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Study of demography risk factors of simple and complex febrile seizure and associated infection in children at tertiary care center

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Abstract

Introduction: Febrile seizures are seizures that occur in children between 6 to 60 months with a temperature of 38°C or higher. It commonly affects male with a peak incidence in below 2 years old. This study aims at identifying the demographic profile of children admitted with the diagnosis of febrile seizure in order to anticipate the condition and counsel the parents.

Method: This is a retrospective cross sectional study conducted in the pediatric ward of Patan Hospital. Medical records of the patients admitted with a diagnosis of febrile seizure (simple or complex) in pediatric ward of Patan Hospital between January 2016 to 2019 were reviewed and data mentioned in the proforma were collected. Ethical approval was taken from the Institutional Review Committee of Patan Academy of Health Sciences (IRC-PAHS). The data was analyzed using Statistical Packages for Social Sciences Version 25 and frequency and proportion was calculated.

Result: Out of 277 cases fulfilling the study criteria, 70.4% had simple febrile seizure whereas 29.6% had complex febrile seizure. The mean age of the patients was 23.13 months \pm 12.8 and the median was 19 months (IQR: 14-29). Around 58.12% were males and 41.88% females. Viral fever accounted for the maximum number of infections in around 22.3% (62/277) of patients and viral URTI in 20.21%(56/277).

Conclusion: The study adds to the existing knowledge of febrile seizure in order to help the clinician anticipate febrile seizure.

Keywords: febrile seizure, fever seasonal variation

Introduction

Febrile seizures are seizures occurring in children between age group of 6 -60 months with a temperature of 38°C or higher in a healthy child.¹ With a prevalence of 2-5% according to the American and European studies, they are the most common seizure disorder in children.² In Nepal, febrile seizure was seen in 4.6% of the admitted children.³ Peak incidence is found at the age of 18 months, is commoner in males and those with family history of febrile seizures.⁴ Globally respiratory viral infection is most commonly seen in cases of febrile seizure.¹ Respiratory tract infection is the commonest cause followed by gastroenteritis in Nepalese children.⁵ Although benign, with rare instances of a long term sequale, they pose a significant apprehension and anxiety to the parents.⁶ Febrile seizure tend to recur in 30–50% of children following the first febrile seizure. They are seen to occur with two seasonal peaks, November to January and June to August, which correspond to peaks of viral upper respiratory infections and gastrointestinal infections respectively.⁷

This study aims at identifying the demographic profile of children admitted in our center with the diagnosis of febrile seizure in order to anticipate the condition, manage them and counsel the parents accordingly. The objective is to determine the frequency of risk factors- history of febrile seizures, epilepsy in family, past history of febrile seizures, birth weight. The study will also determine the infection commonly associated with febrile seizures.

Method

This is a retrospective cross sectional study conducted in the pediatric ward of Patan Hospital. Medical records of the patients admitted with a diagnosis of febrile seizure (simple or complex) in pediatric ward of Patan Hospital between January 2016 to Jan 2019 were reviewed. Data mentioned in the proforma: age, sex, month of admission,

timing of the first seizure, past history of febrile seizure, family history of febrile seizure and epilepsy along with the birth weight were collected. Ethical approval was taken from the Institutional Review Committee of Patan Academy of Health Sciences (IRC-PAHS) (Ref: drs1905191250). Inclusion and exclusion criteria were designated according to the history and examination notes written by the attending doctor. All patients admitted with the diagnosis of febrile seizure (simple or complex) between the age of 6 months to 6 years were included in the study.

Patients with prior episodes of afebrile seizures, delayed developmental milestones and age below six months and above six years were excluded.

