

Evaluation of the Cerebrospinal Fluid Results Analysis and Culture in Infants under 18 Months with Simple Febrile Convulsion, Urmia Motahari Hospital, Iran, 2011 until 2016: A Retrospective Study

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Received 22 October 2020, Accepted for publication 12 March 2021

Abstract

Background & Aims: This study aimed to evaluate the cerebrospinal fluid results analysis and culture in infants under 18 months with the diagnosis of simple febrile convulsion in Urmia Motahari hospital.

Materials & Methods: This retrospective descriptive study was conducted to evaluate the results of lumbar puncture in 223 infants under the age of 18 months with simple febrile seizures from 2011 to 2016. Patients' information such as age and sex and the results of analysis and culture of cerebrospinal fluid culture were extracted from patients' records.

Results: Of 223 infants, 109 (48.8%) were male and 114 infants (51.2%) were female, with an average age of 9 months (age range between 5 to 15 months). Thirty-one of them (13.9%) had abnormal WBC (greater than $5/ \text{mm}^3$) and 192 (86.1%) had normal WBC (less than $5/ \text{mm}^3$). Twenty-four infants (10.8%) had an abnormal cerebrospinal fluid (protein more than 45 mg/dl) and 199 infants (89.2%) had normal cerebrospinal fluid (protein less than 45 mg/dl), 24 infants (10.8%) had abnormal CSF glucose level (less than 50 mg/dl) and 199 infants (89.2%) had normal CSF glucose level (more than 50 mg/dl). In 220 infants (99%), cerebrospinal fluid culture was negative and in 3 infants (1%), it was reported as unresponsive. Four out of 55 medical records (1.79%) were treated as bacterial meningitis and 5 (2.24%) of them were treated as aseptic meningitis.

Conclusion: Findings suggested that the patients under one year with febrile seizures should be carefully examined, regarding decision about conducting lumbar puncture (LP) for them.

Keywords: Fever, Convulsion, Lumbar Puncture, Central nervous system infection

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Introduction

Fever-induced seizures are one of the most common neurological diseases in children that occur in 3-5% of children within the age range of 6 months to 6 years. This type of seizure, which is the most common form of

seizure in children, is usually safe and does not increase the risk of seizures without fever (1). Febrile convulsion is a seizure that is associated with a fever with no evidence of brain infection, metabolic disorders, or a prior history of febrile seizure. These seizures fall into

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two general categories: simple seizures (diffuse seizures without focal features, lasting less than 15 minutes and occurrence of only one seizure) and complex seizures (focal seizures, lasting 15 minutes or more, or repeated seizures within first 24 hours) (2). Although fever-induced seizures are associated with excessive brain stimulation with fever, and the prognosis of children with simple seizures is excellent and have normal intelligence, determining the cause of fever and evaluating these children is important (3). Most seizures are caused by fever due to the upper respiratory tract infections, ear infections, or rubella (4, 5). To prove febrile seizure, as it is defined, it is necessary to rule out other causes including meningitis and encephalitis, electrolyte disorders and other acute neurological diseases. (6) The likelihood of seizure due to meningitis has been a concern in the febrile seizure patients for a long time especially in children younger than 18 months of age. The signs and symptoms of meningitis may be ambiguous in this age group, making it more important (7). There have been several clinical trials worldwide reporting the incidence of meningitis in children with simple seizures (8, 9). Therefore, prior to the diagnosis of simple febrile seizure in children, ruling out the meningitis is essential. Another concern in these children is to make an appropriate decision with regard to performing lumbar puncture (LP) to rule out central nervous system infection (10). Seizures following meningitis are caused by bacterial pathogens such as *Haemophilus influenzae* type B, *Streptococcus pneumoniae*, *Neisseria meningitidis*, and *Staphylococcus aureus*, or viral pathogens including Herpes simplex virus type I (11, 12).

