Original Research Article

Clinical study of risk factors for febrile seizures at a tertiary health center

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Abstract

Background: Febrile seizures is a common benign condition, affecting children below 5 years, which exists only in association with an elevated temperature. Most widely accepted definition of febrile seizure is seizures that occur in febrile children between the ages of 6 and 60 months who do not have an intracranial infection, metabolic disturbance, or history of afebrile seizures. Study of risk factors at local level can help to formulate strategy for prevention, early identification and treatment of patients. Present prospective study was done to study association of various risk factors for febrile seizures in childhood, in paediatric patients admitted at our tertiary health center. **Material and Methods:** Present study was a prospective, observational, institution-based study, conducted in children with history of febrile seizures. 6 months- 5 years age, attended paediatric emergency unit/inpatient wards, parents/caregiver willing for participation. **Results:** During study period, 80 children with febrile seizure fulfilling inclusion criteria were evaluated. Out of 80 children with febrile seizure 44 (55%) were boys and 36 (55%) were girls. We observed boys: girls ratio as 1.2:1. Median age of onset of febrile seizure was 18 months with IQ range of 10-24 months. Febrile seizure is more common among children residing in rural area (61.2%) compared to the urban residence (38.8%). Mean temperature at presentation in present study was 100.51 ± 0.693^0F. 21.3% cases had recurrent febrile seizures in present study. **Conclusion:** The commonest risk factor associated with febrile convulsion in this study were nonexclusive maternal breast feeding, family history of febrile seizure, maternal alcohol consumption and rural residence. Febrile seizures are multifactorial in origin, still can be prevented by strong supervision of children with positive family history, excusive breast feeding for 6 months and avoidance of alcohol consumption during pregnancy.

Key Words: febrile seizure, risk factors, bottle feeding, family history of febrile seizure.

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INTRODUCTION

Febrile seizures is a common benign condition, affecting children below 5 years, which exists only in association with an elevated temperature. Most widely accepted definition of febrile seizure is seizures that occur in febrile children between the ages of 6 and 60 months who do not have an intracranial infection, metabolic disturbance, or history of afebrile seizures.[1] Febrile seizures are of multifactorial origin and different factors associated with its occurrences. Various proposed risk factors for febrile seizures are male sex; family history of febrile seizures; a body temperature of 38°C or higher; underlying cause of fever; antenatal complications; low serum calcium (Ca), sodium (Na), and blood sugar; microcytic hypochromic anaemia, maternal smoking and alcohol consumption during pregnancy. [2] Incidence of febrile seizures is approximately 2-5% in neurologically healthy infant and children but the incidence is as high as 15% in some population.[3] There are two types of febrile seizures: the simple and complex types. While the majority of febrile seizures are simple (70-75%), 9-35% of them are complex.[4] A positive family history for febrile seizures can be elicited

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in 25-40% of patients with febrile seizures. The febrile seizure has a tendency to recur. The overall recurrence rate is 30%. Predictors of recurrence include: complex seizures, positive family history, onset at less 12 months and temperature <40° C at time of seizure.[4,5] Febrile seizures patients are commonly seen in OPD's and IPD's. Study of risk factors at local level can help to formulate strategy for prevention, early identification and treatment of patients. Present prospective study was done to study association of various risk factors for febrile seizures in childhood, in paediatric patients admitted at our tertiary health center.

MATERIAL AND METHODS

Present study was a prospective, observational , institution-based study, conducted in children with history of febrile seizures. Study was conducted in Department of Pediatrics and Adolescent Medicine, BPKIHS from February 20XX-January 20XX (1 year). Ethical committee permission to conduct study was obtained from the Institutional Ethical Review Board (IERB) of B.P. Koirala institute of health sciences, Dharan.

Inclusion criteria

- Child with h/o Febrile seizure , 6 months- 5 years age, attended paediatric emergency unit/inpatient wards, parents/caregiver willing for participation.

Exclusion criteria

- Child with history of epilepsy or afebrile seizure, acute symptomatic seizures apparently proven to be due to CNS insult (for e.g. meningitis or CNS infection) other than febrile seizure
- Seizures due to focal neurological deficit
- Seizures associated with major congenital malformations, developmental delay or genetic abnormality
- Parents not willing for participation.