Febrile seizure were defined as seizures that occur between the age of 6 and 60 month with a temperature of 38°C or higher, that are not the result of central nervous system infection or any metabolic imbalance, and that occur in the absence of a history of prior afebrile seizures.^{1,4} Simple Febrile seizure was defined as a primary generalized, usually tonic-clonic, attack associated with fever, lasting for a maximum of 15 min, and not recurrent within a 24-hour period.^{1,4} Complex Febrile seizure was defined as more prolonged seizure (>15 min), which is focal, and/or recurs within 24 hr.⁴

All children admitted with the diagnosis of febrile seizure fulfilling the inclusion criteria were included in the study. In demography age, sex, and season of presentation were included. Similarly, in risk factors history of febrile seizure, epilepsy in family, past history of febrile seizure and past history of febrile seizure, birth weight were included. Infection that is commonly associated with febrile seizure was derived from the final diagnosis made by the attending physician.

Information was collected as in patient medical records to fill up the proforma as shown below. Sampling was done by convenience sampling method. After, the ethical approval was sought, hospital numbers

of all the patients diagnosed with febrile seizures were generated with the help of the pediatric admissions excel sheet maintained by the Pediatric Research unit. Medical records were retrieved from the recorded section and data from the patients which met the inclusion criteria was collected. This was then data entered in the proforma which later transferred to the excel sheet.

Data was analyzed using Statistical Package for Social Sciences (SPSS) Version 25. Descriptive statistics including frequency and percentage were calculated.

Result

During the study period, 286 patients were diagnosed to have febrile seizures. Nine (%)

patients were later excluded as they were diagnosed to have meningitis. A total of 277 patients who met the inclusion criteria were enrolled in the study. Among them 194(70.4%) had Simple febrile seizures here as 83(29.6%) had Complex febrile seizure The mean age of the patients was 23.1 months \pm 12.8 and the median was 19 months (IQR: 14-29), Table 1. Two records were excluded due to incomplete information regarding the month of admission.

We also determined the frequency of risk factors associated with febrile seizures. Out of the 269 records which had information about the family history, 13(4.83%) had a history of febrile seizures in the paternal side of the family and 3(1.12%) had a history in the maternal side, Table 2.

Table 1. Demographic and clinical characteristics of children presenting with febrile seizure

	Frequency	Percentage
Seizure (N=277)		
Simple	194	70.4
Complex	83	29.6
Demography of children admitted with febrile seizure		
Age (N=277)	Mean \pm SD: 23.13 \pm 12.8	Median: 19, Interquartile range: 14-29, Mode: 24
Sex (N=277)		
Male	161	58.12
Female	116	41.88
Season (N=275)		
Spring(March, April, May)	66	24
Summer (June, July, August)	73	26.55
Autumn (Sep, Oct, Nov)	75	27.27
Winter (Dec, Jan, Feb)	61	22.18

Table 2. Risk factors associated with febrile seizure in children

Risk factors associated with febrile seizure	Frequency	Percentage
Family history of febrile seizure (n=269)		
No	253	94.05
Paternal	13	4.83
Maternal	3	1.12
Family history of epilepsy (n=269)		
No	259	96.2
Yes	10	3.7
Low birth weight (n=182)		
No	155	85.16
Yes	27	14.84
Past history of febrile seizure (n=277)		
No	210	76
Yes	67	24.1

Table 3. Causes of Fever in patients with febrile seizure (N=277)

Commonly associated infection	Frequency	Percentage
Acute Tonsillitis	12	4.3
Acute suppurative otitis media	4	1.4
Bacterial upper respiratory tract infection(URTI)	12	4.3
Dysentery	19	6.8
Occult Bacteraemia	9	3.2
Pneumonia	52	18.7
Sepsis	5	1.8
Suspected enteric fever	2	0.7
Unidentified focus of fever	18	6.4
Urinary Tract Infection	18	6.4
Viral acute gastroenteritis	8	2.8
Viral fever	62	22.3
Viral upper respiratory tract infections	56	20.2

Table 4. Demographic variables and risk factors stratified in simple and complex febrile seizure groups