In recent years, especially after the general vaccination of children against *Haemophilus influenzae* and *Streptococcus pneumoniae* (*Pneumococcus*), the necessity of cerebrospinal fluid puncture in infants with febrile convulsions is well-known (13). In many

American childcare centers, not all infants with febrile convulsion are diagnosed with cerebrospinal fluid analysis. Obviously, in all patients with symptoms suggestive of brain infection, this study will be undertaken and appropriate treatment will be initiated if this is not possible. In some recent studies in the US, France, and the United Kingdom, the prevalence of meningitis in infants 6 to 18 months with febrile convulsion and general good health has been reported to be close to zero (14); therefore, the common practice in most of the pediatric centers in the world is to select cases requiring cerebrospinal fluid examination and the procedure is not routinely conducted (15). In a study of children with their first febrile seizure aging 6 months to 5 years in Tehran, the cerebrospinal fluid puncture was performed in all children, but the prevalence of meningitis was 4.7% (16). Several studies suggested that LP should be considered in patients with febrile convulsion (7, 17, 18). In 2014, a study at the Neuroscience Center of Ali Asghar Hospital in Tehran, examining the lumbar puncture, found that meningitis was more common in patients younger than 18 months with febrile seizure (30). Therefore, the decision to perform LP in patients with febrile convulsion is controversial and, given the inconsistent results of studies and the lack of recent studies in this center, we collected and analyzed LP analysis and culture results to identify, if possible, the indications for conducting LP in infants with simple febrile seizures.

Materials & Methods

This study was a retrospective descriptive study. By survey method, all records related to infants under 18 months with a simple febrile convulsion admitted in Urmia Motahari hospital from 2011 to 2016 were investigated. The inclusion criteria were: 1. Any child under 18 months of age, 2- The first seizure occurred at a temperature above 38 °C, 3- No evidence of infection

and inflammation of the central nervous system, 4- Absence of systemic and acute metabolic and electrolyte disorders, 5. Seizures are mostly generalized and last less than 15 minutes, 6- They only occur once every 24 hours. The exclusion criteria were: 1. A child over 18 months of age, 2. The first seizure occurred at temperature, not above 38 ° C, 3. Evidence of infection and inflammation of the central nervous system, 4- Systemic and acute metabolic and electrolyte disease, 5. Has not been generalized for more than 15 minutes, 6. They occur more than once in 24 hours, 7. Patients with incomplete records.

Patients' demographic and clinical information such as age, sex, results of spinal cord fluid analysis and culture were extracted by checklist from patient records.

Csf analysis was considered abnormal if having WBC

count more than 5/mm³, protein level greater than 45 mg/dl, and glucose level less than 50 mg/dl.

Statistical Analysis:

Statistical analysis was conducted using SPSS, version 21 (IBM Inc., Armonk, NY, USA). Quantitative measurement is expressed by the mean and standard deviation. Qualitative variables are presented as absolute frequency and percentage.

Results

A total of 223 infants with the diagnosis of simple febrile convulsion were included in the analysis. The demographic data of the infants can be found in Table 1. Female patients had a slight majority (51.2%). The mean age of the infants was 9±3 months with an age range between 5 and 15 months.

Table 1. Sample characteristics of 223 infants with the diagnosis of simple febrile convulsion admitted to Motahari hospital, 2011 to 2016

Characteristics	Levels	n	%
Gender	Female	114	51.2
	Male	109	48.8
Age	Mean: 9±3 month [minimum:5 month; maximum:15 month]		

Frequency of WBC abnormalities of Cerebrospinal Fluid:

The incidence of cerebrospinal fluid WBC abnormality in infants under 18 months admitted with

simple febrile seizure was as follows: 13.9% had abnormal WBC readings and 86.1% had normal WBC (Table 2).

Table 2: Frequency of abnormalities of cerebrospinal fluid regarding WBC count in infants under 18

Variable	Levels	n	%
Abnormal WBC	Greater than 5 mm ³	31	13.9
Normal WBC	less than 5 mm ³	192	86.1
Total		223	100

Frequency of Cerebrospinal Fluid Protein:

Table 3 illustrates the frequency of cerebrospinal fluid protein abnormality in infants under 18 months

admitted to Motahari hospital with simple febrile seizures who underwent LP from 2011 to 2016. About 10.8% of infants had abnormal cerebrospinal fluid

protein and 89.2% had normal cerebrospinal fluid protein.

