after immunizations are likely to be febrile, occurring in response to temperature elevation, particularly those occurring within 48 hours of DPT and 7 to 10 day after measles immunization(32)

***1.8.1.* Genetic factor**

It seems clear that febrile convulsions make up an extremely heterogeneous group for which there is no single mode of inheritance(33) .

Causative genes have not been identified in most patients with febrile convulsions;

Mutations in the voltage-gated sodium channel alpha-1, alpha-2 and beta-1 subunit genes (SCN1A, SCN2A and SCN1B) and the GABA(A)receptor gamma-2 subunit gene (GABRG2) have been identified in families with generalized epilepsy with febrile seizures plus’ (GEFS+)(34)Patients with GEFS+ can have febrile seizures followed by afebrile (often generalized) seizures(35)

Currently we know that there is a large role of genetic susceptibility based on a large group of gene variants. This genetic makeup has likely resulted in neuro developmental vulnerability, with alterations in sodium channel expression, hypothalamic dysregulation, and both cortical and hippocampal excitability(30).

***1.8.2.* Prenatal factors**

Maternal ill-health, parental sub-fertility(36), prenatal maternal cigarette smoking(37). and alcohol intake have been associated with the occurrence of febrile convulsions in the offspring. However, population-based studies do not find much evidence that social and maternal factors are significant(37,38,39)

***1.8.3.* Perinatal factors**

A hospital-based series suggested that an abnormal pregnancy or birth history predisposes to febrile convulsions in general and complicated initial febrile convulsions in particular(79).The height or duration of the fever may be important but there are problems in evaluating the temperature recordings because febrile convulsions usually occur randomly at home. Viral infections commonly cause the fever that is associated with febrile convulsions. Synthesis of immunoglobulin in the CSF of children with febrile convulsions has been demonstrated suggesting that encephalitis may sometimes occur and not be recognized(36).There is evidence that human herpes virus-6 (HHV-6) is linked with exanthema subitum, a condition that is frequently complicated by febrile convulsions(40).More recent work suggests that acute HHV infection is a frequent cause of febrile convulsions in young children that do not have the signs of exanthema subitum(41). HHV-6B infection has been shown to be commonly associated with febrile status epilepticus, HHV-7 less frequently so. Together they accounted for one third of the cases in a study of febrile status epilepticus, a condition associated with an increased risk of both hippocampal injury and subsequent temporal lobe epilepsy(42).

Bacterial infections may be associated with febrile convulsions urinary tract infections shigella and pneumococcal bacteremia, for instance. Children with bacterial meningitissometimes have convulsions and it is important to remember this when deciding whether or not to perform a lumbar puncture.

It has been shown that there are increased risks of febrile seizures on the day of receipt of DPT vaccine and 8 to 14 days after MMR vaccine, apparently not associated with long-term adverse consequences(43). A study in the UK found that 6–11 days after MMR vaccine there was an increased risk of complex febrile convulsions lasting more than 30 minutes(44)

However, the risk of febrile convulsions after MMR vaccination was small and transient. Also the long-term rate of epilepsy was not increased in children who had febrile convulsions following MMR vaccination compared with children who had febrile convulsions of a different aetiology(45).

***1.9.* Febrile seizures with iron deficiency anemia**

Febrile seizures and iron deficiency anemia are two common diseases in children worldwide(46) .Iron deficiency is postulated as a risk factor for febrile seizures in children and it is an easily correctable condition(47)

because the latter is more common in children under two years of age and IDA is also common in children of the same age(48). The function of hemoglobin in conveying oxygen to the brain and since fever can exacerbate symptoms that result from anaemia, a relationship between iron deficiency anaemia and febrile convulsions is probable(49,50,51)

