RISK FACTORS FOR FIRST SIMPLE FEBRIL ESEIZURES AMONG CHILDREN IN SULAIMANI GOVERNORATE

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ABSTRACT

Background

Febrile seizures are common problems in children aged between 6-60 months, many studies were conducted on the risk factors associated with the recurrence of simple febrile seizures. However, few research works have been conducted on the risk factors concerning first simple febrile seizures.

Objectives

To determine the risk factors for the development of first febrile seizure attacks among children in Sulaymani governorate.

Patients and Methods

A prospective case-control study was conducted at Dr. Jamal Ahmad Rashid Pediatric Teaching Hospital in Sulaymani governorate, during the period from the 1st of April to the 1st of December 2019. A hundred cases (100) diagnosed to have a first attack of simple febrile seizure who had been admitted to the emergency department, were enrolled in our study, and another sex and age-matched 100 children with fever but without seizures, were selected as controls. The age of both groups (cases & controls) ranged from 6 -60 months. A specially designed questionnaire and oral consent were taken during the interview with the parents.

Results

The study showed that upper respiratory tract infections constituted a major cause of fever among cases, which precipitated febrile seizure (76%) . Significant (,p.value <0.05) association has been noted between the first febrile seizure attack and bottle feeding, prematurity, low birth weight, caesarian section, paternal smoking, as well as family history of febrile seizures has shown a significant value with (P<0.05). Breastfeeding was a protective factor.

Conclusion

There's strong association between upper respiratory tract infections in children younger than five years and first attack of simple febrile seizures. Normal vaginal delivery ,breast feeding and avoidance of smoking are protectives for getting simple febrile seizures in susceptible children.

Keywords: *febrile seizures, Sulaymani , Dr.Jamal A.Rashid pediatric hospital..*

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INTRODUCTION

Febrile seizures represent the most common convulsive disorder in infants and children. It is incidence as much as one in every 25 children, and affected children may experience at least one attack during childhood period. Febrile seizures (also known febrile fit) have been defined by the International League Against Epilepsy (ILAE) as; an event that occurs in infants or children, associated with an elevation in the body temperature more than 38°C, without any evidence of central nervous system infection or afebrile seizures before [1].

They most commonly occur in children between the ages of 6 to 60 months. Most seizures last less than five minutes in duration. However, there is no record of febrile seizures without prior occurrence of fever in the patients. Febrile seizures are divided into two categories: simple and complex seizures [2].

The first sign of febrile seizure may be stiffening of the entire body, children may have symmetric rhythmic synchronous contractions of hands and feet. The eyes may roll up as well, and the head may jerk. Urine and faces may pass involuntarily. Most patients of simple febrile seizures may have a very short postictal state and usually return to their baseline condition and regain consciousness within minutes of seizures [3].

About 2-5 % of neurologically healthy infants and children may experience at least one febrile seizure and usually, it is a simple type. Simple febrile seizures usually do not have an increased mortality rate. However, 2-7 % of children may get epilepsy in the future. However, children who develop later epilepsy may experience such problems [4].

Most febrile seizures occur between 6-60 months of age with a peak incidence around 18 months, approximately 6–15% occur after 48 months, and, the onset is unusual after 72 months. Most research work data support the unique age specificity of the maturing brain's sensitivity to fever [5].

The incidence of febrile seizures in children is slightly higher in males than females, but they tend to occur earlier in females due to more accelerated brain development in female children. A study showed that males are more frequently affected with febrile seizures than females [6]. It's found that children with febrile seizures have a body temperature of at least 38 C [7].

The association between prematurity and the development of febrile seizures is correlated with the effect of intrauterine growth retardation which contributes to brain hypoxia or incomplete myelination of the brain and subsequently, there may be an increased risk for the development of FS [8]. The incidence of febrile seizures is inversely proportional to the birth weight or gestational age, regardless of the family history of febrile seizures [9].

A positive family history of febrile seizures can be elicited in 25–40% of patients with febrile seizures [4]. Recently, the disorder is thought to be inherited and multiple single genes that cause the disorder have been identified in some families. Although, in most cases the disorder appears to be polygenic, the genes predisposing to febrile seizures remain to be identified [4,10].

The study done in western Washington showed cigarette smoking of the mothers has direct effect on inducing febrile seizures [11].

Iron deficiency and iron deficiency anemia were postulated to be associated with febrile seizures [12].

There's no single investigation required for diagnosis of febrile seizure, but we do investigations to know the cause of the fever [2,4].

