



Full Length Research Article

EPIDEMIOLOGICAL, CLINICAL AND LABORATORY FEATURES OF CHILDREN WITH FEBRILE SEIZURES

*Dr. Mabroka Alfoghi, Dr. Ismail Elghuwael and Dr. Amina Abograin

Department of Pediatric, Misurata Teaching Hospital, Misurata University, Faculty of Medicine,
Misurata Hospital, Libya

ARTICLE INFO

Article History:

Received 17th July, 2016
Received in revised form
25th August, 2016
Accepted 09th September, 2016
Published online 31st October, 2016

Key Words:

Febrile seizures,
Epidemiology,
Etiology,
Seasonal variation.

ABSTRACT

Objectives: With respect to the issue that febrile seizures (FS) is the most common seizure type in children, the purpose of this study was to determine the epidemiological, clinical and laboratory features of children admitted to Misurata Teaching Hospital with febrile seizures in 2015 – 2016 and its comparison with similar studies in other parts of the world.

Patients and Methods: Descriptive (Longitudinal hospital based) study where children were admitted to pediatric department in Misurata Teaching Hospital 6 months – 6 years of age presented with fever and seizure, from 1st June 2015 to 30th of May 2016 are included in the study, patient's data retrospectively collected based on information registered in hospital medical files including history, demographics, clinical examination and laboratory findings.

Result: During the study period, 292 children with FS were studied, The proportion among all admitted patients was 4%. The mean age of patients with FS was 21.69 ± 13.71 months, the highest frequency was seen in 6 to 18 months age group, which included 163 children (55.4%), Male to female ratio was 1.7:1, Two hundred ninety one (97.9%) children were presented with generalized seizures and 6 (2.1%) had focal seizures. Two hundred eight (71.2%) children had Simple Febrile Seizure, Seventy one children (24.3%) had Complex Febrile Seizure and Febrile Status Epilepticus in 13 (4.5%). The majority of patients 215 (73.6%) had an episode of FS early in the course of illness, The mean temperature of our patients was $38.9 \pm 0.70^\circ\text{C}$. Two hundred eighty two of children (96.6%) were born at term, only 10 (3.4 %) had less than 37 weeks of gestational age at birth, majority with average birth weight, with only 21 (7.2%) was below 2500 gm. at birth. Ninety (30.8%) of the patients had family history of FS and family history of epilepsy was positive in 19 (6.5%), The mean duration of stay in hospital during the illness was 29.67 ± 15.06 hours. Upper respiratory tract infections was the most common cause of fever, 209 of patients (71.6%), (p-value <0.001), higher frequency (36%) of them were admitted in the winter months of year, especially in January (15.4%) (P-value < 0.001).

Conclusions: Based on our study, the highest frequency of FS was seen in 18 month-old children or younger, except for the lower incidence of positive history of prematurity, low percentage of focal seizure type, results of the present study are relatively similar to other studies. Leukocytosis, low serum sodium and microcytic hypochromic anemia may be another risk factors in occurrence of FS need to be studied in comparison with healthy control group.

Copyright©2016, Dr. Mabroka Alfoghi et al. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

INTRODUCTION

Febrile seizures (FS) are among the leading causes of pediatric emergency hospital admissions affects 2 – 5% of all young children. The National Institute of health (NIH) consensus statement defines febrile seizures "an event in infancy and

childhood usually occurring between 6 months and 6 years of age associated with fever with a temperatures of 38°C (100.4°F) or higher but without evidence of intracranial infection or defined cause of the seizure". The International League Against Epilepsy (ILAE) defines FS as "a seizure in association with febrile illness in absence of central nervous system infection (CNS) or acute electrolyte imbalance in children older than one month of age without prior a febrile seizure. single seizure of < 15 min duration in the presence of fever without focal features was defined as a simple febrile

*Corresponding author: Dr. Mabroka Alfoghi

Department of Paediatric, Misurata Teaching Hospital, Misurata University, Faculty of Medicine, Misurata Hospital, Libya.