Generally the children between 6 months to 5 years are more prone to this disease. However, age for peak incidence is 14 to 18 months which overlaps with that of iron deficiency anemia which is from 6 to 24 months(52,53,54). furthermore ,There are many hypotheses appear that threshold of neuron excitation affected by iron deficiency anemia(55),which is the most common nutritional deficiency and hematological disease of infancy and childhood which is affecting between 500 million and two billion people worldwide(56). Iron is a nutritional element that essential for enzymes involved in neurochemical reactions(57).Neurological symptoms like poor attention span,

learning deficits, weak memory, delayed motordevelopment and behavioural disturbances caused byiron deficiency are well known.(57,58,59)

Iron is a vital micronutrient that is used by every cell and organ system in the body. It has been found to act as a cofactor in many enzymatic reactions at the cellular level, and affects neurotransmitter production and function, hormone function and DNA replication(60,61)

So Iron is essential for the metabolism of brain and neurotransmitters, and in the production of myelin which is required for nerve cells and can change the amplitude and the threshold of neurons excitation(62)

***1.10.*Risk factors for iron deficiency anemia**

* **Maternalrelated factors**

-Medical conditions/complications during pregnancy and postnatal e.g., haemorrhagic disease /infection

-Untreated maternal anaemia during pregnancy

-Vegetarian and vegan diets: if insufficient iron-rich foods in the diet

-Twin or multiple pregnancy(63,64)

* **Child related factors**

-Premature and low birth weight infants(65)

-Delayed introduction of solids

-Gastrointestinal disease affecting iron absorption

-Faltering growth

-Chronic infections or parasitic infections(66,67,68)

-Intake of cow’s milk before 12 months of age(69)

-High intake of cow’s milk (which is a poor source of iron) in infants >12 months of age

* **Environmental related factors**

-Residence in tropical environments(66,67,68)

-Low socio-economic status(70,71,73).

-Food insecurity/access to iron rich foods(72,73)

***1.11.* Diagnosis of IDA**

Iron deficiency (ID) is a state in which there is insufficient iron to maintain the normal physiological function of blood and tissues, such as the brain and muscles. The more severe stages of ID are associated with anemia. Iron-deficiency anemia (IDA) occurs when the hemoglobin concentration is below two standard deviations (–2SD) of the distribution mean for hemoglobin in an otherwise normal population of the same sex and age(73).IDA is generally characterized by a hemoglobin level of less than 110 g/L, plus a measure of poor iron status(74).

IDA is diagnosed by fulfilling the following criteria: Hb level below normal according to age, peripheral blood smear reveals microcytic and \ or hypochromic red blood cells, and Hb level rises after two months of iron supplementation , in addition, one or more the following criteria must be met: RDW >14% and Mentzer index >13(85).

The diagnostic tests widely used for IDA are CBC, SI, TIBC, and serum ferritin level.

Since serum ferritin level is expensive and not available, an inexpensive, simpler test is needed. The Mentzer index (MCV\RBC ) has been used identified hypochromic microcytic anemia with good validity(86)

Table (1.1) : Hematological parameter of IDA

|  |  |
| --- | --- |
| Measurement (87) | IDA |
| MCV\MCH  |  |
|  Serum iron |  |
| TIBC |  |
| Transferrin saturation |  |
| Serum ferritin |  |
| Serum TfR |  |
| Bone marrow iron stores |  |
| Erythroblast iron |  |

**Table(1.2) : Normal values: Hb, indices, RDW(88)**

|  |  |  |
| --- | --- | --- |
|  | Age | Normal levels |
| S Iron (μg/dl)  | **All age** | **22-184** |
| TIBC (μg/dl)  | **Infants****Thereafter**  | **100-400****250-400** |
| S Ferritin (ng/ml)  | **0-6 wks****7 wks-1 year****1-9 yrs****10-18 yrs male female**  | **0-400****10-95****10-60****10-300****10-70** |
| TLC (cells/mm3)  | **0-30 days****1-23 mo****2-9 yrs** | **9100-34000****6000-14000****4500-12000** |
| Neutrophil (%)  | **All age** | **54-62** |
| Hemoglobin (g/dl)  | **1-23 mo****2-9 yrs** | **10.5-14****11.5-14.5** |
| MCH(pg/cell)  | **1-23 mo****2-9 yrs** | **24-30****25-31** |
| MCHC(%)  | **All age** | **32-36%** |
| MCV(fl)  | **1-23 mo****2-9 yrs** | **72-88****76-90** |
| RDW(%)  | **1 mo- 24 mo****25-60 mo** | **<16.5****<15** |

|  |
| --- |
|  |

***1.12.* IDA Treatment**

Successful treatment of IDA depends on three essential steps:

