

# HOW FREQUENT IS THE CEREBROSPINAL FLUID PLEOCYTOSIS IN INFANTS WITH FEBRILE SEIZURES?

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**Abstract-** Febrile seizure is the most common type of convulsion yet described in man. It is a convulsive event mainly occurring in children between the ages of 6 to 60 months and is not accompanied by any type of electrolyte imbalance and CNS infections, which are very difficult to be ruled out in infancy. To determine the frequency of cerebrospinal fluid (CSF) pleocytosis in infants under the age of eighteen months with febrile seizure who routinely undergo lumbar puncture, we studied 159 cases (from 3 to 18 months of age, mean of 11, SD of 4 months), referred to Takhti Children Hospital from September 1995 to September 1996 because of Febrile Seizures. There were only 5 patients (3.1%) with pleocytosis in our case series. Significant correlation was found between pleocytosis and high erythrocyte sedimentation rates (CI=99%, Chi square=5.94) in our patients. There was also a positive correlation between pleocytosis and the duration between the beginning of fever and occurrence of seizure (CI=98%, Chi square=7.58). We concluded that there was little risk for our patients to have CSF pleocytosis. We also strongly recommend further investigations to exam the relationship of various signs and symptoms with meningitis in infants with seizure and fever, preferably in the form of likelihood ratios. It is noteworthy to emphasize that performing a lumbar puncture in any infant less than 18 months of age is practically rational until more precise and specific indications emerge from further such well-designed studies in the future.

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**Key words:** Seizures, febrile, cerebrospinal fluid, meningitis, spinal puncture, febrile seizures

## INTRODUCTION

Seizures occurring in association with fever are the most common neurological disorders in pediatric age group and affect 2% to 4% of all children in the Great Britain and the United States (1). Simple febrile seizures are brief (<15 minutes), generalized, and occur in association with fever and only once during a 24 hour period (2, 3). The indications for lumbar puncture in infants and children have been reviewed by several investigators with a great degree of controversy (4-8). To determine the frequency of cerebrospinal fluid (CSF) pleocytosis in infants under the age of eighteen months with presumed febrile

seizure who routinely undergo spinal puncture, and also to find some predictive factors for meningitis, we conducted the following study.

## MATERIALS AND METHODS

In our case series we reviewed the files of 182 patients with seizure and fever (from 3 to 18 months of age, mean of 11, SD of 4 months), referred to Takhti Children Hospital (one of the main pediatric referral centers in Tehran) from September 1995 to September 1996.

Lumbar puncture was done routinely for all the patients according to the American Academy of Pediatrics Subcommittee on febrile seizure's recommendation. Patients whose files lacked tap results were excluded from the study. White cells count of more than 10 in the CSF smear considered as pleocytosis.

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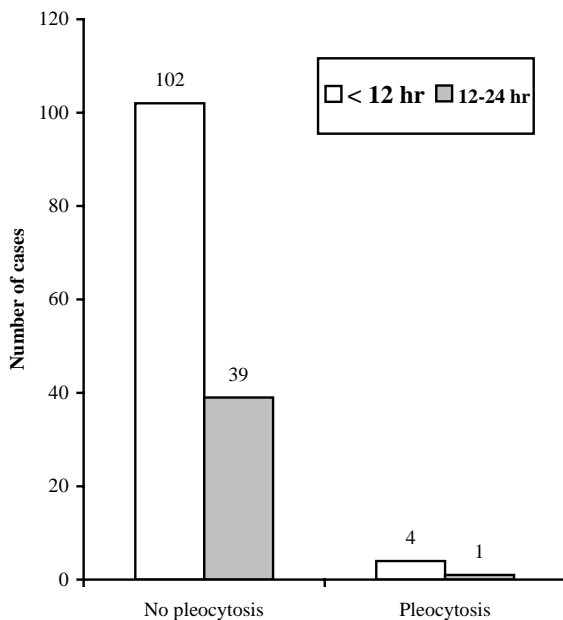
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## RESULTS

After reviewing 182 files, 23 patients were excluded because of lack of tap results. Sixty one out of 159 (38.5%) of the remaining patients were female and 61.5% (98 out of 159) were male. The peak age frequency of febrile seizures was slightly earlier among boys than girls (10-12 vs. 16-18 months, respectively).

One hundred fifty four (96.9%) of our patients had normal CSF and only five (3.1%) had CSF pleocytosis. From those who had pleocytosis 80% were female and 20% were male (Table 1). Generalized tonic-clonic seizures (GTCS) were the predominant type of seizure seen (86.2%) and it was also the only type of seizure in the patients with CSF pleocytosis. The other types of convulsions were tonic (8.2%), as well as focal (2.5%) and other types (3.1%), such as myoclonic seizures. One hundred thirty patients (81.7%) had only one attack and the remainder (8.3%) had two or more. Three out of five patients with CSF pleocytosis had once and two had twice or more attacks during their febrile episode. One hundred forty five cases (92%) had short seizures lasting less than 15 minutes and the remainder had more prolonged convulsions. There were no significant differences between patients with and without pleocytosis in this regard.



