https://doi.org/10.48047/AFJBS.6.15.2024.15449-15459

African Journal of Biological Sciences

Journal homepage: http://www.afjbs.com

Research Paper Open Access

Frequency of Meningitis in Children (Age 06 Months-60 Months) presenting with Fever and First Episode of Seizure

Dr. Mohammad Arif[1], Dr. Muhammad Kamran[2*], Dr. Aizaz Raheem[3], Dr. Aamir Karim[4], Dr. Maryam Hayat[5], Dr. Sadiqullah[6]

[1]Professor, Department of Pediatrics, North West General Hospital, Peshawar, Pakistan
[2*]Senior Registrar, Department of Pediatrics, North West General Hospital, Peshawar, Pakistan
[3]Registrar, Department of Pediatrics, North West General Hospital, Peshawar, Pakistan
[4]Resident Pediatrician, Department of Pediatrics, Khyber Teaching Hospital, Peshawar, Pakistan
[5]House Officer, Department of Pediatrics, Northwest General Hospital, Peshawar, Pakistan
[6]Resident Pediatrician, Department of Pediatrics, Northwest General Hospital, Peshawar, Pakistan

*Corresponding author's Email: kamranbebrak495@gmail.com

Received: 06 Aug, 2024
Accepted: 05 Oct, 2024
Published: 30 Oct, 2024
doi:10.48047/AFJBS.6.15.2024.15449-15459

Background

To determine the frequency of acute meningitis (bacterial + viral/aseptic) among children (06 – 60 months old) with '1st episode of febrile seizures at a tertiary care hospital and the utility of lumbar puncture as a diagnostic tool in such patients'

Methods

A retrospective cross-sectional study was conducted at Department of Pediatrics, Medicine, Northwest General Hospital and Research Centre, Peshawar'. From January 2021 to July 2023. A total number of 145 children who presented with 1st episode of febrile seizures, aged 06 – 60 months, were included in this study. Data regarding age, gender, residential area, family history of seizures/febrile seizures, vaccination status of patients, type (simple/complex) of seizure, meningeal signs, and lumbar puncture status were taken for each child. 'Cerebrospinal fluid

(CSF) was analyzed to determine the frequency of meningitis among children presenting with fever and a first attack of seizure'.

Results

The Mean age of children was 20.04 months ± 16.278, and the median of 12 months. There were 101 (69.70%) male children and 44 (30.30%) 'female children'. 'There were 53 (36.6%) children having a positive family history of seizures/febrile seizures. 103 (71%) children were from urban areas, and the rest were from rural areas'. Meningitis was found in 73 (50.30%) children, among them 39 (26.9%) were found to be acute bacterial, while 34 (23.4%) were of acute viral meningitis cases.

Conclusion

The occurrence of meningitis among children presenting with febrile seizures was found to be considerably high in this study. Acute bacterial meningitis was diagnosed in 26.9% of children experiencing their first episode of febrile seizure. Based on these findings, lumbar puncture is strongly advised for children aged 6 to 12 months, as this age group demonstrated a higher incidence of meningitis. Similarly, children who are partially vaccinated or unvaccinated should also undergo lumbar puncture when presenting with febrile seizures, given their increased susceptibility to central nervous system infections.

Key words: Febrile Seizures, Bacterial Meningitis, Viral/Aseptic Meningitis, Lumbar Puncture, Cerebrospinal Fluid.

INTRODUCTION

Normal body temperature in healthy children ranges from 36.5°C to 37.5°C, with a typical daily variation of around 0.5°C (1). A temperature above 38.5°C is generally considered a fever in children, and above 38.0°C in infants under three months. Seizures, particularly febrile seizures, are common in pediatric emergencies, affecting 2–5% of children in Europe and North America, and up to 8% in Japan (2-3). These seizures usually occur in children aged 6 to 60 months during febrile episodes without an underlying neurological cause.

Febrile seizures are classified as simple or complex (4). Simple seizures are brief, generalized, and non-recurrent within 24 hours. Complex seizures, however, may involve focal features, last longer than 15 minutes, recur within 24 hours, or be associated with neurological deficits or prior conditions like developmental delay (5,6).