Table 3: Frequency of cerebrospinal fluid abnormality regarding protein level in infants under 18 months admitted to Motahari hospital with simple febrile seizure who underwent LP, 2011 to 2016

Variable	Levels	n	%
Abnormal cerebrospinal fluid protein	Greater than 45 mg/dl	24	10.8
Normal cerebrospinal fluid protein	Less than 45 mg/dl	199	89.2
Total		223	100

The Prevalence of Cerebrospinal Fluid abnormality regarding Glucose level:

Table 4 shows the frequency of cerebrospinal fluid glucose in infants under 18 months who were admitted

to Motahari hospital with simple febrile seizure and under LP from 2011 to 2016. About 10.8% of infants had abnormal cerebrospinal fluid glucose and 89.2% had normal cerebrospinal fluid glucose.

Table 4: Frequency of cerebrospinal fluid glucose in infants under 18 months who were admitted to Motahari hospital with simple febrile seizure and under LP, 2011 to 2016

Variable	Levels	n	%
Abnormal cerebrospinal fluid glucose	Greater than 50 mg/dl	24	10.8
Normal cerebrospinal fluid glucose	Less than 50 mg/dl	199	89.2
Total		223	100

Cerebrospinal Fluid Cultures:

Table 5 shows the frequency of cerebrospinal fluid cultures in infants under 18 months admitted to Motahari hospital with simple febrile seizures who underwent LP

from 2011 to 2016. About 99% of infants had negative cerebrospinal fluid cultures and 1% were reported as non-responsive.

Table 5: Frequency of cerebrospinal fluid cultures in infants under 18 months who were admitted to Motahari hospital with simple febrile seizure and under LP, 2011 until 2016.

Variable	n	%
Negative	220	99
Non-responsive	3	1
Total	223	100

Four patients out of 55 medical records (7.27%) with meningitis probability based on CSF tests, received

antibiotic treatment for bacterial meningitis. However, 5 patients (9%) were diagnosed with aseptic meningitis, for whom antibiotic treatment was discontinued

according to the consultation with an infectious disease subspecialist.

The analysis of cerebrospinal fluid in children with bacterial meningitis was as follows:

- 1- 5-month-old son with total cell = 15235, pr = 74, Glu = 79, WBC = 30 seg = 60%, lym = 40% RBC = 15200 who received negative culture received 10 days of meningitis treatment.
- 2- A 9-month-old girl with total cell = 250, pr = 25, Glu = 75, WBC = 40 seg = 60%, lym = 40% RBC = 210 who received negative culture received 7 to 10 days of meningitis treatment.
- 3- A 9-month-old girl with total cell = 667, pr = 30, Glu = 55, WBC = 325 seg = 70%, lym = 30% RBC = 342 who had negative culture received 7 to 10 days of meningitis treatment.
- 4- A 12-month-old boy with total cell = 720, pr = 45, Glu = 51, WBC = 64 seg = 65%, lym = 35% RBC = 80 who received negative culture received 7 to 10 days of meningitis treatment.

Discussion

The study was conducted to answer this important question that should lumbar puncture be performed for all children under 18 months with the first fever-induced seizure? According to the data in Tables 1 and 2, 223 infants were retrospectively studied, of them, 109 were male and 114 were female, 31 (13.9%) had abnormal WBC (greater than 5mm) and 192 (86.1%) had normal WBC. (Less than 5mm). Previous studies reported different results regarding this issue. In the study of Kimia et al.(19), the number of WBC was high in 10 cases (3.8%). In the study conducted by Son et al.(7), 5 (6.7%) patients showed pleocytosis in cerebrospinal fluid. In the study of Sadek et al. WBC count (CSF pleocytosis) was abnormal in 23.5% of patients (20). One explanation for this discrepancy might be the existence of different sample sizes in each of the mentioned studies, and the impact of seasonal variations

and changing viral infection patterns. It is recommended to investigate this topic in a separate study with a larger sample size and in a larger statistical population to obtain more reliable results.