Meningitis should be considered in the differential diagnosis, and a lumbar puncture should be performed for all infants younger than 6 months of age who present with fever and convulsion , or if the child is ill appearing or at any age if there are clinical signs or symptoms suspecting a possible meningitis [13]. A lumbar puncture is an option in a child 6-12 months of age who is deficient in Hemophilus influenza type b and Streptococcus pneumonae immunizations or for whom immunization status is unknown [13,14] .

Electroencephalogram (EEG) is not indicated in a neurologically healthy child with a first simple febrile seizures [2].

If an EEG is done, it should be performed for at least 20 min in a wakefulness and in sleep (according to international guidelines) to avoid misinterpretation and errors. At times, if the patient does not recover immediately from a seizures, then an EEG can help distinguish between ongoing seizures activity and a prolonged postictal period . EEG can also be helpful in patients who present with febrile status epilepticus, because the presence of focal slowing present on the EEG obtained within 72 hours of the status has been shown to be highly associated with MRI evidence of

acute hippocampal injury [15].

A CT or MRI of the brain individualized. This can include an EEG and neuroimaging, particularly if the child is neurologically abnormal child [16].

Approximately 11% of children with febrile status epilepticus are reported to have (usually) acute unilateral swelling of their hippocampus, which is followed by a subsequent long-term hippocampal atrophy [17]. In general, the treatment with antiepileptic therapy is not recommended for children with one or more simple febrile seizures.. If the seizures lasts for longer than 5 min, acute treatment with diazepam, lorazepam, or midazolam is needed . Rectal diazepam is often prescribed to be given at the time of reoccurrence of a febrile seizures lasting longer than 5 min. Alternatively, buccal or intranasal midazolam may be used and is often preferred by parents. Intravenous benzodiazepines, phenobarbital, phenytoin, or valproate may be needed in the case of febrile status epilepticus . If the parents are very anxious concerning their child's seizures, intermittent oral diazepam (0.33 mg/kg every 8 hours during fever) or intermittent rectal diazepam (0.5 mg/kg administered as a rectal suppository every 8 hours), can be given during febrile illnesses. Intermittent oral nitrazepam, clobazam, and clonazepam (0.1mg/kg/day) have also been used. Such therapies help reduce, but do not eliminate, the risks of recurrence of febrile seizures [2].

Antipyretics can decrease the discomfort of the child but do not reduce the risk of having a recurrent febrile seizures, probably because the seizures often occurs as the temperature is rising or falling [17] .

Febrile seizures recur in approximately 30% of those experiencing a first episode, in 50% after 2 or more episodes, and in 50% of infants younger than 1 year old at febrile seizures onset [2,4].

Although approximately 15% of children with epilepsy have febrile seizures, only 2-7% of children who experience febrile seizures proceed to develop epilepsy later in life [4, 17].

Incidence of Epilepsy after a febrile seizures is in this way : Simple febrile seizure 1% ,recurrent febrile seizures 4%, complex febrile seizures (more than 15 min duration or recurrent within 24 hr.) 6%,duration of fever <1 hour before febrile seizures 11%, family history of epilepsy 18% , complex febrile seizures (focal) 29% and neurodevelopmental abnormalities [2]

Aim of the study :To determine the risk factors for the development of first simple febrile seizures among children in sulaymani governorate . To identify the most common causes of fever which precipitated febrile seizures.

PATIENTS AND METHODS

A prospective case- control study was conducted at Dr. Jamal Ahmad Rashid Pediatric Teaching Hospital, in sulaymani governorate ,during the period from first of April to the first of December 2019 .

The main source of data were obtained directly from parents/ relative of the enrolled children by questionnaire method and oral consent were taken from the parents.

Hundred cases diagnosed to have first attack of simple febrile seizures who were admitted to the emergency department included in the study. Another 100 children with fever but no seizures and they were sex and age matched were selected as controls. The age of both groups (cases & controls) ranged from 6 -60 months. Both groups underwent full history,

physical examinations and indicated investigations.

Cases with first attack of febrile seizures had fever ≥38^{o} C (100.4F) and another 100 control cases who were had fever ≥38^{o} C (100.4F) with no seizures , in infants and children, aged from 6 months to 60 months old Cases were diagnosed as febrile convulsion depending mainly upon the consideration of their clinical features as well as the judgment of the specialist . Twenty cases were required LP ,on assumption of possible meningitis, and all revealed normal CSF finding . Cases with proved meningitis , epilepsy , or complex febrile seizures were excluded from the study.The exclusion criteria of the cases and control group were:

Children with central nervous system infection, children with previous afebrile seizures. Previous medical history of epilepsy, Organic causes of seizures, Metabolic diseases. And age less than 6 months and older than 60 months.