Meningitis, an inflammation of the meninges, remains a serious concern despite medical advances, with a mortality rate approaching 25%. It may present subtly in infants, where febrile seizures could be the sole initial symptom(7-10). Thus, differentiating between febrile seizures and seizures caused by meningitis is critical, especially since complex seizures may heighten the risk.

Lumbar puncture (LP), essential for diagnosing meningitis, is often debated due to procedural risks. While older guidelines recommended routine LP in children under one year, current practice allows room for clinical judgment.

This study aims to determine the frequency of meningitis in children aged 6–60 months presenting with fever and their first seizure, specifically assessing those with simple or complex febrile seizures. Additionally, it evaluates the utility of routine LP in detecting central nervous system infections requiring urgent treatment in this population.

METHODS

This retrospective cross-sectional study used medical records from the pediatric emergency unit at Northwest General Hospital in Peshawar, a tertiary care referral center. The research included children between 6 and 60 months of age who were diagnosed with acute bacterial meningitis, viral meningitis, or febrile seizures upon discharge. The data spanned from January 2021 to July 2023. Relevant cases were identified by reviewing discharge records coded under the International Classification of Diseases, 11th Revision (ICD-11) for meningitis and febrile seizures. After initial identification and screening, 145 eligible patients were selected. Ethical approval was obtained from the institutional review board of Northwest General Hospital and Research Center, Peshawar.

Children were considered febrile if their axillary temperature was measured above 100.4°F in the emergency department. Febrile seizures were defined as convulsions occurring in the context of fever, with or without signs such as tongue biting, incontinence, or abnormal body movements noted by parents or medical staff.

A diagnosis of meningitis was made when children with fever and seizures exhibited all of the following cerebrospinal fluid (CSF) findings: white cell count greater than 5/mm^3, protein concentration above 40 mg/dL, and CSF glucose level less than two-thirds of the corresponding blood glucose value.

In cases where a traumatic lumbar puncture occurred, white blood cell counts were adjusted using the following formula:

Corrected WBC = CSF WBC – (CSF RBC / 500).

When CSF samples showed bacterial growth or a positive Gram stain, bacterial meningitis was confirmed. Any samples contaminated with non-pathogenic organisms were excluded.

When CSF samples displayed elevated cell counts dominated by mononuclear cells and CSF and blood cultures were negative without recent antibiotic exposure,the case was classified as aseptic meningitis. However, if a child had similar CSF findings and had received antibiotics within the past week, bacterial meningitis was presumed, and the child was treated accordingly. Such cases were included as bacterial meningitis in the final analysis.

Collected data included age, gender, seizure type, family history of febrile seizures, signs of meningeal irritation (e.g., neck stiffness, Brudzinski’s or Kernig’s signs, altered consciousness, feeding difficulties in infants), vaccination history, residence (urban vs. rural), and results from lumbar puncture and CSF culture.

Children were excluded if they had a prior diagnosis of epilepsy, known brain malformations, immunodeficiency, malnutrition, or any chronic systemic illness such as cardiac, renal, metabolic, oncological, or autoimmune diseases, and if they presented with seizures.

The descriptive statistical analysis was performed using SPSS statistical software (version 25). Data were expressed as percentages for categorical variables. The categorical variables are number (n) and percentage (%).Participants were selected through non-probability consecutive sampling. A p-value of ≤ 0.05 was set as the benchmark for statistical significance in all analyses.

RESULTS

The study groups consisted of 145 patients with a diagnosis of febrile fits, bacterial meningitis, and viral meningitis. The mean age was 20.04 months± 16.278 and the median of 12 months (06–60 months), and 69.70% (n = 101) were male while 30.30% (n = 44) were female.Patients were also divided into groups based on age ranges. 76 (52.4%) patients were in age range 06 months – 12months, 25 (17.2%) patients in age range 13 months – 24 months, 23 (15.9%) patients in age range 25 months – 42 months while 21 (14.5%) patients were in age range of 43 months – 60 months respectively.

The mean stay in hospital was 03.27 ± 3.1 days, with the median of 02 days. 143 (98.6%) patients were admitted to the paediatric ward while only 02 (1.4%) were admitted to the Paediatric ICU. Among them, 144 (99.3%) patients were treated and discharged, while only 01 (0.7%) patient expired.