A written informed consent was taken from parents/caregiver for participation in present study. History was taken from parents/caregiver. A complete description of episode of seizure, any recurrence was taken. Details such as age, gender, nature of illness, maternal history of smoking/alcohol consumption/use of recreational drugs, obstetric factors like gestational age at delivery/prolonged labor/mode of delivery, birth weight, feeding practices such as exclusive MBF, top up feed, bottle feed family history, duration and level of fever, birth weight and immunization status was collected. Clinical examination, anthropometric measurements, head to toe examination, neurologic assessment and developmental assessment was carried in detail. Laboratory investigations for fever were sent. Serum sodium was done in all patients and serum iron in patients with anaemia. In cases where lumber puncture was done. CSF samples were sent in 2 vials with 8 drops in each for CSF routine examination, CSF biochemistry and CSF culture sensitivity. All details were collected in a proforma and entered Microsoft excel sheet. Statistical analysis analysed with software SPSS version 20. Statistical analysis was done using descriptive statistics. For comparing categorical variable among groups Chi square test and fisher's exact test were used. A p value of <0.05 was considered significant.

RESULTS

During study period, 80 children with febrile seizure fulfilling inclusion criteria were evaluated. Out of 80 children with febrile seizure 44 (55%) were boys and 36 (55%) were girls. We observed boys: girls' ratio as 1.2:1. Minimum age of presentation was 6 month and maximum age of presentation was 60 month with median age of presentation was less than 18 months (63%). Median age of onset of febrile seizure was 18 months with IQ range of 10-24 months. Febrile seizure is more common among children residing in rural area (61.2%) compared to the urban residence (38.8%).

Table 1: Age distribution

Age of onset	No. of patients	Percentage
Age < 18 months	50	63%
Age > 18 months	30	38%

Mean temperature at presentation in present study was 100.51 ± 0.693^{0}F. Level of temperature at seizure onset was 102.54±0.841^0 F. Median gap between onset of fever and onset of seizure was 12 hours. Most of the cases of febrile seizure (46.3 %) occurred at a temperature ≥102^{0}F (38.9^{0}C).

Table 2: Fever characteristics among febrile seizure

Temperature at presentation	Mean ± SD - 100.51±0.693^{0}F Range=100-102^{0}F
Level of temperature at seizure onset	Mean ± SD=102.54±0.841^0 F Range=101-101^{0}F
Gap between onset of fever and onset of seizure	Median=12 hours IQ=6-20 hours Range=1-72 hours

Most of the febrile seizure occurred within 24 hours of the onset of fever with 57.5% of cases occurring within 12 hours of

fever onset.

Table 3: Distribution of duration of seizure onset after fever

Duration	No. of patients	Percentage
<12 hours	46	57.5
12-24 hours	22	27.5
>24 hours	12	15
Total	**80**	**100.0**

21.3% cases had recurrent febrile seizures in present study.

Table 4: Type of febrile seizure.

Seizure	No. of patients	Percentage
First	63	79
Recurrent	17	21

Of total cases one cases each were exposed to maternal smoking in-utero and drugs in form of oral and intravenous antibiotics and 19 cases had exposure to maternal alcohol in utero.

Table 5: Antenatal exposure to risk factors among cases and control

Risk factors	No. of patients	Percentage
smoking	1	1.3 %
alcohol	19	23.8 %
Drugs, (intravenous/oral) antibiotics	1	1.3 %

In present study, most common cause of fever among febrile seizures was upper respiratory tract infection (66%) followed by viral exanthematous fever (13%) and urinary tract infection (13%).

Table 6: Causes of fever in febrile seizure cases

Cause of fever	No. of patients	Percentage
Upper respiratory tract infection (URTI)	53	66%
Viral exanthematous fever	10	13%
Urinary tract infection (UTI)	10	13%
Acute gastroenteritis (AGE)	4	5%
Pneumonia	3	4%

Gestational age at delivery was 38.93 ± 1.73. Average birth weight was 2.77 ± 0.44 kg. 46% children had not received exclusive breast feeding during first six months.

Table 7: Obstetric factors and breastfeeding

Birth history	No. of patients	Percentage
Place of delivery		
Home delivery	42	53%
Hospital delivery	38	48%
Prolonged labor	5	6%
Instrumental delivery	7	9%
Gestational age (mean ± SD)	38.93 ± 1.73 weeks	
Birth weight (mean ± SD)	2.77 ± 0.44 kg	
Breast Feeding		
Exclusively breast fed	48	60%
Bottle-fed babies	32	40%

Family history of febrile convulsion in first degree relative was 14%.

Table 8: Family history of febrile convulsion and epilepsy

Past history	No. of patients	Percentage
Family history of febrile seizure in first degree relative	11	14%
Family history of febrile seizure in second degree relative	1	1%
Family history of epilepsy in second degree relative	1	1%
Family history of epilepsy in third degree relative	2	3%

Among febrile seizure patients 20 cases (25%) had moderate wasting and 3 case (3.8%) had severe wasting and stunting.

