



ORIGINAL ARTICLE

Prevalence and risk factors of seizure in children with acute bacterial meningitis: updating previous evidence using an epidemiological design

How to Cite This Article: Ataei Nakhaei A , Bakhtiari E, Ghahremani S, Akhondian J, Sasan MS, Movahed M, Aelami MH . Prevalence and risk factors of seizure in children with acute bacterial meningitis: updating previous evidence using an epidemiological design. Iran J Child Neurol. Summer 2021; 15(3): 47-54

Alireza ATA EI NAKHAEI MD¹,
Elham BAKHTIARI MD²,
Sara GHAREMANI MD¹,
Javad AKHONDIAN MD³,
Mohammad Saeed SASAN MD⁴,
Malihe MOVAHED MD¹,
Mohammad Hassan AELAMI MD⁴

1. Department of Pediatrics,
Faculty of Medicine, Mashhad
University of Medical Sciences,
Mashhad, Iran
2. Eye Research Center, Mashhad
University of Medical Sciences,
Mashhad, Iran
3. Department of Pediatric Neu-
rology, Faculty of Medicine,
Mashhad University of Medical
Sciences, Mashhad, Iran
4. Infection Control & Hand Hy-
giene Research Center, Mashhad
University of Medical Sciences,
Mashhad, Iran

Corresponding Author

Aelami MH MD.
Infection Control & Hand Hy-
giene Research Center, Mashhad
University of Medical Sciences,
Mashhad, Iran
Email: Aelamimh@mums.ac.ir

Received: 23-Jul-2018

Accepted: 18- Jan-2020

Abstract

Objective

The current study aimed to investigate the prevalence and risk factors of seizure in acute bacterial meningitis.

Materials & Methods

In the present study, a total of 180 children (age range, 2 months to 14 years) with acute bacterial meningitis, were separated into two groups based on the diagnosis of seizure. The study was conducted in Mashhad (Iran) from 2002 to 2016.

Results

Seizure occurred in 37.4% of children with bacterial meningitis. *Streptococcus pneumonia* (*S. pneumonia*) was the most common organism. Most of the children with seizures (53.7%) had more than one episode. Also, 35% of patients had neurologic complications. Complications were more related to the seizure occurrence, the number of episodes, prolonged seizure, and being younger than 12 months. Age categories of less than 1 year and 1-5 year were associated with increased risk of seizure (odds ratio: 4.33 and 6.54, respectively). The more episode of seizure was associated with more complications (odds ratio: 6.33).

Conclusion

The prevalence of seizures in acute bacterial meningitis was 37.4%. Besides, the seizure was associated with more complications. Hence, timely diagnosis and treatment of bacterial meningitis are necessary for preventing future consequences.

Keywords: Meningitis; Child, Seizure; Iran.

DOI: 10.22037/ijcn.v15i2.22250

Introduction

Acute bacterial meningitis (ABM) is a life-threatening infection with high morbidity and mortality in neonates and young children (1, 2). Every year it claims more than 171000 life worldwide (3). The mortality rate of bacterial meningitis ranges from 2 to 30% (3). Also, 10-20% of survived cases suffer from epilepsy and mental retardation (1). The mortality rate of ABM depends on age, pathogen, and geographic location (3). Furthermore, its epidemiology has changed considerably in the countries that adopted the conjugate vaccines against *Haemophilus influenzae* type b, *Neisseria meningitidis*, and *S. pneumoniae* (4). The ABM carries a higher burden in developing countries (4). Seizure is a common and unwelcome outcome of bacterial meningitis. The incidence rate of seizure in patients who suffer from ABM varies from 25 to 50% (5-7). Our literature review revealed that no recent study has been conducted on this issue in Iran, as a developing country. Hence, following a retrospective design (2002 to 2016) the current study aimed to evaluate the prevalence and risk factors of seizure in infants and children with acute bacterial meningitis in Iran.

Patients and methods

The current clinical study was conducted retrospectively in Imam Reza hospital, as a referral healthcare center, affiliated to the Mashhad University of Medical Sciences, Mashhad (Iran) from 2002 to 2016. The study is approved by the Ethics Committee of the Mashhad University Medical Sciences (IR.MUMS.FM.REC.1394.245). A total of 180 children (age range, 2 months to 14 years) with acute bacterial meningitis, were separated into two groups based on the diagnosis of seizure. The study was conducted in Mashhad

(Iran) from 2002 to 2016. The diagnosis of acute bacterial meningitis was documented based on the World Health Organization (WHO) protocol: Bacterial meningitis is defined by fever, headache, and one of the following signs: neck stiffness, altered consciousness, or other meningeal signs. Bacterial meningitis can be confirmed by isolation of a bacterial pathogen from a normally sterile clinical specimen such as CSF or identification of a bacterial antigen in normally sterile fluids or gram stain results.

Sample size

Following the enumeration method, the sample size was estimated at 180 subjects.