Seventy-two patients (49.7%) had the discharge diagnosis of febrile fits, 39 (26.9%) had the discharge diagnosis of bacterial meningitis, while 34 (23.4%) had the discharge diagnosis of viral/aseptic meningitis. Among those patients in 79 (54.5%) had lumber puncture advised and were performed, while in 66 (45.5%) patients, lumber puncture was not advised.

Patients were also divided based onthe type of seizure, and those having meningeal signs. Based onthe type of seizures, 124 (85.5%) patientswere having simple febrile seizures (for less than 15 minutes) while 21 (14.5%) patients were having complex febrile seizures (for more than 15 minutes). Based on meningeal signs in 35 (24.14%) patients, meningeal signs were present, while in 110 (75.86%) patients,there were no meningeal signs.

In 53 (36.6%) of the patients, there was a positive family history of seizures/febrile seizures, while in 92 (63.4%) of the total patients,there was no family history of seizures/febrile seizures. In our data, 103 (71%) patients were from urban areas, while 42 were from rural areas, and 97 (66.9%) of the patients were completely immunized, 25 (17.2%) were partially immunized, while 23 (15.9%) were not immunized.

Table 01: Demographic Characteristicsand Vaccination Status:

	Total Patients (n=145)
Age, months, mean ± SD, median (range)	20.04 ± 16.278, 12 (06-60)
Age distribution, *n*, (%)	
06 Months – 12 Months	76 (52.4)
12 Months –24 Months	25 (17.2)
25 Months – 42 Months	23 (15.9)
43 Months – 60 Months	21 (14.5)
Gender, male, *n*, (%)	101 (69.7)

Gender, female,*n*,(%)	44 (30.3)
Family History of Fits, *n*, (%)	
Present	53 (36.6)
Not Present	92 (63.4)
Residence, *n*, (%)	
Urban	103 (71)
Rural	42 (29)
Vaccination Status, *n*, (%)	
Completely Vaccinated	97 (66.9)
Partially Vaccinated	25 (17.2)
Unvaccinated	23 (15.9)

Table 02: Seizure Type, Meningeal Signs, Diagnosis, LP status, Stay in Hospital, Outcome:

	Total Patients (n=145)
Seizure Type, n, (%)	
Simple	124 (85.52)
Complex	21 (14.48)
Meningeal Signs, n, (%)	
Present	35 (24.14)
Absent	110 (75.86)
Diagnosis, n, (%)	
Febrile Fits	72 (49.7)
Bacterial Meningitis	39 (26.9)
Viral/Aseptic Meningitis	34 (23.4)
LP Status, n, (%)	
Done	79 (54.5)
Not Done	66 (45.5)
Stay in Hospital, n, (%)	
Paediatric Ward	143 (98.6)
Paediatric ICU	2 (1.4)
Days Spent in Hospital, mean ± SD, median	3.27 ± 3.1, 02

Stratification of final diagnoses with different variables and*P* – P-values were also calculated for each stratification.

Stratification based on age group with final diagnosis was performed;the group with ages between 06 months and 12 months had 27 (35.52%) cases of febrile fits, 28 (36.84%) with bacterial meningitis, while 21 (27.63%) cases were of viral/aseptic meningitis. In the group with ages between 13 months – 24 months, 18 (72%) cases were diagnosed as febrile fits, 2(8%) cases as bacterial meningitis, while 5 (20%) as viral/aseptic meningitis. In the third group, the ages were between 25 months –42 months, in which 16 (68.57%) patients were having febrile seizures, 3

(13.04%) were having bacterial meningitis, while 4 (17.39%) were having viral/aseptic meningitis. In the last group,where patients aged between 43 months – 60 months were there, 11 (45.83%) had febrile seizures, 6 (28.57%) had bacterial meningitis as a final diagnosis, while 4 (19.05%) hadviral/aseptic meningitis. *P* – value for this stratification was 0.049.