1. Iron therapy

 2. Dietary changes

3. Lab monitoring for assessment of response(75)

***1.12.1.* Iron Therapy**

Oral iron therapy is finest administered as oral ferrous sulphate as it is the a lot of budget- friendly. Dosage is 3- 6 mg/kg/d of important iron (maximum is 150 mg)(76).

* + 1. **Dietary Changes**

 Bottle feeding leads to consumption of huge amount of milk(77). Eliminating the container is an important initial step in the treatment. Unmodified cow's milk need to be avoided under 1 y of age and if inescapable as a result of failure of breast feeding and absence ofaffordability of formula feed, it is necessary to offer iron supplementation and monitor for IDA. For children greater than 1 y of age, milk consumption should not be greater than 500 ml/d. Consumption of iron abundant food should be encouraged.

* + 1. **Monitoring Response**

 A repeat CBC after 1 month of iron therapy ought to show a rise in hemoglobin by 1 g/dl. Confirm normalization of hemoglobin (as each age adjusted normal values) by repeating a CBC every 2-3 month and proceed iron supplementation for a more 3 month after normalization of hemoglobin to replenish the storage space swimming pool(73).

* 1. **Treatment of FS**

A full clinical assessment about type of seizure, its etiology, precipitating factors and concomitant illness should be done and accordingly management is planned.

Aim of the treatment is to control seizure to improve quality of life and to prevent complications(78)

First initial assessment the convulsion should be stopped if it is continuing. Then the temperature should be measured to confirm that the child is febrile (the rectal temperature is more reliable than oral or axillary). The history and the general physical examination may provide clues: if there is an exanthematous rash or evidence of an upper respiratory tract infection

If the child presents in a convulsion the situation should be reassessed when it has stopped. Even when there is evidence of an infection outside the nervous system it may be important to exclude an intracranial infection by performing a lumbar puncture(79).

* Clothing should be removed and the child covered with a sheet.
* The child should be on its side or prone with its head to on side since vomiting with aspiration is a hazard.
* Rectal diazepam is the drug of choice, producing on effective blood

concentration of anticonvulsant within ten minutes. Dose: 0.5 mg/kg state.

* Repeat same dose if convulsion is not controlled within half an hour.
* It can be repeated after 30 minutes if convulsion is not controlled. Paracetamol 12-15 mg/kg/dose 4-6 hourly.
* Avoid physical methods such as fanning, cold bathing and tepid sponging-their use in controversial as they are felt to cause some discomfort and minimal benefit(80,81).
	+ 1. **Criteria for admission**

Most children with a first febrile convulsion do not need to be admitted . The main concern is the possibility of missing a more serious diagnosis such as meningitis Strongly consider admission for observation, lumber puncture or treatment if any of the following factors are present:.

• Age under 18 months (May have meningitis without meningeal signs).

• Signs of meningitis (neck stiffness, photophobia, kernig's sign, brudzinski's signs, bulging fontanelle, depressed level of consciousness).

• Child was drowsy before the seizure or is irritable, systemically unwell or "toxic".

• Petechial rash

• Recent or current treatment with antibiotics (because partially treated meningitis may not have meningeal signs).

• Complex convulsion (i.e. lasting longer than 10 minute, or with focal features, e.g. jerking affecting only one limb or repeated in the same episode of illness or with incomplete recovery within 1 hour).

• Early review by a doctor not possible.

• Inadequate home circumstances.

• The cause of the fever requires hospital management in its own right(82,83,84)

many parents witnessing a child's first convulsion thinks that their child is dying or is already dead. Try to decrease parental anxiety by counseling. Reassurance and education is thus very important. Instructions on the future management of possible recurrences should be given with emphasis on practical issues of how to manage a child with febrile convulsion at the scene.