seizure (SFS), whereas seizures were defined as complex (CFS) if they lasted >15 min, had focal features, or occurred more than once in 24 hours, and rarely a third category called Febrile status epilepticus (FSE) is a FS lasting longer than 30 min without neurological recovery. SFS are mostly benign, even though they are concerning to the parents when they first witness them but a prolonged (Complex) FS can have long term consequences and approximately 2-fold long-term increase in mortality, as compared to the general population, probably secondary to coexisting pathology. Most children who have a febrile seizure have normal health and development after the event, but there is recent evidence that suggests a small subset of children that present with seizures and fever may have recurrent seizure or develop epilepsy (2-7%) later in life. FS arise from a wide array of genetic and developmental factors, Various risk factors are said to play a role in the etiology of FS as gender, development delay, sudden high body temperature, family history, bacterial and viral infections, certain vaccinations, discharge from a neonatal unit after 28 days, day care attendance and iron deficiency. Despite its benign nature, the underlying cause of fever must be identified, In these patients, in most cases, fever is the result of respiratory system infection, gastroenteritis and urinary tract infection. Bacterial meningitis which is common differential diagnosis was rarely observed but necessary to be ruled out if clinically indicated.

Objectives:

With respect to the issue that FS is the most common seizure type in children, the purpose of this study was to determine the epidemiological, clinical, etiological and laboratory features of children admitted to Misurata Teaching Hospital during one year period with FS in 2015 - 2016 and its comparison with similar studies in other parts of the world.

MATERIALS AND METHODS:

Study design:

Descriptive (Longitudinal hospital based) study.

Inclusion criteria:

children was admitted to pediatric department in Misurata Teaching hospital 6 months - 6 years of age presented with fever and seizure from 1st June 2015 to 30th of May 2016.

Exclusion criteria:

Patients with:

- Past history of unprovoked seizures.
- Metabolic disorders.
- Known illnesses of central nervous system and neurological deficits.

Patient's data retrospectively collected based on information registered in hospital medical files including: age, gender, date of admission, type of seizure (simple, complex, status), duration of seizure, temperature at time of seizure, duration of fever before seizure attack, pretreatment with antibiotics, gestational age at birth, mode of delivery, birth weight, duration of stay in NICU, family history of febrile seizures, familial background of epilepsy, laboratory data, length of stay in hospital and underlying causes of fever. Laboratory data

was considered abnormal out of range of normal levels according to (Table 1).

Statistical analysis:

The collected data was entered in excel and analyzed using (SPSS) statistical software program (version 18), and displayed in appropriate tables and graphs. Data was summarized and expressed as frequency and percentage, Significance of difference was tested by chi-square test and the results is considered significant when P < 0.05.

Table 1. Normal laboratory Values

Blood Study	Normal ranges
WBC	5 - 14 × 10 ⁹ cells/L
HB	> 10.5g/dl (5-24mo) > 11.5g/dl (>24mo)
MCV	72 - 88fL (5 - 24mo) 76 - 90 fL (> 24mo)
MCH	24 - 30 fL/cell (5- 24mo) 25 -31 fL/cell (> 24mo)
Platelet	150 - 450 × 10 ⁹ cells/L
Blood Sugar	60 -120 mg/dL
Calcium	8.4 - 10.4mg/dL
Sodium	134 - 145 mmol/L
CSF finding	WBC < 5 cells/mm ³ , Sugar >2 / 3 Bl.S, normal protein and sterile culture

RESULTS

During the study period, 292 children with FS were studied. The proportion of patients with FS among all admitted patients was 4%, The mean age of patients with FS was 21.69 ± 13.71 months, We had subdivided our patient's age group at six months interval i.e. from age group 6 months to 12 months, 12 months to 18 months and so forth. The highest frequency of FS was seen in 6 to 18 months age group, which included 163 children (55.4%), In contrast, the lowest frequency belonged to the age group of 37 - 66 months, which contained only 32 children (11%) (Fig. 1).