**Fig. 1.** Frequency of pleocytosis in accordance to the time between the onset of fever and seizures

**Table 1.** Patients' gender in two groups (cases with and without CSF pleocytosis)\*

Gender	Patients without CSF pleocytosis	Patients with CSF pleocytosis
Male	99 (62.3%)	1 (0.62%)
Female	55 (34.6%)	4 (2.48%)
Total	154 (96.9%)	5 (3.1%)

\*Data are given as number (percentage)

None of the patients had cutaneous signs. Neck stiffness as well as meningeal signs was not detected in any of our cases. There was also a longer interval (Fig.1) between the onset of fever and seizures in the cases with pleocytosis in comparison with the patients with normal CSF results (CI=98%, Chi square=7.58). In patients who had normal CSF results, there was also a normal erythrocyte sedimentation rate (ESR) in 96% of cases. But almost all patients with CSF pleocytosis had an ESR of more than 30 mm/hour (CI=99%, Chi square=5.94).

## DISCUSSION

The prevalence of meningitis among children with seizures and fever in North American pediatric emergency departments is between 1% and 2% (9), and through selective referral, may be as high as 7% in a European country (10). These figures are in accordance with the finding of 3.1% CSF pleocytosis in our case series, and also indicate that a large number of "unnecessary" lumbar punctures would be done if a lumbar puncture is being performed in all children with a seizure associated with fever.

Indications for lumbar puncture in a febrile child age 18 months to 5 years old include presence of meningeal signs and toxicity consistent with the diagnosis of meningitis. Lumbar puncture has been strongly considered in this age group for children who present with seizure activity at the time of arrival in the emergency department, or with findings on physical examination such as rash, cyanosis, hypotension, respiratory distress, or abnormal neurological examination (2, 4). Children with complex febrile seizures should also be strongly considered for performance of a lumbar puncture (5).

But there are some controversies about children with fever and seizure who are younger than 18 months. Some authors believe that if the child had been previously healthy, has not been treated previously with an antibiotic, and has a simple febrile seizure, he/she is managed as any child with an acute

fever. In other words, they believe that all children who presented with fever, seizures, and meningitis appeared extremely ill, had meningeal signs, or had febrile seizures with complex features (2, 6, 7). On the other hand, the American Academy of Pediatrics (AAP) subcommittee on febrile seizure recommends, "After the first seizure with fever in infants younger than 12 months, performance of a lumbar puncture must be strongly considered and in a child between 12 and 18 months of age, a lumbar puncture should be considered, because clinical signs and symptoms of meningitis may be subtle" (8).

Looking for studies that investigate the relationship of various signs and symptoms with meningitis in children with seizures and fever, preferably in the form of likelihood ratios (LRs), only one study is found that actually provides sensitivity, specificity, and LRs for the various clinical indicators of meningitis (10). This study tried to identify criteria, based on age, specific clinical indicators, or the results of initial blood tests that could serve as indications for performing lumbar puncture. Among 309 children aged 3 months to 6 years consecutively seen with a first seizure associated with fever in the emergency departments of 2 major children's hospitals in the western part of the Netherlands, 23 cases of meningitis (7%) were diagnosed. These 23 cases were then compared with a reference group of 69 children with seizures associated with fever, but without meningitis, selected at random from the remaining 286 children. Several clinical signs and symptoms were examined for their ability to differentiate children with from those without meningitis. The presence of petechiae, nuchal rigidity, and/or coma identified 16 (70%) of the 23 children with meningitis. In children who did not have meningitis, these "major" signs of the disease were not found; the LR when any of these signs is present (LR+) is, therefore, infinite (95% CI, 6.0 to infinity), and the meningitis probability approaches 100% (95% CI, 31%-100%). In the absence of meningeal irritation, petechiae, or complex features of the seizure, there were no meningitis cases in the study. The child's age, sex, degree of fever, and results of routinely performed blood tests did not have any diagnostic value (10). In our case series, there was a positive correlation between CSF pleocytosis and ESR higher than 30mm/hr, and also the time between the onset of fever and seizures.

The major drawback is that these two studies were both retrospective review of the medical records of children presenting with seizure and fever. In Netherlands' review, the study group was limited to

children aged 3 months to 6 years with first-time seizure and fever (10). The pretest probability of meningitis is likely to be different in another group of children. In addition, nuchal rigidity may not be a strong predictor in young children (especially the infants below 18 months of age). However, these results indicate that it is indeed unusual for a child with meningitis to present only with a seizure. Also, a fair number of children without meningitis will present with the risk factors mentioned above, that is, the specificity of these "clinical tests" is far from 100%. For determining some highly sensitive and specific predictive signs or symptoms for meningitis in children with seizure and fever, we suggest to design prospective studies in wider range of age groups. That will better provide the sensitivity, specificity, and likelihood ratios for the various clinical indicators of meningitis. At last but not at least, it should be mentioned that performing a lumbar puncture in any infant less than 18 months of age is practically rational until more precise and specific indications emerge from further well-designed studies in the future.

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