Our findings in Tables 3, 4, and 5 showed that 10.8% of infants had abnormal cerebrospinal fluid protein and 89.2% had normal cerebrospinal fluid protein. The same results were obtained for cerebrospinal fluid glucose. Cerebrospinal fluid cultures in 220 cases (99%) were negative and in 3 cases (1%) were unanswered. Kimia et al, inconsistent with our results, concluded that all cerebrospinal fluid cultures were negative (19). Similar to our results, in the study of Son et al. *Streptococcus pneumonia* (2 patients) and *Klebsiella pneumonia* (1 patient) were isolated in cerebrospinal fluid (7). In our study, 4 out of 55 cases with possible meningitis based on CSF tests, (7.27%) received antibiotic treatment for bacterial meningitis. Aseptic meningitis was diagnosed in 5 (9%) cases and their antibiotic treatment was discontinued after consultation with an infectious disease subspecialist. In a retrospective study carried out in Yazd by Golestan et al. (in children within the age range of 6 months to 6 years old), 3% of patients (3 cases) had aseptic meningitis, only one of whom was under one year of age, but no case of bacterial meningitis was reported (21). In a retrospective study conducted by Ehsanipour et al. (22) in Tehran on children within the age range of 5 to 6-year-old; 3.6% had meningitis and 1.6% had bacterial meningitis, all of whom were less than 18 months old with their first febrile convulsion. According to another study by Batra et al. in India on infants aged 6-18 months with their first febrile seizures, 86% of infants with simple febrile convulsion and 4.8% of infants with complex febrile convulsion had meningitis. None had meningeal irritation symptoms, but at least one of the symptoms of neurological deficits or lethargy was recorded. (13). Also, according to a cross-sectional study conducted by Siddiqui et al. in Pakistan on children 6 months to 6 years old, 6.7% of

bacterial meningitis was reported (6.41% in the 6-12 months age group, 3.33% in 12-18 months age group and 0.25% in the over 18 months age group) and patients had at least one symptom of malaise, bulging fontanel, neck stiffness, and eating disorder (23). The findings of previous studies in the USA and French (19, 24) are in disagreement with our results. In the aforementioned studies, the risk of bacterial meningitis in children with their first simple seizure between 6 and 18 months was very low, and no case was diagnosed as bacterial meningitis. These results may be due to the high coverage of vaccination in these countries against common types of meningitis in childhood.

Conclusion

As vaccination against pneumococcus is not included in our national vaccination program and considering it in the findings of current study, still 1.7% of those admitted as simple febrile seizures turned out to have meningitis; all of whom were under one year, it seems that the decision to conduct LP or not is still a matter of clinical judgment especially in those under twelve months. Until the inclusion of pneumococcal vaccine in our national vaccination program, we have to rely on CSF analysis to manage patients with febrile seizures.

Acknowledgments

We thank all personnel of Motahari Hospital of Urmia University of medical sciences.

Author's contribution

Ezatolah Abbasi was the major investigator of the study, collected the data and wrote the article. Ahad Ghazavi and Amir Nasimfar has designed and supervised the study. Mina Mokhtari and Hashem Mahmodzadeh have analyzed the data and interpreted the results.

Conflict of interest

The authors reports no conflicts of interest in this work.

References

1. Sattar S, Saha S, Parveen F, Banu L, Momen A, Ahmed A, et al. Intermittent prophylaxis of recurrent febrile seizures with clobazam versus diazepam. *Mymensingh Med J* 2014;23(4):676-85.
2. Subcommittee on Febrile Seizures; American Academy of Pediatrics. Neurodiagnostic evaluation of the child with a simple febrile seizure. *Pediatrics* 2011;127(2):389.
3. Rosman NP. Evaluation of the child who convulses with fever. *Paediatr Drugs* 2003;5(7):457-61.
4. Hoberman A, Wald ER. Urinary tract infections in young febrile children. *Pediatr Infect Dis J* 1997;16(1):11-7.
5. Kayastha N, Rai GK, Karki S. Use of Lumbar Puncture for First Episode of Febrile Seizure among Children 6 Months to 18 Months of Age: A Cross Sectional Study. *Birat Journal of Health Sciences* 2018;3(2):399-402.
6. Chung J, Ou X, Kulkarni RP, Yang C. Counting white blood cells from a blood smear using Fourier Ptychographic microscopy. *PloS one* 2015;10(7):e0133489.
7. Son YY, Kim G-H, Byeon JH, Eun S-H, Eun B-L. Need for lumbar puncture in children younger than 12 months presenting with simple febrile seizure. *Pediatr Emerg Care* 2018;34(3):212-5.
8. Kimia A, Ben-Joseph EP, Rudloe T, Capraro A, Sarco D, Hummel D, et al. Yield of lumbar puncture among children who present with their first complex febrile seizure. *Pediatrics* 2010;126(1):62-9.
9. Ahmadzadeh J, Mansorian B, Attari MM-A, Mohebbi I, Naz-Avar R, Moghadam K, et al. The association between hematological parameters and metabolic syndrome in Iranian men: A single center large-scale study. *Diabetes Metab Syndr* 2018;12(1):17-21.
10. Najaf-Zadeh A, Dubos F, Hue V, Pruvost I, Bennour A, Martinot A. Risk of bacterial meningitis in young children