Based on gender stratification, in patients with febrile seizures, 51 (70.83%) were male, while 21 (29.17%) were female. 24 (61.54%) patients of bacterial meningitis weremale, while 15 (38.46%) were female, while in cases with viral meningitis/aseptic, 26 (77.47%) were male and 08 (23.53%) cases were female.*P* – value for this stratification was 0.746.

The stratification is based on residency in urban and rural areas. 57 (79.17%) patients with febrile seizures were from urban areas, while 15 (20.83%) were from rural areas. In the patients with bacterial meningitis group, 24 (61.52%) were from urban areas, while 15 (38.46%) were from rural areas. 22 (64.70%) patients with viral/aseptic meningitis were from urban areas, while 12 (35.30%) were from rural areas. *P* – value for this stratification was 0.073.

When stratification based on vaccination status of the patients was done, 65 (90.28%) of the patients with febrile seizures were fully vaccinated, 4 (5.55%) were partially vaccinated, while 3 (4.17%) patients were unvaccinated. In the bacterial meningitis group, 16 (41.02%) cases were fully vaccinated, 12 (30.77%) patients were partially vaccinated, while 11 (28.20%) were unvaccinated. In patients with viral/aseptic meningitis, 16 (47.05%) were fully vaccinated, 9 (26.47%) were partially vaccinated, while 9 (26.47%) patients were unvaccinated. *P* – value for this stratification was < 0.001.

Based onthe family history of seizures/febrile seizures, stratification was also done. In cases with febrile seizures,27(37.75%) cases had having positive family history, while 45 (62.25%) had having negative family history of seizures. In cases with bacterial meningitis, 12 (30.77%) cases had positive results, while 27 (69.23%) cases had no family history of seizures. In viral/aseptic meningitis cases, 14 (41.18%) had positive while 20 (58.82%) had having negative family history of seizures.*P* – value was 0.852.

Stratification based on types of seizures was as follows. In the febrile seizure group, 72 (100%) had simple febrile seizures, while none had complex febrile seizures. In the bacterial meningitis group, 18 (46.15%) patients had simple seizures while 21 (53.85%) hadcomplex seizures. 34 (100%)patients among the viral/aseptic meningitis group had simple seizures, while none hadcomplex seizures.*P* – value for this stratification was <0.001.

Based onmeningeal signs, 3 (4.17%) patients from the febrile seizures group had meningeal signs, while 69 (95.83%) patients had no meningeal signs. In patients with bacterial meningitis, 27 (69.23%) had meningeal signs while 12 (30.77%) did not have meningeal signs. In the viral/aseptic meningitis group, 5 (14.70%) patients hadmeningeal signs, while 29 (85.30%) did not. *P*– value was <0.001 for this stratification.

Stratification with patient outcome was also performed. In the febrile fits group, 72 (100%) patients were treated and discharged. 38 (97.43%) patients with bacterial meningitis were treated and discharged, while 1 (2.57%) expired in the paediatric ICU. All patients with viral/aseptic meningitis were also treated and discharged.*P* – value for this stratification was 0.749.

The immunization status of patients was also compared with their residence. In patients residing in urban areas, 74 (71.84%) patients were fully vaccinated, 23 (22.33%) were partially vaccinated, while 6 (5.82%) were unvaccinated. In patients residing in rural areas, 23 (54.76%) were fully vaccinated, 2 (4.76%) were partially while 17 (40.48%) patients were unvaccinated. *P* – value for this stratification was <0.001.

In patients with simple febrile seizures, lumbar puncture was advised and performed in 58 (46.77%) cases, while lumbar puncture was not performed in 66 (53.23%) cases. In patients with complex febrile seizures, lumbar puncture was advised and performed in 21 (100%) cases. *P* – value was <0.001.