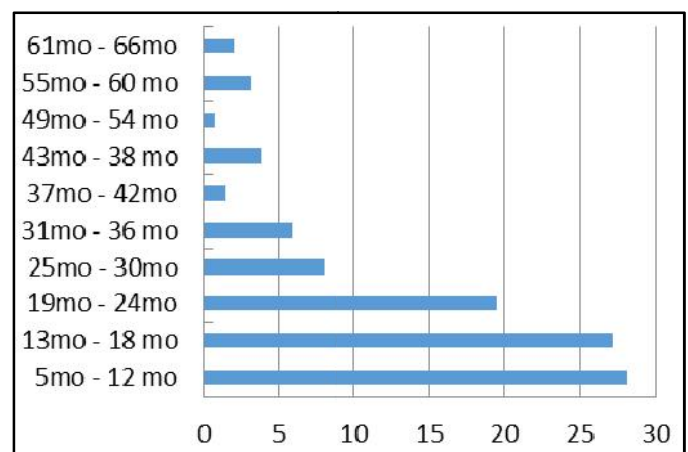


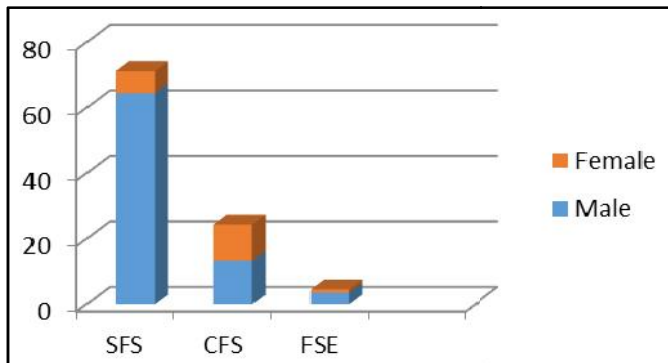
Figure 1. Distribution of febrile seizures incidence (Percentage) versus age groups

Male to female ratio was 1.7:1, 184 patients (63%) were boys and 108 patients (37 %) were girls. The majority of patients 215 (73.6%) had an episode of FS early in the course of illness (Table 2), The mean temperature of the patients was 38.9 ± 0.70°C.

Table 2. Time interval between fever and seizure episode

Duration	Cases number	%
< 24 hours	215	73.6%
24 – 72 hours	61	20.9%
>72 hours	16	5.5%

Two hundred ninety one (97.9%) children were presented with generalized seizures and 6 (2.1%) had focal seizures. Two hundred eight (71.2%) children had SFS, 71(24.3%) children had CFS and FSE in 13 (4.5%) (Fig. 2.) Of children with CFS, 54 patients (18.5%) the seizure was recurrent within 24 hrs, 33 patients (11.3%) presented with prolonged seizure, and the seizure was of focal type in 6 children (2.1%).

**Figure 2. Frequency of seizure types between males and females**

Two hundred eighty two of children (96.6%) were born at term. Also, only 10 (3.4 %) had less than 37 weeks of gestational age at birth. 184 (63%) delivered vaginally and 108 (37%) by Caesarean section (P- value 0.134), majority with average birth weight, with only 21 (7.2%) was below 2500gm at birth, non of our patients had history of prolonged stay (>28 days) in NICU. Ninety (30.8%) of the patients had family history of febrile seizures and family history of epilepsy was positive in 19 (6.5%). Forty eight patients (16.4%) had background pretreatment with antibiotic during the same illness. The mean duration of stay in hospital during the illness was 29.67 ± 15.06 . Frequency of Abnormal Laboratory Findings in our study in Patients with FSs Shawn in [Table 3]. In children with complex febrile seizure which was recurrent within 24 hrs of same illness (54 patients), hyponatremia was reported in 36(66.6%) (P-value 0.000). Lumbar puncture was done in 144 (47.9 %) of patients (as clinically indicated), Aseptic meningitis observed only in two infants, Bacterial meningitis was not observed in our patients who did and also in patients who did not undergo the puncture, no meningitis later diagnosed. Cerebral imaging was not conducted in any of the cases.