**Aim of study**

To assess the effect of iron deficiency anemia in febrile seizure in children between 6 months to 60 months.

**Chapter Two**

**Subject**

**And**

**Methods**

***2.* Subjects and Methods**

***2.1.* Subjects**

**2.1.1. Patients**

A Case-control study has been carried out to determine association between simple febrile convulsion and IDA. Permission was taken from hospital ethical committee. Thirty patient present with of simple febrile convulsion admitted to BintAl-huda teaching hospital in Thi-Qar governorate in south of Iraq from first of July to December 2018,age, sex and weight were documented. Diagnosis of simple convulsion was made after detailed history and examination.

**2.1.2. Control group**

Control group of 30 febrile patient with same age and gender but without convulsion were selected to compare with cases group.

***2.2.* Inclusion criteria**

* Children aged 6 months to5 years presenting with simple 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.

***2.3.* Exclusion criteria**

* Atypical febrile convulsion.
* Diagnosed organic cause of convulsion.
* Delayed milestones, neurological defects.
* Central nervous system infection- meningitis, encephalitis.
* Anemia resulting from other causes – hemolysis, bleeding.
* Refusal of Consent.

***2.4.* Data collection**

A special questionnaire was designed for the purpose of the study including the following data:

Name, 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** are seizures occurring among children, 6 months to 5years at temperature 38 C° (100 F°) or higher without CNS infection or any metabolic imbalance.

**Simple febrile seizures** are generalized, tonic clonic associated with fever, lasting not more than 15 minutes and not recurring within 24 hours.1 In 2–5% children, it occurs at least one time. Peak age is 18 months

***2.5.* Methods**

**Laboratory procedures:**

A One milliliter of venous blood sample were collected in to tubes with EDTA from all patients and controls then send to laboratory to find the hemoglobin (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 could not be done as this facility was not available inhospital and patients were not able to afford it .

verbal consent was taken from the parents, and the study was approved by the ethics committee of Bint Al-huda teaching hospital.

***2.6.* Statistical analysis**

All statistical analyses were carried out using the Statistical Packages for Social Sciences (SPSS) software version 17. Comparisons of proportions were performed by cross tab using Chi-Square test when each cell has an expected frequency of five or more, and the Fisher's exact test was used when one or more of cells have an expected frequency of less than five in 2×2 table. P values less than 0.05 were considered statistically significant.

**Chapter Three**

**Results**

**Results*:***

. ***3.1.* selected characteristics of febrile convulsion patients and controls**

We studied 30 children (19 males and 11 females) with FC and a control group of 30 febrile children without convulsion (20males and 10 female)which was more frequent among male , their ages ranged from 6-60 months The mean age of patients in the case and control groups was (21.166±16.354) months and (24.266±17.824) months, respectively, that mean FC more common below 2 years. According to mean weight of cases was (10.213± 4.020) lower than control group which was(11.233± 4.290),and the peak of body temperature was 38.983± 0.688 which was higher among case group in compare with control group which was 38.883± 0.762.Demographic characteristic variable among two groups inform of age, gender, parent Consanguinity, resident and iron therapy show in table 3-1))

**Table(3-1):Baseline characteristics of two groups.**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| P-Value | Total | Controls(30) | Cases(30) | Variable |
| **%** | **N** | **%** |  **N** |
| 0.396 | **36** | **56.7** | **17** | **63.3** | **19** | **23-6** | **Age (months)** |
| **24** | **43.3** | **13** | **36.7** | **11** | **60-24** |
| 0.181 | **39** | **66.7** | **20** | **63.3** | **19** | **Male** | **Gender** |
| **21** | **33.3** | **10** | **36.7** | **11** | **Female** |
| 0.219 | **30** | **56.7** | **17** | **43.3** | **13** | **Present** | **Consanguinity** |
| **30** | **43.3** | **13** | **56.7** | **17** | **Absent** |
| 0.200 | **25** | **43.3** | **13** | **40.0** | **12** | **Urban** | **Resident** |
| **35** | **56.7** | **17** | **60.0** | **18** | **Rural** |
| 0.500 | **1** | **3.3** | **1** | **0** | **0** | **Yes** | **Iron therapy** |
| **59** | **96.7** | **29** | **100** | **30** | **No** |