Table 03: Comparison of Final Diagnosis with Different Variables, Total Patients (n=145)

Variables	**Final Diagnosis**			***P* – value**
	Febrile Seizures	**Bacterial Meningitis**	**Viral/Aseptic Meningitis**	
Age Groups (months)				0.049
06 – 12 (n=76), n, (%)	27 (35.52)	28 (36.84)	21 (27.63)	
13 – 24 (n=25), n, (%)	18 (72)	02 (08)	05 (20)	
25 – 42 (n=23), n, (%)	16 (69.57)	03 (13.04)	04 (17.39)	
43 – 60 (n=21), n, (%)	11 (45.83)	06 (28.57)	04 (19.05)	
Gender				0.746
Male (n=101), n, (%)	51 (70.83)	24 (61.54)	26 (77.47)	
Female (n=44), n, (%)	21 (29.17)	15 (38.46)	08 (23.53%)	
Residency				0.073
Urban (n=103), n, (%)	57 (79.17)	24 (61.54)	22 (64.70)	
Rural (n=42), n, (%)	15 (20.83)	15 (38.46)	12 (35.30)	
Vaccination Status				<0.001
Fully Vaccinated (n=97), n, (%)	65 (90.28)	16 (41.02)	16 (47.05)	
Partially Vaccinated (n=25), n, (%)	04 (05.55)	12 (30.77)	09 (26.47)	
Unvaccinated (n=23), n, (%)	03 (04.17)	11 (28.20)	09 (26.47)	
Family History for Seizures				0.852
Positive (n=53), n, (%)	27 (37.75)	12 (30.77)	14 (41.18)	
Negative (n=92), n, (%)	45 (62.5)	27 (69.23)	20 (58.82)	
Seizure Type				<0.001
Simple (n=124), n, (%)	72 (100)	18 (46.15)	34 (100)	
Complex (n=21), n, (%)	00 (00)	21 (53.85)	00 (00)	
Meningeal Signs				<0.001
Present (n=35), n, (%)	03 (04.17)	27 (69.23)	5 (14.70)	
Absent (n=110), n, (%)	69 (95.83)	12 (30.77)	29 (85.30)	
Outcome				0.749
Treated (n=144)	72 (100)	38 (97.43)	34 (100)	

Expired (n=01)	00 (00)	01 (02.57)	00 (00)	

DISCUSESSION

Meningitis is a medical emergency in children and should not be overlooked in any youngster who has a fever and is having seizures. The connection between seizures and meningitis is widely recognized and has been documented in approximately 12% to 27% of cases (11-13). The likelihood of meningitis, particularly bacterial meningitis, occurring in a child with a fever has diminished significantly due to universal vaccination against bacterial pathogens; this remains a big worry in any child who exhibits febrile seizures, particularly in populations with poor immunization rates. 'In 2011, the American Academy of Pediatrics (AAP) updated its guidelines for the neurodiagnostic assessment of individuals experiencing simple febrile seizures'. The updated recommendations supported lumbar puncture as an option for infants presenting with simple febrile seizures and incomplete or unknown immunization status. However, they did not recommend its routine use among fully immunized infants, particularly those immunized against Hib and S. pneumoniae (13-15).

Meningitis was found in 73 of the 145 cases (including bacterial and viral/aseptic), indicating that meningitis affects nearly half of the children who report to the Northwest General Hospital with an apparent febrile seizure. According to Al-Eissa YA from Saudi Arabia, bacterial meningitis occurs 3.5% of the time in children with febrile seizures, but only 1.5% of those between the ages of 3 and 60 months (15).'According to Casasoprana A et al from France, the occurrence of bacterial meningitis was reported at 1.9% among cases experiencing their first febrile seizure and who were younger than 18 months of age'.Ghobti and Shiva's research findings also documented a rate of 4.7% for bacterial meningitis among children who had experienced febrile seizures (16)In a separate study conducted at KCH (Kanti Children's Hospital), it was revealed that 10.9% of patients who appeared to be experience ng their first febrile seizure had meningitis (17).In another study done in Kanti Children's Hospital, Kathmandu, Nepal, the incidence of bacterial meningitis among children aged 06 – 60 months presenting with first febrile seizure was 17.1 percent (18).

Study conducted in a children's hospital, Multan, the incidence of bacterial meningitis was 4.5% among patients aged 06 – 60 months (19).In another study conducted in the pediatric department of Lahore General Hospital, bacterial meningitis was 7.3%.Our finding was comparatively higher than from studies done both outside and inside the country, mainly because most of the patients with meningitis were partially vaccinated or unvaccinated, and those who were vaccinated, proper vaccination charts were not available with them. Given the high frequency of meningitis cases identified, it is advisable to consider meningitis as a preliminary diagnosis for all children who present with fever accompanied by seizures in our setup.