- with a first seizure in the context of fever: a systematic review and meta-analysis. *PLoS One* 2013;8(1):e55270.
11. Galetto-Lacour A, Zamora SA, Andreola B, Bressan S, Lacroix L, Da Dalt L, et al. Validation of a laboratory risk index score for the identification of severe bacterial infection in children with fever without source. *Arch Dis Child* 2010;95(12):968-73.
 12. Rezaeian S, Ahmadzadeh J. Assessment of food habits and their association with cardiovascular risk factors in employees. *International Journal of Collaborative Research on Internal Medicine and Public Health* 2012;4(4):339-43.
 13. Ghotbi F, Shiva F. An assessment of the necessity of lumbar puncture in children with seizure and fever. *Headache* 2009;2(1):0-06.
 14. Davis J, Lehman E. Fever Characteristics and Risk of Serious Bacterial Infection in Febrile Infants. *J Emerg Med* 2019;57(3):306-13.
 15. Bank AM, Bazil CW. Emergency Management of Epilepsy and Seizures. *Semin Neurol* 2019;39(1):73-81.
 16. Osman NM, Gai JPG. Assessment of the necessity of routine lumbar puncture among children with fever and convulsions. *Sudan Journal of Medical Sciences* 2019;14(3):162-71.
 17. Ameen DM, Hassan FA, Moosa AI. Is Lumbar Puncture Mandatory for First Simple Febrile Seizures Among Children 6 to 18 Months of Age. *Kerbala Journal of Medicine* 2012;5(11):1262-7.
 18. Ahmed M, Ejaz M, Jahangeer A, Khan S, Hashmi SSR, Jawaid T, et al. Frequency and Associated Factors of Parental Refusal to Perform Lumbar Puncture in Children with Suspected Central Nervous System Infection: A Cross-sectional Study. *Cureus* 2019;11(9): e5653.
 19. Kimia AA, Capraro AJ, Hummel D, Johnston P, Harper MB. Utility of lumbar puncture for first simple febrile seizure among children 6 to 18 months of age. *Pediatrics* 2009;123(1):6-12.
 20. Sadek AA, Mohamad MA, Ali SH, Hassan IAA-A, Hussein MF. Diagnostic value of lumbar puncture among infants and children presenting with fever and convulsions. *Electronic physician* 2016;8(4):2255.
 21. Golestan M, Fallah R, Akhavan-Karbasi S. Evaluation of CSF in 100 children admitted with febrile seizures. *J Shaheed Sadoughi Univ Med Sci* 2009;16(5):3-7.
 22. Ehsanipour F, Khodapanahandeh F, Aslani Z. The prevalence of meningitis in children with febrile seizure hospitalized at Hazrat Rasoul hospital (1997-2002). *Razi Journal of Medical Sciences* 2005;11(44):907-11.
 23. Siddiqui HB, Haider N, Khan Z. Frequency of acute bacterial meningitis in children with first episode of febrile seizures. *J Pak Med Assoc* 2017;67(7):1054-8.
 24. Guedj R, Chappuy H, Titomanlio L, Trieu TV, Biscardi S, Nissack-Obiketeki G, et al. Risk of Bacterial Meningitis in Children 6 to 11 Months of Age With a First Simple Febrile Seizure: A Retrospective, Cross-sectional, Observational Study. *Academic Emergency Medicine* 2015;22(11):1290-7.