Table 9: Nutritional status distribution among cases

Nutritional status	No. of patients	Percentage
Normal	57	71%
moderate wasting	20	25%
severe wasting and stunting	3	4%

Mean hemoglobin in case group was 10.9±1.19 g/dl. 61cases (76.25%) were anemic out of which 46 cases (75.4%) had simple febrile seizure and 15 cases (24.6%) had complex febrile seizure.

Table 10: Anemia among febrile seizure patients

	anemia (n=61)	No anemia (n=19)
Simple febrile seizure	46 (75%)	12 (63%)
complex febrile seizure	15 (25%)	7 (37%)
Total (n=80)	61 (76%)	19 (24%)

Rural residence (61.30%), home delivery (52.50%), bottle feeding (40%), maternal alcohol consumption (23.80%) and family history of febrile seizure (15%) were most common risk factors associated with febrile seizures in present study.

Table 11: Common risk factor among children with febrile seizure

Risk factor	No. of patients	Percentage
Residential setting (rural)	49	61.30%
Home delivery	42	52.50%
Bottle feed	32	40%
Maternal alcohol	19	23.80%
Family history of febrile seizure	12	15%

We compared risk factors among simple febrile seizure and complex febrile seizure group . Level of temperature at seizure, maternal smoking, family H/O febrile seizure, gestational age(weeks), anemia, malnutrition, birth weight(Kg) were significant risk factors among complex febrile seizure patients as compared to simple febrile seizure patients.

Table 12: Comparison of risk factors among simple febrile seizure and complex febrile seizure group

Risk factor	Simple febrile seizure (n=58)	complex febrile seizure (n=22)	P value
Hemoglobin	10.80±1.09	11.17±1.42	0.135
Level of temperature at seizure	102.52±0.80	102.59±0.959	0.19
Maternal smoking	0%(n=0)	4.5%(n=1)	0.275
Family H/O febrile seizure	1.7%(n=1)	0%(n=0)	0.306
Gestational age(weeks)	38.98±1.331	38.77±2.544	0.336
Anemia	79.31%(n=46)	68.18%(n=15)	0.379
malnutrition	22.41%(n=13)	31.8%(n=7)	0.399
Birth weight(Kg)	2.77±0.425	2.78±0.502	0.461
Prolonged labour	5.17%(n=3)	9%(n=2)	0.612
Family history of epilepsy	3.4%(n=2)	4.5%(n=1)	0.641
Temperature	100.52±0.682	100.50±0.740	0.75
non immunized	8.6%(n=5)	9%(n=2)	0.786
Age of onset <18months	63.8%(n=37)	59.1%(n=13)	0.797
Maternal alcohol	24.13%(n=14)	22.72%(n=5)	1
Maternal drug	1.7%(n=1)	0%(n=0)	1
Exclusive MBF	56.89%(n=33)	54.54%(n=12)	1
Bottle feed	39.65%(n=23)	40.9%(n=9)	1

DISCUSSION

Febrile seizures are not associated with problem behavior or executive functioning in preschool children, but the results suggest that children with recurrent febrile seizures might be at risk for delayed language development.[6] Increased incidence was noted in children from rural area. Higher incidence of infections in rural setting due to poor hygiene and living conditions, low Socioeconomic status and lack of knowledge regarding febrile seizure in rural population of Nepal may be the contributing factors.[7] The simple type is characterized by a single episode of generalized tonic-clonic seizure lasting less than 15 min within 24 hrs. of onset of fever. A complex febrile seizure is more prolonged (>15 min), is focal, and/or recurs within