Independent Variables	Simple frequency (%)	Complex frequency (%)	Total
Sex			
Female	87 (75%)	29 (25%)	116
Male	107 (66.5%)	54 (33.5%)	161
Season			
Spring	45 (68.2%)	21 (31.8%)	66
Summer	52 (71.2%)	21 (28.8%)	73
Autumn	50 (66.7%)	25 (33.3%)	75
Winter	45 (73.8%)	16 (26.2%)	61
Time of the day			
06-12 (morning)	34 (59.6%)	23 (40.4%)	57
12-18 (afternoon)	51 (77.3%)	15 (22.7%)	66
18-00 (evening)	48 (80%)	12 (20%)	60
00-06 (night)	22 (56.4%)	17 (43.6%)	39
Family history of febrile seizure			
No	178 (70.4%)	75 (29.6%)	253
Paternal	10 (76.9%)	3 (23.1)	13
Maternal	1 (33.3%)	2 (66.7%)	3
Family H/O epilepsy			
No	177 (68.3%)	79 (30%)	259
Yes	6 (60%)	4 (40%)	10
Low birth weight (<2.5kg)			
No	114 (73.5%)	41 (26.5%)	155
Yes	16 (59.3%)	11 (40.7%)	27
Past history of febrile seizure			
No	163 (77.6%)	47 (22.3%)	210
Yes	40 (59.7%)	28 (41.8%)	67

The study also looked at the incidence of the common infections in children presenting with febrile seizures. A total of 259 infections were noted in 277 patients. In 18 (6.4%) of children, focus of infection was not identified. Viral infections were the most commonly encountered infections. Viral fever accounted

for the maximum number of infections in around 62 (22.3%) of patients and viral URTI in 56 (20.21%), Table 3.

In this study we also determined the demographic parameters like age, sex and seasonality in both the simple and complex febrile seizure groups.

Frequency of family history of seizures, epilepsy, past history of seizures and low birth weight was also categorized according to the type of seizure in Table 4. The frequencies of complex febrile seizures were more in males (33.5%) as compared to females (25%). Seasonal variation was not seen across both the simple and complex febrile seizure groups. Around 66(30%) episodes of seizures occurred in the afternoon out of which 51 (77.3%) were simple and 15 (22.7%) were complex febrile seizures.

Discussion

Our findings suggest that 70.4% children had simple febrile seizure whereas 29.6% had complex febrile seizures. This was similar to that seen in 151 Australian children where seizures were complex in 33% patients.⁸ A study conducted in 176 Polish children show that 94.89% of children developed simple febrile seizures and only 5.11% of children suffered complex ones

However, Winkler, et al., report complex febrile seizures in 71.4% of patients in a hospital based study of 197 children. This difference may be attributed to the ethnicity and genetic predisposition to seizures.¹⁰

Their findings are similar to a community based random cluster survey in Tanzania where the incidence of complex seizures was 65%. A large number of seizures in this group were more than 15 mins but were generalized and did not recur within a 24hour period, indicating possible overestimation of complex seizures.¹¹

In our study, most of the enrolled patients were males. Sharwat, et al., also report male gender to be significantly associated with a risk of a febrile seizure.¹² A retrospective cohort study of 75,593 Danish children with febrile seizures report 21% higher risk of seizures in boys as compared to girls.¹³ Majority of the studies have reported the median age of the first febrile seizure. In a case control study including 70 Indian children, the mean age of presentation was

24.9±16.1 months.¹² Although the mean age of presentation was less than 2 years in our study, our findings may not be truly comparable to these studies since we have included all seizures irrespective of recurrences.

A case control study done in 428 Indian children shows that iron deficiency, family history of febrile seizures and epilepsy in first degree relatives, day care attendance, and prematurity were found to be the independent risk factors for simple febrile seizures in children.¹⁴ We determined that family history of febrile seizures were present in 5.9% of patients and 3.7% had a history of epilepsy in the family. Our findings are comparable to a study done in western Nepal which reports 8.3 % of patients have had a family history of febrile seizure whereas a history of epilepsy in the family was found in 2.3%. However, Kumari, et al., report a positive family of history of febrile seizures in 30 %of patients%.¹⁴ Shankar P et al also report a family history in around 30% children.¹⁷ The difference in the incidences may be due to genetic predisposition in various populations. It can largely be affected by the lack of awareness about past seizures in the parents or any members of the family.