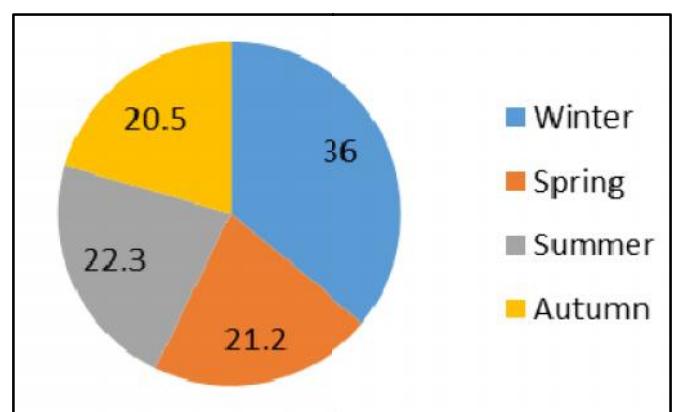
Table 3. Frequency of Abnormal Laboratory Findings in Patients With FSs

Laboratory Abnormality	Number of cases	%
Leukocytosis	88	29.8
Leukopenia	1	0.3
Anemia (Microcytic, hypochromic)	79	27
Thrombocytosis	0	-
Thrombocytopenia	1	0.3
Hypoglycemia	0	-
Hyperglycemia	9	3
Hyponatremia	207	66.8
Hypernatremia	0	-
Hypocalcemia	14	4
CSF abnormality	2	0.7
Cerebral Imaging	0	-

Upper respiratory tract infection (URTI), was the most common cause of fever in our patients, small number are associated with LRTI, AGE (P-value < 0.001), (Table 3), higher frequency (36%) of them were admitted in the winter monthsof year specially in January (15.4%) (P-value< 0.001), (Fig. 3).

Table 4. Distribution Frequency of Etiology of Fever in Patient With FSs

Etiology of Fever	Cases No.	%
URTI	209	71.6%
LRTI	27	9.2%
AGE	20	6.8%
UTI	9	3.1%
Otitis Media	3	1%
Aseptic meningitis	2	0.7%
Chicken pox	2	0.7%
Unclassified	20	6.8%

**Figure 3. Seasonal variation in occurrences of febrile seizures**

DISCUSSION

Febrile seizures is the most common type of seizure during childhood which occurs in 2-5 % of children. It usually occurs in children between 6 months and 6years. Fortunately, most febrile seizures are benign and rarely cause brain damage. Although febrile seizures are benign in nature, when seizures occur, they may lead to fear and anxiety of parents and behavioral disorders may manifest due to the lack of sufficient information of parents about febrile seizures. In comparison to other studies, the majority of children in our study were under 2 years old and our findings were similar to other studies in which FS was in the age range of 6 months to 3 years with peak incidence at the age of 18 months. In the present study, prevalence of FS was slightly predominant in males than females with ratio 1.7:1 and the mean axillary temperature of patients was 38.9 ± 0.70 °C, this in agreement with other studies. The majority of children with febrile seizures were born at term in many studies, Compared to the Al-Zwaini study in which the history of prematurity existed in 13 percent of cases, and the Danish (Aarhus, Aalborg-Odense, Danish National) Birth Cohorts have demonstrated that low birth weight and short gestational age are significant risk factors for FS, in our study, only 10 (3.4 %) had less than 37 weeks of gestational age at birth, and only 7.2% was below 2500 gm. at birth, which is less than other studies in this respect, also there is no difference between children born by vaginal delivery and those born by caesarean section in occurrence of FS (P- value 0.134).