24 hr. Febrile status epilepticus is a febrile seizure lasting >30 min. Present study showed incidence of simple febrile seizure as 72.5%, complex febrile seizure as 27.5% and febrile status as 2.55%. Leung *et al.* in their study found simple febrile seizure in 85%.[8] In present study we noted that febrile seizure increases with temperature level and most febrile seizure (46.3 %) occurred at a temperature ≥102^{0}F (38.9^{0}C). Mahyar *et al.* in Iranian hospital-based study found that the mean temperature at seizure onset was 38.9±0.37^{0}C.[9] Sadlier *et al.* mentioned that the temperature of at least 380C is required for seizure onset.[10] Elevating brain temperature in itself alters many neuronal functions, including several temperature-sensitive ion channels and causes seizures.[11] We noted that the median duration of seizure onset after fever was 12 hours with Inter Quartile range of 6-20 hours. Mukherjee *et al.* mentioned that the incidence of febrile seizure occurring within 1hr of fever onset is 21% between 1- 24 hrs. is 57% and after 24 hrs in 22%.[12] Shrestha *et al.*[7] in a retrospective hospital-based study found majority of children developed seizure within 24 hours of onset of fever with mean of 9.3 (±7.4). In present study recurrent episode of febrile convulsion was found in 21.3%. Offringa *et al.* stated thirty per cent of children have recurrent febrile seizures during subsequent illnesses.[13] Knudsen *et al.* pointed out approximately 30% to 40% of children who experience a febrile seizure will have a recurrence, but less than 10% will have three or more recurrences.[14] Talebian *et al.* found recurrences in twelve children (24%) out of the fifty.[15] Risk factor for recurrence for febrile seizure are Age <1 yr., Duration of fever <24 hrs., Day care, Male gender, Lower serum sodium. Having no risk factors carries a recurrence risk of about 12%; 1 risk factor, 25-50%; 2 risk factors, 50-59%; 3 or more, 73-100%.[16] In this study the important causes of fever are Upper respiratory tract infection, viral exanthema, Urinary tract infection, acute gastroenteritis and pneumonia. Berg *et al.* found Nonspecific cause in 26%,otitis media in 65% gastroenteritis in 9% invasive bacterial infection in 6%.[17] Rantala *et al.* found URTI in 67%, gastroenteritis in 10%,otitis media in 7%, exanthema subitum in 9%.[18] In Iranian hospital-based study found upper respiratory tract infections 53.8%,gastroenteritis in 24.4%, acute otitis media in 9%, urinary tract infection in 6.4%, and pneumonia in 3.8%.[9] The cause of fever varies among different geographical location depending upon prevalence, disease pattern and hospital presentations of different diseases. Viral infections were presumed in majority of these children with upper respiratory tract infection based on clinical features and the course of illness. Viral URTI is the most common cause of febrile seizure. HHV 6 and HHV 7 are most commonly implicated viral cause of febrile seizure.[19,20] In present study 23% children with febrile seizures had history of maternal alcohol ingestion. Ingestion of alcohol during pregnancy has also been reported to have two-fold risk of developing febrile seizures with a strong dose-response relationship.[21] The hypothesis behind alcohol as a risk factor for febrile seizure is supported by low to moderate average alcohol intake may affect fetal brain development, especially if large volumes are consumed on single occasions and high peak blood concentrations are reached.[22] Khet *et al.* found an indirect correlation between in incidence of febrile convulsion and length of breast- feeding.[23] Akhodian *et al.* suggested that exclusive breast-feeding in the first 6 months of life does not have a significant effect on febrile seizure, but it may protect children from complex febrile seizure which is a predisposing factor for epilepsy.[24] Greenwood *et al.* in a British cohort study found increase incidence of febrile convulsion in a non-breast fed group.[25] A positive family history for febrile seizures can be elicited in 5-25% of patients with febrile seizures.[13,17] In addition to the positive history in a first or second degree relative, monozygotic rather than in dizygotic twins, human herpes virus-6 infection[20], influenza viral infection[26] and iron deficiency anemia[27]. The febrile seizure gene have been mapped to chromosomes 2q23-34, 5q14-15, 6q22-24,8q13-21, 18p11.2, 19p13.3, and19q.[28] The risk of subsequent epilepsy is for Simple febrile seizure 1%, Neurodevelopmental abnormalities 33%,Focal complex febrile seizure 29%, Family history of epilepsy 18%,Fever <1 hr before febrile seizure 11%, Complex febrile seizure, any type 6%, and Recurrent febrile seizures 4%.[16] Level of temperature at seizure, maternal smoking, family H/O febrile seizure, gestational age(weeks), anemia, malnutrition, birth weight(Kg) were significant risk factors among complex febrile seizure patients as compared to simple febrile seizure patients. Nelson *et al.* in US cohort prenatal risk factor study mentioned that the risk of a complex seizure was approximately the same for the first as for each subsequent febrile seizure.[29] Rural residence (61.30%), home delivery (52.50%), bottle feeding (40%), maternal alcohol consumption (23.80%) and family history of febrile seizure (15%) were most common risk factors associated with febrile seizures in present study. Present study was observational, small sample size, hospital-based study. Large sample, comparative studies will be helpful to identify risk factors for febrile seizures.

CONCLUSION

The commonest risk factor associated with febrile convulsion in this study were nonexclusive maternal breast feeding, family history of febrile seizure, maternal alcohol consumption and rural residence. Febrile seizures are multifactorial in origin, still can be prevensted by strong supervision of children with positive family history,

excusive breast feeding for 6 months and avoidance of alcohol consumption during pregnancy.

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