This Table shows that 19 (63.3%) of FC children are younger than24 months, FC was noticed more in male (63.3%) than female (36.7%) , As well as (60%) are rural in their resident

There is no statistically significant difference concerning sex, age, Consanguinity, Iron therapy and residence between FC patients and control group (p-value >0.05)

**3.2. Demographic characteristics of patients with febrile convulsion*.***

Selected variables for patients with febrile seizure as Family history of F.C and Family history ofepilepsy show in table (3-2) and causes of fever among cases and controls that show in table (3-3)

**Table (3-2):family history among case group**

|  |  |  |  |
| --- | --- | --- | --- |
| P-Value | Total | Cases(30) | Variable |
| % | N |
| 0.001\* | **11** | **36.7** | **11** | **Present** | **Family history of F.C** |
| **19** | **63.3** | **19** | **Absent** |
| 0.001\* | **0** | **0** | **0** | **Present** | **Family history of epilepsy** |
| **30** | **100** | **30** | **Absent** |

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| p-value | Odd's ratio | Total | Control | Case | Variable |
| **%** | **N** | **%** | **N** |
| 0.431 | **1.96** | **24** | **33.3** | **10** | **46.7** | **14** | **Gastroenteritis** |
| **0.510** | **12** | **23.3** | **7** | **16.7** | **5** | **Upper Respiratory tract infection** |
| **1.428** | **6** | **6.7** | **2** | **13.3** | **4** | **lower Respiratory tract infection** |
| **0.595** | **11** | **20.0** | **6** | **16.7** | **5** | **Urinary tract infection** |
| **0.285** | **7** | **16.7** | **5** | **6.7** | **2** | **Nonspecific underlying case** |

This table show that family history among case group for febrile convulsion and epilepsy,

Positive for FC was (36.7%) while absent was (63.3%) with significant value (0.001) using Fisher's Exact Test

**Underlying causes of fever among cases and controls.:Table (3.3)**

Table (3-3) show that the gastroenteritis{cases (46.7%),control (33.3%)} are the most frequent cause of fever followed by respiratory diseases, Odd's ratio significance in gastroenteritis (1.96) and lower respiratory tract infection (1.42).

**Table(3.4):Type of feeding among two groups**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| p-value | Odd's ratio | Total | Control | Case | Variable |
| **%** | **N** | **%** | **N** |
| 0.427 | **0.5** | **5** | **6.7** | **2** | **10.0** | **3** | **Breast feeding** |
| **2** | **8** | **6.7** | **2** | **20.0** | **6** | **Bottle feeding** |
| **0.380** | **22** | **46.7** | **14** | **26.7** | **8** | **Mixed feeding** |
| **0.333** | **3** | **6.7** | **2** | **3.3** | **1** | **Complimentary feeding** |
| **0.8** | **22** | **33.3** | **10** | **40.0** | **12** | **Same family diet** |

 This table show the type of feeding among case group more common was same family diet (40.0%),while the common type of feeding among control was mixed feeding (46.70%) .

Odd's ratio significant among bottle feeding (2).

**3.5.Hematological parameters of cases and control*s***

CBC indices inform of Hb, MCV, MCH, MCHC, RBC count, RDW and PLT used to diagnose IDA, Mentzer index which is the ratio between MCV\RBC count also use as a diagnostic parameter for IDA, all of these indicator show in table 3-5 .