From large number of international studies, it has been reported that a family history of febrile seizures or epilepsy are powerful prognostic risk factors for recurrent febrile seizures or epilepsy later on. In our study, ninety patients (30.8%) had a positive family history of FS, and this is in agreement with the results of other studies, Nineteen patients (6.5%) in this study had a positive family history of epilepsy, while this frequency varied from 1.6% to 9% in other studies. Regarding type of seizure, Two hundred eight (71.2%) children were suffering from SFS that is similar to the other studies, and 24.9% had complex features, this was lower in comparison with most hospital-based studies, which quoted figures of between 32 to 35%. However, what was striking in this study was the low incidence of focal seizures type, occurring in only 2.1 % of the patients, This was far less than that found in hospital-based studies elsewhere, which reported incidences of between 16 to 29%, This apparent difference in incidence might be a true reflection of variation among different population groups or due to lack of uniformity in classification and assessment of focality of seizure. like other studies e.g: study conducted by Millar JS and Anne T Berg which had findings that the height of temperature plays a role in eliciting a FS and that most of the episodes occurred in the initial part of illness, we found same results, 73.6% of our patients, the seizures occurred within the first 24 hours after onset of fever and Forty eight patients (16.4%) had a background of antibiotic consumption during the current illness.

The American Academy of Pediatrics Practice Parameter does not recommend serum electrolytes be obtained routinely in evaluation of a child with a first febrile seizure unless clinically indicated. In our hospital, blood studies (serum electrolytes and complete blood count) are routinely recommended in the work-up of a child with a first febrile seizure, values may be abnormal in children after a febrile seizure, but this should be suggested by precipitating or predisposing conditions elicited in the history and reflected in abnormalities of the physical examination. relationship between iron deficiency anemia and FS has been suggested by several studies, although there are conflicting results, some studies indicated a lower iron status and lower hemoglobin levels as a possible cause of febrile seizures as iron is involved in the metabolism of several neurotransmitters and iron deficiency has variably been associated with behavioral and developmental disturbances. Pisa cane *et al* reported that anemia was more common in children younger than 2 years with febrile seizures, where as in contrast, Kerensky *et al*. reported that iron deficiency raises the threshold for seizures. 27% of patients in the present study had microcytic hypochromic anemia (iron status was not investigated), which may be a risk factor for development of FS. Also, 88 patients (29.8%) in our study had raised leukocyte count, as many other Studies conducted by e.g Lahat *et al*, Ulich *et al*, explained that the stress from fever or seizure is the main cause of leukocytosis with neutrophilic predominance following release of epinephrine and interleukin 1. The hyponatraemia is unlikely to be the cause of the seizure, but probably may predisposes the child to a subsequent seizures during the same febrile illness, Two studies in Europe have demonstrated a relationship between low serum sodium levels and an increased risk of developing recurrent seizures within the same febrile illness, One study by Kiviranta and Airaksinen and other prospective study by Hugen *et al*. reported that sodium levels were significantly lower in children with recurrent FS as compared with SFS without recurrences, in our study

hyponatremia reported in 36 (66.6%) of those (54 patients) with recurrent FS with in 24 hrs of same illness (P-value 0.000).