The data of cases and controls were obtained by questionnaire method including :

Questions related to the children: These include, gender,age ,residences, degree of body temperature at time of admission corrected (axillary- temperature),

underlying illness associated with the fever, maturity at time of birth as well as weight at birth, neonatal history and type of feeding pattern during the first 6 months of life.

Questions related to the mothers during pregnancy were history of parental smoking during pregnancy, ante-natal events ; (hypertension, diabetes mellitus,vaginal bleeding or any significant infection) as well as the mode of delivery.

Questions related to the family history of febrile seizures and epilepsy were asked. Investigations were done for both cases with first simple febrile seizures and controls were hemoglobin level (HB) as a screening test for anemia ; Random blood sugar (RBS) ; Serum electrolytes as (sodium & potassium).

STATISTICAL ANALYSIS

To measure the strength of association of the risk factors for first attacks of simple febrile seizures , comparison between cases and controls was performed using odd ratio calculation and 95% CI (confidence interval)to measure the statistical significance, Chi-squire test; four fold table; (2 X2) with one degree freedom(Pearson) .P- Value is considered significant if < 0.05. All statistical analysis were performed using IBM SPSS statistics for window , version 23(IBM Corp, Armond ,N.Y., USA).

RESULTS

In table (1) , there was largest number of cases(56%) aged beteen 6-24 months old,80% of them were from urban areas and only 3% of their mothers had hypertention during pregnancy.

Table 1. Distribution of cases and controls according to the age groups, Geographical distribution &maternal complication during pregnancy.

Age	Cases(N)	Controls(N)
-(6-24 months)	56 (56%)	64(64%)
-(25-60) months	44(44%)	36(36%)
-Mean (SD)	27.1(±7)	22.1(±5)
Geographical distribution. Rural	20(20%)	10(10%)
-Urban	80(80%)	90(90%)
Complicated pregnancy.		
-Diabetes mellitus.		
-Antepartum	2(2%)	4(4%)
hemorrhage.	2(2%)	1(1%)
–Hypertension	3(3%)	2(2%)

N= number, SD= standard deviation.

Table 2. Comparison between cases with febrile seizures and controls regarding possible risk factors and their statistical significance.

Risk factors	Cases(n.)	Controls(n.)	Odded Ratio	95%CI	p.value
N.V.D	20	36			
C.S.	80	64	2.2500	1.1890-4.2579	<0.05
Prematurity	14	4	3.9070	1.238-12.3228	<0.05
Full term	86	96	6.76.92	2.12387-12.3228	
Low birth weight	10	2	5.444	1.1614-25.5219	<0.05
Breast feeding in first 6 months	36	62			
Bottle feeding	64	38	0.345	1.6334-5.151	<0.001
Paternal smoking	49	25	2.88.24	1.5837-5.2459	<0.001
Family history of febrile seizure	36	2	27.5625	6.4117-118.4854	<0.0001
Family history of epilepsy	6	2	3.12.77	0.6158-15.8861	0.1691
Hemoglobin <11gm/d	30	20	1.7143	0.8949-3.2851	0.1043
Body temperature 38-39C	60	53	0.7857	0.461-13387	0.375
Body temperature>39	40	44	0.848	0.483-1.488	0.573
Age<12 months	24	30	0.7368	0.3935-1.379	0.3400
Sex Male	32	34			
Female	68	66	0.921	0.526-1.61.35	0.7752

NVD ;normal vaginal delivery, C.S; cesarean section.

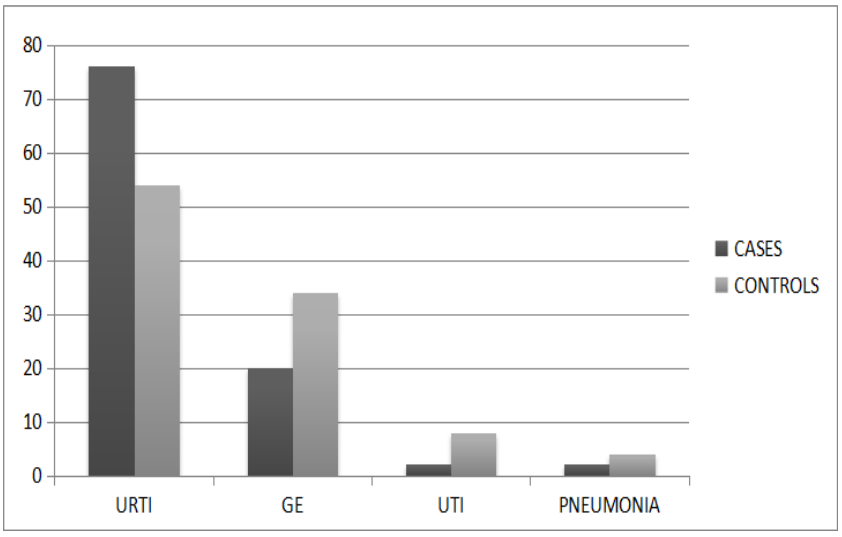

Figure 1. Showing the distribution of cases and controls regarding the underlying causes of fever.