***Table (3.5): complete blood count and Mentzer index among two group.***

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| p-value\* | t-test | Control | Case | Variable |
| **SD± mean** | **SD± mean** |
| 0.274 | **1.104** | **1.46±11.03** | **1.55±10.60** | **Hb** |
| 0.072 | **1.834** | **8.73±74.07** | **7.96±70.11** | **MCV** |
| 0.729 | **0.349** | **3.34±24.33** | **4.49±33.98** | **MCH** |
| 0.765 | **0.301** | **1.85±33.15** | **2.47±33.32** | **MCHC** |
| 0.740 | **0.333** | **0.50±4.59** | **0.54±4.64** | **RBC Count** |
| 0.002 | **3.267** | **2.24±14.42** | **2.14±16.27** | **RDW** |
| 0.678 | **0.418** | **117.23±295.13** | **120.57±307.96** | **PLT** |
| 0.157 | **1.434** | **2.86±16.31** | **2.63±15.29** | **Mentzer index** |

This table show the amount of Hb, MCV,RDW are statistically among case group are lower than control group according to mean and standard deviation. In this study we observe near significant MCV and significantly higher RDW in FS cases compared to control.

**T-test was used measure p-value for all variables.**

**Chapter Four**

**-Discussion**

**-Conclusions**

**-Recommendation**

**-References**

***4.1.* Discussion**

Febrile seizure ,also known as a febrile fit or febrile convulsion , is associated with a high body temperature but without serious underlying health issue ,long term out comes are generally good with little risk of neurological problems or epilepsy(55). Many risk factors like genetic predisposition, gender, age, perinatal exposure to drugs, smoking and alcohol ingestion during pregnancy had been studied(13). Age for peak incidence of febrile seizures is 14 to 18 months which overlaps with that of iron deficiency anaemia which is from 6 to 24 months(96) .In this prospective case –control study ,the majority of febrile convulsion occur between 6 months to 60 months with more frequent below two years ,that similar to studies done by ,Sudhir et al ,E. Dinesh Kumar et al ,and Jeetam et al in India(55,56,93) show febrile seizure was more frequent below two years . while study of Tejesh et al in Nepal(9)found no differences in frequency among two groups according to age . The current study show the male gender two time more risk for febrile seizure than female among case group ,this in agreement with Jateem et al in India(93).WhereasKhawaja et al in Iran(13)didnot reported significant differences among both gender, possibly due to limitation of collection data and dependence on hospital that could not generalized . Genetic factor play an important role in febrile seizure .however, genetic inheritance is not fully understood . in this study revealed that half of patient with febrile seizure their parent were relative also had positive family history of febrile convulsion .similar result concluded in a study was carried out by Hasim et al in Turkey(92). Gastroenteritis and respiratory diseases are more frequent causes of fever among cases and controls groups ,This study reported that the gastroenteritis more frequent cause in occurrence of febrile seizure than respiratory diseases . This result in agreement to that reported by Hasim et al done in Turkey(92).But it is in contrast to that reported by Sudhir et al in India(56) showed that respiratory diseases were more frequent than other causes that can be explained due to the collection of data and research done in different season. As dietary habits of children would have an important influence on iron intake ,In this study ,the odds ratio of bottle feeding for febrile seizure group was nearly two time that of control group ,these result in contrast with Ghasmi et al study that done in Iran(48) ,which was showed that breast feeding is more frequent among case group than bottle formula .this difference could be due to unfortified formula that use among case group as mean source of diet Iron Deficiency Anemia is a major risk factor found aggravating simple febrile fits in many studies .Fever can worsen the negative effects of anemia or of iron deficiency on the brain and a seizure can occur as a consequence. Some studies showed protective effects on it and others found no association with simple febrile fits(13). This study showed low mean Hb in children with febrile seizure as compared with to mean Hb in children in control group. Mean and SD of MCV which was low among case group as compared with control group and showed statistically near significant .This resultis similar to that reported by Pisacaneet et al in Italy(94) showed that in a case-control study less than 2 years of age and report that anemia was significantly more common in case than control . other study done by Fallah et al Iran(95) showed low Mean Hb in case group as compared to control group which was significant ,Similarly Ambreen Sultan et al in a Pakistani(13) study done in Abbottabad in 2013 by two time had low Hb with febrile fits as compared to children with fever but without febrile fits ,also another study done by Boshra et alIn Egyptian (96)children, showed mean hemoglobin, hematocrit and MCH significant low in simple febrile fits case as compared to control group. And similarly, an Indian study done by Srinivasa et al(97) showed low Hemoglobin, MCV, MCHC in febrile fits cases as compared to control tow time . Other hematological indicator that use in diagnosis of iron deficiency anemia in this study is RDW which was higher in cases than controls and it was statistically significant .This result is in agreement to that reported by Khawaja et al in Iran(13). All of these study described an association between iron deficiency anemia and febrile convulsion . On other hand some studies showed no association of iron deficiency anemia with increased risk of febrile fits. Salehi Omran MR et al In Iran (98)study done in 2009 showed difference was not statistically significant. The differences between the result of present study and other studies are because of different in sample size and using different patient age group and differences in diagnostics criteria of iron deficiency anemia between their and this study