It is clearly important to consider and, where appropriate, exclude meningitis or encephalitis In any child who presents with FS. Consequently, one of the most common decisions is whether lumbar puncture (LP) is necessary. The estimated incidence of meningitis in children who present with an apparent FS is 2–5%. The yield of positive findings from LP varies between studies, and is generally low in the absence of risk factors Including focal seizures, and suspicious clinical findings. The AAP guidelines were based on retrospective analyses of the risk for bacterial meningitis presenting as a SFS with no other symptoms of meningitis, In a 20-year review of 503 consecutive children with bacterial meningitis, no child presented solely with an SFS. A more recent study of 6- to 18-month old children presenting with a first SFS found no cases of bacterial meningitis, CFS and FSE are more frequently associated with meningitis than SFS, finding that was found in many studies. In our study no cases of bacterial meningitis was detected. Upper respiratory tract infections was the most common cause of febrile illness in patient with FS in many studies, findings consistent with the current study in which 71.6% and 9.2% of patients had febrile illnesses resulting from upper and lower respiratory tract infection respectively, 6.8% percent of cases had gastroenteritis, other causes of fever are shown in (Table 4). Considering many reports about the increased frequency of the occurrence of Febrile seizures in special seasons occur in the setting of febrile illnesses, the occurrence in our study was significantly more common in winter, especially in January (P - value <0.015) this in agreement with other studies in which seasonal variations was observed in children in Finland [1], are reported also in Japanese [2] and in US children [3], The frequency of FS is highest in the winter and lowest in summer months in all 3 geographic areas.

Conclusion

Based on our study, the highest frequency of FS was seen in 18 month-old children or younger. Except for the lower incidence of positive history of prematurity, low percentage of focal seizure type, results of the present study are relatively similar to other studies regarding parameters such as age, gender, type of convulsion, peak body temperature, family history, underlying cause of fever, incidence of meningitis, and seasonal variation. Leukocytosis, low serum sodium and microcytic hypochromic anaemia may be another risk factors in occurrence of FS need to be studied in comparison with healthy control group.

Limitations

The main limitation of this study was to order iron study to support many studies that find significant relation between iron deficiency anemia and FS, because of it's known potential confounding effect of serum ferritin as an acute-phase reactant agent. This limitation could be overcome by predicting the time when ferritin level returned to its baseline value after the acute-phase reaction.

Recommendations

Studies needs to be carried out aims to:

- Find out the relationship between fever, seizure and leucocytosis
- Assess the association of FS with iron deficiency anemia in comparison with healthy control group.
- The role of serum sodium levels in prediction of seizure recurrence during the first 24 hours of illness.