Gender and meningitis did not significantly correlate, according to our research. This runs concurrently with other research. It was noted that the younger the patient, the higher the risk of developing meningitis. In the 6 – 12 months age group, 64% had meningitis compared to 28 % in the 12 – 24 months age group and 18 % in the more than 24 months age group. Other research

studies have also come to the same results. Therefore, the younger the age, the greater the chance that a child presenting with fever and seizure may have meningitis.

Meningeal signs were found to be significantly associated with meningitis, with a *P* – P-value of <0.001, but the lack of these signs does not exclude meningitis in younger patients. The increased risk of meningitis when meningeal signs are present in a patient with fever and seizures appears consistent with findings from other studies (20). 'Our study could not note any significant association of family history of fits/febrile fits or residency (urban/rural) with the prevalence of meningitis'.

Our findings indicated that complex seizure symptoms were present in most children with bacterial meningitis. This is comparable to Casasoprana's outcomes (21) discovered that the risk of bacterial meningitis or encephalitis in infants with uncomplicated febrile seizures and a normal physical examination is quite low. According to Rossi et al, a complex seizure could be an important distinguishing factor between patients with and without meningitis in children younger than 3 years old with no neurological symptoms.

In our study, lumbar puncture was performed in all patients presenting with complex seizures, which was comparable to other studies (22).

Researchers from many parts of the world have observed a lower incidence of meningitis/bacterial meningitis among febrile seizure cases and have related those to higher immunization rates in their community. Pakistan, a developing nation, needs to increase its immunization rates generally, which are now around 50%, and in provinces like Khyber Pakhtunkhwa, where the vaccination refusal rate is relatively high. Enhancing immunization coverage and ensuring prompt meningitis diagnosis can unquestionably reduce the 'prevalence of this life-threatening condition among children in Pakistan, with a particular focus on the province of Khyber Pakhtunkhwa'.

Our study has a few limitations worth noting. A lumbar puncture was not performed on all patients, and some patients with aseptic/viral meningitis (with no major clinical symptoms) may have been overlooked. Moreover, vaccination charts for every patient were unavailable; most patients' vaccination status was determined by their parents' vaccination history and by the presence of a BCG scar during an examination.

CONCLUSION

Our findings revealed a noteworthy proportion of meningitis among children presenting with febrile seizures, emphasizing the importance of considering meningitis as a differential diagnosis in such cases within pediatric emergency settings. Particularly in infants aged 6 to 12 months experiencing their first seizure episode associated with fever, a lumbar puncture is strongly recommended even without classical signs of meningeal irritation due to the higher risk of meningitis in this age bracket. Furthermore, lumbar puncture should also be prioritized in children who are incompletely vaccinated or unvaccinated, as they face a heightened vulnerability to invasive infections when presenting with febrile seizures for the first time.