***4.2.* Conclusions**

1. Iron deficiency anemia is more prevalent in children with simple febrile seizure than in children with febrile illness without seizure.
2. A positive family history of FS among first-degree relatives isthe important risk factor for developing FS.
3. A family history ofepilepsy was also significantly related with FS.
4. Majority of children with FC are younger than24 months.
5. FC was noticed more in male than female .
6. The amount of Hb, MCV,RDW among children with FC are lower than control group.

**Limitation in this study**

1. unavailability of many important relevant investigations like serum ferritin,serum iron,total iron binding capacity,blood film.
2. A case–control study might bemisleading if cases were identified from hospital admissions andadmission to hospital was influenced not only by the presence andseverity of disease but also by other variables, such as social class.
3. Limited our knowledge of statistical methods and difficulty in dealing with different types of data.

***4.4.* Recommendations**

1. children with febrile seizures are suggested to be monitored for diagnosis and treatment ofiron-deficiency anemia. Furthermore, it is advisable to prescribe the iron supplements sooner and more carefullyto children who have important and well-known risk factors for febrile convulsion, such as family history offebrile convulsion.
2. It will be worthwhile to conduct a study to follow up children with iron deficiency, whichstricken by the febrile convulsions after the treatment of iron deficiency, in terms of the recurrence rate of febrileconvulsions.
3. An interventional large prospective cohort study should bedone for those children presenting with febrile seizure.
4. The need to counseled people to stop their children from taking non-nutritious foods such as artificial juices , chips and large amounts of milk to reduce occurrence of iron deficiency anemia.
5. Screening and early diagnosis of IDA in high risky group like premature children ,low social class,cyanotic CHD and febrile convulsion
6. Educate people about the benign nature of febrile convulsion and the low chance of serious complications.
7. The need to conduct an expanding studies on other risk factors of febrile convulsion such as electrolytes disturbance and some viral infections

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**Appendices**

**QUSITIONNAIR PAPER FOR GROUP 1 (febrile child with simple febrile convulsion)**

Name ; Age (m.) ; Sex; male

 Female

Current weight; Parents consanguinity; present

 Absent

Family history of febrile convulsion; present Temperature;

 Absent

 Family history of epilepsy; present Type of febrile convulsion; Simple

 Absent complex

Type of feeding; breast feeding Cause of fever; URTI other

 Bottle feeding LRTI

 Mixed feeding UTI

 Complimentary diet GE

 Same family diet Vaccine

History of iron therapy; Yes

 No

Hb MCV MCH MCHC

RBC Count RDW PLT

**QUSITIONNAIR PAPER FOR GROUP 2 (febrile child without convulsion)**

Name ; Age (m.) ; Sex; male

 Female

Current weight; Parents consanguinity; present

 Absent

 Temperature;

Type of feeding; breast feeding Cause of fever; URTI other

 Bottle feeding LRTI

 Mixed feeding UTI

 Complimentary diet GE

 Same family diet Vaccine

History of iron therapy; Yes

 No

Hb MCV MCH MCHC

RBC Count RDW PLT