REFERENCES

- Abdulhafeez, M., Khair and Dalal Elmagrabi, 2015. Febrile Seizures and Febrile Seizure Syndromes: An Updated Overview of Old and Current Knowledge. *Neurology Research International*, Article ID 849341, 7 pages.
- Al-Zwaini, E.J. 2007 Epidemiological and clinical features of hospitalized patients with febrile seizures in Ramadi, West of Iraq. *J. Pediatr Neurol*, 5(4):311-315.
- Berg, A.T., Berkovic, S.F., Brodie, M.J., et al, 2010. Revised terminology and concepts for organization of seizures and epilepsies: report of the ILAE Commission on Classification and Terminology, 2005–2009, *Epilepsia* 51(4): 676–685.
- Berg, A.T., Shinnar, S., Shapiro, E.D., Salomon, M.E., Crain, E.F. and Hauser, W.A. 1995. Risk factors for a first febrile seizure: a case-control study. *Epilepsia*. 36(4): 334-341.
- Berg, A.T., Steinschneider, M., Kang, H., Shinnar, S. 1992. Classification of complex features of febrile seizures: interrater agreement. *Epilepsia*, 33:661-6.
- Chin, R.F., Neville, B.G., Scott, R. C. 2005. Meningitis is a common cause of convulsive status epilepticus with fever. *Arch Dis Child*. 90(1):66-69.
- Christophfr, M. Verity, 2015, Febrile convulsions a practical guide, Chapter 08, Child Development Centre, Adden brook's Hospital, Cambridge.
- Delpisheh, A., Veisani, Y. and Sayehmiri, K.A. 2014, Febrile Seizures: Etiology, Prevalence, and Geographical Variation. *Iran J Child Neurol. Summer*, 8(3):30-37.
- Duffner, P.K., Baumann, R.J. 1999. A synopsis of the American Academy of Pediatrics' practice parameters on the evaluation and treatment of children with febrile seizures. *Pediatr Rev*, 20(8): 285-7.
- Elham Bidabadia, Mehryar Mashoufb, 2009. Association between iron deficiency anemia and first febrile convulsion: A case- control study. *Seizure*, (18), 347–351.
- Farwell, J.R., Blackner, G., Sulzbacher, S., Adelman, L., Voeller, M. 1994. First febrile seizures. Characteristics of the child, the seizure and the illness. *Clin Pediatr (Phila)* 33:263-7.
- Ghasem Miri Aliabad, Ali Khajeh, Afshin Fayyazi, Leila Safdari, 2013, Clinical, Epidemiological and Laboratory Characteristics of Patients with Febrile Convulsion, *J Compr Ped.*, 4(3):134-7.
- Green, S.M., Rothrock, S.G., Clem, K.J., et al. 1993. Can seizures be the sole manifestation of meningitis in febrile children? *Pediatrics.*, 92 (4): 527-534.
- Heydarian, F., Ashrafzadeh, F., Kam, S., 2009. Simple Febrile Seizure: The Role Of Serum Sodium Levels In Prediction Of Seizure Recurrence During The First 24 Hours, *Iran J Child Neurology*. June: 31 – 34.
- Hugen, C.A., Oudesluys-Murphy, A.M. and Hop, W.C. 1995. Serum sodium levels and probability of recurrent febrile convulsions. *Eur J Pediatr.*, 154(5): 403-5.
- Janet, L. Patterson; Stephanie A. Carapetian, Joseph R. Hageman, and Kent R. Kelley, 2013. Febrile Seizures: *Pediatric Annals*, December, 42:12.
- Jayashree Nadkarni, Ila Binaykiya, Utkarsh Sharma, Rashmi Dwivedi, 2011. Role of serum sodium levels in prediction of seizure recurrence within the same febrile illness, *Neurology Asia*, 16 (3) 195 – 197.
- Jenniferl. Trainor, Louisc. Hampers, Stavene. Krug, 2001, Children with first-time Simple Febrile Seizures are at low Risk of Serious Bacterial Illness. *Academic Emergency Medicine*, August, Volume 8, Number 8.
- John J. Millichap and J. Gordon Millichap, 2015, Diurnal and Seasonal Occurrence of Febrile Seizures, *Pediatric Neurology Briefs*, Vol. 29, No. 4: 29.
- Juliane, S. Dalbema, Heloise, H. Siqueirab, Mariano, M. Espinosabe Regina, P., 2015. Febrile seizures: a population-based study, *J Pediatr (Rio J)*, 91(6):529 -534.
- Kimia AA, Ben-Joseph E, Prabhu S, et al, 2012, Yield of emergent neuroimaging among children presenting with a first complex febrile seizure, *Pediatr Emerg Care*, 28:316–321.
- Kimia, A.A., Capraro, A.J, Hummel, D., et al. 2009. Utility of lumbar puncture for first simple febrile seizure among children 6 to 18 months of age. *Pediatrics*. 123(1): 6-12.
- Kiviranta, T. and Airaksinen, E.M. 1995. Low sodium levels in serum are associated with subsequent febrile seizures. *Acta Paediatr*, 84 (12): 1372-4.
- Mikkonen, K., Uhari, M., Pokka, T. and Rantala, H. 2015; Diurnal and seasonal occurrence of febrile seizures. *Pediatr Neurol*. 52(4):424-7.
- Millichap, J.J. and Millichap, J.G. 2008. Methods of investigation and management of infections causing febrile seizures. *Pediatr Neurol*. 39(6):381-6.
- Mogens Vestergaard, Marianne Giørtz Pedersen, John R Østergaard, Carsten Bøcker Pedersen, Jørn Olsen, Jakob Christensen, 2008, Death in children with febrile seizures: a population-based cohort study, *Lancet*; 372: 457–63.
- Mohammad Reza Sharif, Davood Kheirkhah, Mahla Madani, Hamed Haddad Kashani, 2016, The Relationship Between Iron Deficiency and Febrile Convulsion: A Case-Control Study, *Global Journal of Health Science*; Vol. 8, No. 2, 185-189.
- Narges Habibian, Abbas Alipour, Abbas Rezaianzadeh, 2014; Association between Iron Deficiency Anemia and Febrile Convulsion in 3- to 60-Month-Old Children: A Systematic Review and Meta-Analysis, *Iran J Med Sci.*, November Vol 39, No 6: 496 – 505.
- National Institutes of Health, 1980. Febrile seizures: consensus development conference summary, Vol.3. Bethesda: No (2).
- Ogihara, M., Shirakawa, S., Miyajima, T., Takekuma, K. and Hoshika, A. 2010. Diurnal variation in febrile convulsions. *Pediatr Neurol*. 42(6):409-12.
- Pierre-Marie Preuxa, VoaRatsimbazafya, Jeremy Jost, 2015, Epidemiology of febrile seizures and epilepsy, a call for action, *J Pediatr (Rio J)*. 91(6):512-514.
- Reese C. Graves; Karen Oehler; and Leslie E. Tingle, 2012, Febrile Seizures: Risks, Evaluation, and Prognosis, *American Family Physician* Volume 85, 149-153.
- Robert M. Kliegman, Bonita Stanton, Joseph St. Geme and Nina F Schor. Febrile Seizures: Nelson Textbook of Pediatrics, 2-Volume Set, 20th Edition, Copyright, 2016.
- Rutter, N. and Smales, O.R.C. 1977. Role of routine investigations in children presenting with their first febrile convulsion. *Arch. Dis. Child*. 52, 188-191.
- Sheilaj. Wallace, 1972. Aetiological Aspects of Febrile Convulsions, Pregnancy and perinatal factors, *Archives of Disease In Childhood*, No (47): 171-178.