There was no seasonal variability in presentations to the hospital. This was similar to the findings reported by Pokhrel, et al.¹⁵ In a nationwide cohort study in Denmark, the onset of a first febrile seizure had a seasonal variability and cases were double in winter months as compared to summer but this variability was not noticed in the subsequent episodes of seizures.¹⁶

A study among 60 Indian children shows that majority presented in the monsoon season(June)and in the morning hours.¹⁷ In our study, maximum number of seizures occurred during the afternoon but the diurnal variation couldn't be commented. Melatonin (N-acetyl-5-methoxytryptamine),secreted mostly at night seems to possess some anticonvulsant effects and few studies suggest an association between melatonin and the occurrence of

febrile seizures).¹⁸ Mikkonen, et al., report children to experience their first febrile seizure mostly in the evenings and less frequently at nights.¹⁹ Similarly, a Japanese study reports, febrile seizures to occur five times more often in the evenings than in the mornings, peaking in incidence at 4 PM and reaching its lowest at 4 AM.²⁰

Around 15% of our children presenting with seizures had their birth weight less than 2.5kg. The risk of febrile seizures is substantially higher in children born premature and with a low birth weight compared to those born at full term with a normal birth weight. In a register-based cohort study of Danish children, incidence of a first febrile seizure increased with decreasing birth weight probably due to higher susceptibility to infective episodes.¹³

Out of the total evaluated for febrile seizures, 24.1% had a history of febrile seizures in the past. A 5-year data collected from the Korea National Health Insurance Review and Assessment Service reports an overall recurrence rate was 13.04% (13.81% for boys and 12.09% for girls).²¹ Febrile seizure is seen to recur in 30-50% of the children following the first episode and additional seizure increases the risk of further recurrence indicating that each episode lowers the risk for future seizures.¹

Viral Infections were the commonly encountered infections associated with febrile seizures but the causative pathogen was not determined in this study. Viral fever accounted for maximum number of cases followed by viral URTI. Our findings are similar to the study done in 4890 Nepali children where URTI is reported to be the most common etiology of fever.¹⁵ Common viral infections like Influenza A, B virus, Parainfluenza virus and Adenoviruses are more frequently associated with febrile seizures.¹ Similarly, a study in Chinese children also demonstrated Viral URTI as the most frequent causative agent for fever in febrile seizure.²² A study performed in Australian children reports that influenza, rhinovirus

and adenovirus were frequently detected in the nasopharynx of children with febrile seizures. Various factors like, coinfections with different viruses, increase susceptibility to respiratory viral infections and prolonged viral shedding may increase the risk of developing febrile seizures in children aged 6 months to 5 years.⁸

We have attempted to look at the frequency of commonly associated risk factors in a patient presenting with febrile seizures but determining the association is beyond the scope of this study. The data might not be a true representation of the febrile seizures nationwide, as a large number of children might not seek medical attention especially in brief episodes of seizure. Prospective studies involving the outpatient department or if feasible population based studies may be a better method to look at the true incidences in Nepali population.

Conclusion

Febrile seizures are more common in males especially below 2 years of age. Family history of seizures and epilepsy are common risk factors with Viral URTI being the commonest associated infection.

This study helps clinicians to identify the common risk factors in a child presenting with febrile seizures and helps in anticipating the condition and providing necessary counseling to the parents.

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Conflict of Interest

None

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None

Author Contribution

Concept, design, planning: DP, AN; Literature review: DP, AP, SS, BP; Data collection: DP,

AP; Data analysis: DP; Draft manuscript: DP, AN; Revision of draft: DP; Final manuscript: DP, AN, AP, SS, BP; Accountability of the work: DP, AN, AP, SS, BP

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