URTI = upper respiratory tract infection, GE = gastroenteritis, UTI = urinary tract infection

DISCUSSION

This study determines the risk factors that contribute to the development of the first simple febrile seizures. On reviewing the reports of previous researches studies, mostly they touched the risk factors for the recurrence of febrile seizures in general and few researches about first simple febrile seizures.

Our study found that bottle feeding has a significant association with the development of first simple febrile seizures, while breast feeding had a protective role. Mitsudi N., et al. in their study reported a similar finding [18]. The importance of breast feeding work as a protective from occurrence of first simple febrile seizures by reducing the occurrence of upper respiratory tract infection which is the most common cause for first attack of febrile seizures [18,19].

A study conducted by Sharawat I.k. et al ,found that significant associations were noted between the family history of febrile seizures, the low serum sodium level, similar to our study outcome. On the contrary of our study, they considered that the male gender, the hypochromic microcytic anemia, and the peak body temperature, are possible risk factors for the development of first simple attack of febrile seizures [20].

It thought that the fever increases the metabolism of the brain, and in addition, the negative effects of anemia on the brain has more impacts that consequently causes febrile seizures. Therefore, it might be possible to reduce the risk of febrile seizures through prevention and treatment of anemia while our study displayed no significant association between the level of hemoglobin(as a screening test for anemia) and the occurrence of febrile seizures. A study performed about the role of anemia in first simple febrile seizures by Heydarian F. et al, concluded that anemia has similar finding like our finding [21].

Another research also reported by Heydarian F.et al; concerning the update for risk factors for first febrile seizures ; they concluded that caesarian section

family history of febrile seizures, and upper respiratory tract infection appeared to be possible risk factors [22], like our outcome findings.

In our study we couldn't find the effect of mothers smoking on children with febrile seizures because it was not a usual habit in our community,but paternal smoking studied and found that it has a significant effect,it was similar to a study done by Majeed Mohammed Z.et al [23].

According to the age, the present study revealed that majority of cases were age group between 6 - 24 months; (56%of patients with febrile seizures) , and have significant association with FS . this result is compatible with study done in by Meri Aliabad et al that found the majority of cases of febrile seizures occurred during the second year of life (13 to <25 months), with the peak age at 18 months [24] .

Our study found that (68%) of patients with febrile seizures were males and (42%) were females, and when compared with the controls, no significant association was noted . Preponderance of males was clarified in the study performed by Pathan HG et al., who studied (83) cases and found (62.35%) were males and (37.35%) females[25]. There was no satisfactory explanation for this sex predominance, but a study was done in Finland attributed that finding to the earlier maturation of female's brain [26].

In our study we found that the mode of delivery is not a significant risk factor for the development of febrile seizures , most of our women delivere their babies by caesarian section , using formula feeding ,

The study revealed that low birth weight, prematurity, bottle feeding, family history of febrile seizures, paternal smoking have an association with the emergence of the first simple febrile seizures attacks as show statistical significance were P value <0.05 , while no significant association were noted with the gender, the degree of body temperature or anemia , as there is no statistical significance P value > 0.05. It wes similar to a study conducted by . Yousif A. , Hafez L. , Benkhail F et al, found that the most frequent significant risk factors for febrile convulsion were bottle feeding, prematurity, and a positive family history of FS [27].

CONCLUSIONS

The following conclusions were obtained from our study:

1- Upper respiratory tract infection constituted a major cause of fever among cases of febrile seizures.

2-The following factors were emerged as a risk factors for development of febrile seizures among study Samples: Bottle feeding, prematurity and low birth weight , caesarian section, parental smoking , as well

as family history of febrile seizures.

Recommendations

*Improve the awareness of parents with a positive family history of FS.

* Encourage breast feeding especially in first year of life , as a protective from occurrence of FS in the future.

* Avoid smoking especially during the risk period of getting febrile seizures inside the

houses.

* Good antenatal care with close observation of mother during pregnancy to

prevent prematurity , low birth weight and encouraging normal vaginal delivery.

*Febrile seizures are benign conditions,not rising chance of epilepsy in the future too

much.