REFERENCES

1. Fever in children: Overview. 2019 Jun 6 [cited 2023 Sep 6]; Available from: https://www.ncbi.nlm.nih.gov/books/NBK279455/
2. Fever in children: Overview - InformedHealth.org - NCBI Bookshelf [Internet]. [cited 2023 Sep 6]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK279455/
3. Pallin DJ, Goldstein JN, Moussally JS, Pelletier AJ, Green AR, Camargo CA. Seizure visits in US emergency departments: epidemiology and potential disparities in care. International Journal of Emergency Medicine 2008 1:2 [Internet]. 2008 Jun 5 [cited 2023 Aug 28];1(2):97–105. Available from: https://intjem.biomedcentral.com/articles/10.1007/s12245-008-0024-4
4. Armon K, Stephenson T, Gabriel V, MacFaul R, Eccleston P, Werneke U, et al. Determining the common medical presenting problems to an accident and emergency department. Arch Dis Child [Internet]. 2001 May 1 [cited 2023 Aug 28];84(5):390–2. Available from: https://adc.bmj.com/content/84/5/390
5. Fetveit A. Assessment of febrile seizures in children. Eur J Pediatr [Internet]. 2008 Jan 2 [cited 2023 Aug 28];167(1):17–27. Available from: https://link.springer.com/article/10.1007/s00431-007-0577-x
6. 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 [Internet]. 2013 Jan 28 [cited 2023 Aug 28];8(1):e55270. Available from: https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0055270
7. Joffe A, McCormick M, DeAngelis C. Which children with febrile seizures need lumbar puncture? A decision analysis approach. Am J Dis Child. 1983;137.
8. Waruiru C, Appleton R. Febrile seizures: an update. Arch Dis Child [Internet]. 2004 Aug [cited 2023 Aug 28];89(8):751–6. Available from: https://pubmed.ncbi.nlm.nih.gov/15269077/
9. Shinnar S, Glauser T. Febrile seizures. J Child Neurol. 2002;17.
10. Fetveit A. Assessment of febrile seizures in children. Eur J Pediatr. 2008;167.
11. Verburgh M, Bruijnzeels M, Wouden J van der, Suijlekom-Smit L van, Velden J van der. Incidence of febrile seizures in the Netherlands. Neuroepidemiology. 1992;11.
12. Stuijvenberg M van, Moll H, Steyerberg E, Gijssel E van, Moons K. The duration of febrile seizures and peripheral leukocytosis. J Pediatr. 1998;133.
13. Green SM, Rothrock SG, Clem KJ, Zurcher RF, Mellick L. Can seizures be the sole manifestation of meningitis in febrile children? Pediatrics. 1993;92(4):527–34.
14. Offringa M, Beishuizen A, Derksen-Lubsen G, Lubsen J. Seizures and fever: can we rule out meningitis on clinical grounds alone? ClinPediatr (Phila). 1992;31.
15. Seltz L, Cohen E, Weinstein M. Risk of bacterial or herpes simplex virus meningitis/encephalitis in children with complex febrile seizures. PediatrEmerg Care. 2009;25.

16. Dubos F, Rocque FD la, Levy C, Bingen E, Aujard Y. Sensitivity of the bacterial meningitis score in 889 children with bacterial meningitis. J Pediatr. 2008;152.
17. Tunkel AR, Hartman BJ, Kaplan SL, Kaufman BA, Roos KL, Scheld WM, et al. Practice Guidelines for the Management of Bacterial Meningitis. Clinical Infectious Diseases [Internet]. 2004 Nov 1 [cited 2017 Nov 27];39(9):1267–84. Available from: https://academic.oup.com/cid/article-lookup/doi/10.1086/425368
18. Adjunctive dexamethasone treatment in acute bacterial meningitis. Lancet Neurol [Internet]. 2004 Jan 1 [cited 2017 Nov 27];3(1):54–62. Available from: http://www.sciencedirect.com/science/article/pii/S1474442203006239
19. Leppert D, Leib SL, Grygar C, Miller KM, Schaad UB, Holländer GA. Matrix Metalloproteinase (MMP)-8 and MMP-9 in Cerebrospinal Fluid during Bacterial Meningitis: Association with Blood-Brain Barrier Damage and Neurological Sequelae. Clinical Infectious Diseases [Internet]. 2000 Jul 1 [cited 2017 Nov 27];31(1):80–4. Available from: https://academic.oup.com/cid/article-lookup/doi/10.1086/313922
20. Wispelwey B, Tunkel AR, Scheld WM. Bacterial meningitis in adults. Infect Dis Clin North Am [Internet]. 1990 Dec [cited 2017 Nov 27];4(4):645–59. Available from: http://www.ncbi.nlm.nih.gov/pubmed/2277193
21. Pomeroy SL, Holmes SJ, Dodge PR, Feigin RD. Seizures and Other Neurologic Sequelae of Bacterial Meningitis in Children. New England Journal of Medicine [Internet]. 1990 Dec 13 [cited 2017 Nov 27];323(24):1651–7. Available from: http://www.nejm.org/doi/abs/10.1056/NEJM199012133232402
22. Trainor J, Hampers L, Krug S, Listernick R. Children with first-time simple febrile seizures are at low risk of serious bacterial illness. AcadEmerg Med. 2001;8.