- Shrestha, D. Dhakal, A.K., Shakya, H., Shakya, A., Shah, S.C. and Mehata, S. 2014, Clinical characteristics of children with febrile seizure, *Journal of Nepal Health Research Council*, Vol.12, No. 28: 162–166,
- Shrestha, S.K., 2010. Role of CSF Analysis for the First Episode of Febrile Seizure among Children between Six Months to Five Years of Age, *J. Nepal Paediatr. Soc.*, Vol 30/Issue 2, 90-93.
- Soheila Zareifar, Hamid Reza Hosseinzadeh, Nader Cohan, 2012, Association between iron status and febrile seizures in children, *Seizure*, (21) 603–605.
- Srinivasa, S. and SaiPraneeth Reddy, 2014, Iron deficiency anemia in children with simple febrile seizures-A cohort study. *Curr Pediatr Res.*, 18 (2): 95-98.
- Syndi Seinfeld and John M. Pellock, 2013. Recent Research on Febrile Seizures: A Review, *J Neurol Neurophysiol*, ISSN: 2155-9562 JNN. 4: 165.
- Tejesh Malla¹, Kalpana K Malla, Brijesh Sathian, Prabha Chettri, Sandip Singh, Amrita Ghimire, 2015, Simple Febrile Convulsion and Iron Deficiency Anemia A Correlation in Nepalese Children. *American Journal of Public Health Research*. Vol. 3, No. 5A, 11-16.
- Tonia Jones and Steven J. Jacobsen, 2007, Childhood Febrile Seizures: Overview and Implications, *International Journal of Medical Sciences*, 4(2):110-114
- Vestergaard, M. and Christensen, J. 2009. Register-based studies on febrile seizures in Denmark. *Brain Dev*, 31: 372-377.
- Wallace, S.J. 1975, Factors predisposing to a complicated initial febrile convulsion. *Arch Dis Child*; 50:943
- Waruiru, C. and Appleton, R. 2004 Febrile seizures: an update. *Arch Dis Child*; 89(8):751-756.