*Dowing further studies on this problem with larger samples and with more updatingSimilar studies

REFERENCES

1.Kantamalee w, Katanyuwong k, Louthrenoo O. Clinical characteristics of febrile convulsion and riskfactors of its recurrence in Ching Mai University Hospital.Neurology Asia; 2017;22(3):203-208.

2. Graves, RC; Oehler, K & Tingle, LE"Febrile seizures: risks, evaluation, andprognosis". American Family Physician;2012; 85 (2): 149–153.

3. Sajun Chung MD. Febrile Seizures. Korean Journal of Pediatrics. 2014; 9

(57): 384–395.

4. American Academy of pediatrics: Clinical practice guideline for long-term management of the child with simple febrile seizures, Pediatrics;2008; 121:1281-1286.

5. Jensen FE, Sanchez RM. Why does the developing brain demonstrate heightened susceptibility to febrile and other provoked seizures. In: Baram TZ,Shinnar S, eds. Febrile seizures. San Diego: Academic Press; 2002:153– 168.

6. Ashrafzade T., Hashemzadeh A. , Malek Acute otitis media in children with Febrile Convulsion .Iran J Otorhinlogy go .2002;16(35) :33-39.

7. Moyer VA.Offrngia M. Evidence based management of seizure. associated with fever.BMJ,2002,323(7321):1111-1114.

8. Al-Eissa YA.Febrile seizure :rate and risk factors of febrile seizure journal child Neural ;1998;10(4)315-319.

9. Olsen AW. Prenatal and maternal complication related to preterm delivery .AMJ Obs Gynecol ; 2003;189(1):222-227.

10. Singh R, Scheffer IE, Crossland K.. Generalized epilepsy with febrile seizures plus: a common childhood-onset genetic epilepsy syndrome. 1999;45:75–81.

11..Law K ,Smoking during pregnancy and newborn .neurobehavioral Pediatric; 2003,111(6),p1318-1323.

12.Ullrich C, Wu A,Armsby C,et al. Screenings healthy infants for iron deficiency using reticulocyte hemoglobin content .JAMA ;2005;294(8)8:224-930.

13.Kneen R, Solomon T, Appleton RE. The role of lumbar puncture in suspected CNS infection-a disappearing skill? Arch Dis Child;2002;87:181–3

14.American Academy of Pediatrics: Clinical practice guideline—febrile seizures: guideline for the neurological diagnostic evaluation of the child with a simple febrile seizure, Pediatrics;2011, 127:389.

15.Nordli DR Jr, Moshé SL, Shinnar S, et al:Acute EEG findings in children with febrile status epilepticus: results of the FEBSTAT study, Neurology ;2012;,79(22):2180–2186.

16. Shinnar S, Bello JA, Chan S, et al: MRI abnormalities following febrile status epilepticus in children: the FEBSTAT study, Neurology;2012; 79(9):871–877. 17. Strengell T, Uhari M, Tarkka R, et al: Antipyretic agents for

17.preventing recurrences of febrile seizures, Arch Pediatr Adolesc Med ; 2009; 163:799–804.

18.Mitsuda N., Hosokawa T., Eitoku M.,Fujieda M., Suganuma N.; Breast feeding and risk of febrile seizure in infants; The Japan Environment and children study ; Brain and development,2019;41(10);839- 847.

19.Taha AY, Jeffrey MA , Taha NM , Bala S , Burnaham WM. Acute administration of decosahexaenoic acid increase resistance to pentylentetrazole induced seizures in rats Epilepsy Behave , 2010 ;17:336-343.

20.Sharawat I. K. , Singh J., Dawman L.(Evaluation of risk Factors associated with first episode febrile seizure) Journal of Clinical and Diagnostic Research; 2016; 10(5): 10-13

21.Heydarian F.,Vatankhab H.; The role of anemia in first simple febrile seizure in children aged 6 months to 5 years old; neurosciences;2012;17(3); 226-229.

22.Heydarian F., Bakhtiari E., Yousefi S., et al: The first febrile seizure: An updated study for clinical fisk Factors, Iran J Pediatric;2018; 28(6):69761.

23.Majeed M.,Mohammad Z.: Risk factors of febrile convulsion among children under 5 years, IJDR ;2018; 8(10):23471-23476.

24.Miri Aliabad G, Khajeh A, Fayyazi A, et al. Clinical, epidemiological and laboratory characteristics of patients with febrile convulsion. J Compr Ped ;2013; 4(3):134-7.

25. Pathan HG et al. Int J Contemp Pediatr ;2017;4(6):2093-2097.

26.Yousif A.,Hafez L. , Benkhail F et al. Risk factors of febrile seizure in Benghazi ,Libya : acase –control study , Alexandria Journal of pediatric ; 2017; 20(2): 68-73.