Analysis

Data were analyzed using SPSS version 16 (SPSS Institute, Inc., Chicago, IL, USA). All experimental values are presented as Mean \pm standard deviation (SD). The t-test was used to compare the study groups. The association between qualitative variables was calculated by the chi-square test. Risk factors were calculated according to the logistic regression model. Statistical significance was considered when p -value < 0.05 .

Results

Demographic

Of 180 participants, the seizure was observed in 67 patients (37.4%). Also, 111 patients (61.67%) were male and 69 (38.33%) were female. Besides, 55 patients with seizure (67.2%) and 66 without seizure (58.9%) were male, with no significant difference concerning the variable of gender ($p=0.2$). The mean age of participants was 36.25 ± 42.51 months, with a median of 13 months. The youngest and oldest participants were 2 and 158 months old. Forty-six patients with seizure (68.7%) and 36 without seizure (32.1%) were

aged less than 1 year, with a significant difference ($p=0.001$). Six patients (3.3%), including 4 with seizure and 2 without seizure, died during the study period. The demographic characteristics of participants are presented in Table 1.

Organisms

According to smear and CSF culture, *S. pneumoniae* was found in 16 (23.9%) patients with seizure and 25 (22.7%) without seizure. *H. influenza* type b was found in 4 (6%) and 12 (10.9%) patients with and without seizure, respectively. Forty-four (65.7%) and 67 patients (60.9%) with and without seizure had negative results, respectively. There was no significant difference between the study groups concerning the responsible organism ($p=0.54$). Also, the type of the organism was not different in patients with and without seizure. The results are presented in Table 2.

Seizure characteristics

Of 180 eligible patients, 67 (37.4%) had at least one episode of seizure. Type of seizure was generalized in 53 patients (79.1%). Also, 63 patients (35%) experienced neurologic complications including hydrocephaly ($n=20$; 31.7%), subdural effusion ($n=14$; 22.2%), and hearing impairment ($n=11$; 17%). Among patients with generalized seizure, 28 (52.8%) developed at least one complication. Of 67 patients with seizure, 36 (53.7%) had more than one episode of seizure. The prolonged seizure was observed in 17 (15.2%) patients. Seizure occurred before hospitalization in 23 patients (34.3%) and on the first day of admission in 22 patients (32.8%). Seizure characteristics are presented in Table 3. There was a significant difference concerning

the seizure occurrence, the number of seizure episodes, prolonged seizure, and being younger than 1 year old ($p=0.002$, 0.002, 0.007, and 0.0001, respectively). Complications were not significant according to the type of seizure, time of first seizure episode, gender, and mortality ($p>0.05$).

Laboratory characteristics

Among patients with seizure, 45 (69.2%) had CSF glucose less than 40 mg/dl. For patients without seizure, 70 cases (63.1%) had CSF glucose less than 40 mg/dl. The difference was not significant ($p=0.4$). Thirty patients (44.8%) with seizure had more than 1000 leukocytes in the CSF sample but in patients without seizure. In addition, 63 patients (56.2%) had more than 1000 leukocytes in the CSF sample; However, the difference was not significant ($p=0.2$).

Among patients with seizure, 58 (89.2%) had the CSF protein more than 40 mg/dl. In patients without seizure, 103 (92.8%) had the CSF protein more than 40 mg/dl ($p=0.4$). The results are presented in Table 4.

Risk factors

According to the results of the logistic regression, age less than 1 year and the age group of 1 to 5 years old had a significant association with seizure occurrence (OR= 4.33; CI: 4.33-42.22, $P=0.0001$; and OR=6.54; CI: 1.95-21.95, $P=0.002$, respectively). Again, according to the logistic regression, the number of seizure episodes had a significant association with complications incidence (OR= 6.33; CI: 1.77-22.63, $p=0.005$). Data are presented in Tables 5 and 6.

Prevalence and risk factors of seizure in children with acute bacterial meningitis

Table1. Demographic characteristics of 180 patients with acute bacterial meningitis

Variable	with seizure	without seizure	Total population	P value
Age				0.0001*
Less than 1 year	46 (68.7%)	36 (32.1%)	82 (45.8%)	
1-5 years	17 (25.4%)	32 (28.6%)	49 (27.2%)	
More than 5 years	4 (6%)	44 (39.3%)	48 (26.7%)	
Gender				0.27
Male	45 (67.2%)	66 (58.9%)	111 (61.7%)	
female	22 (32.8%)	46 (41.1%)	69 (38.3%)	

*Significant in chi square

Table2. Responsible organisms detected by smear and CSF culture in 180 patients with acute bacterial meningitis.

Variable	Streptococcus pneumoniae	Haemophilus influenza type b	Neisseria meningitides	Other oraginisms	No organism	Total	P value
With seizure	16 (23.9%)	4 (6%)	0	3 (4.5%)	44 (65.7%)	67 (100%)	0.54*
Without seizure	25 (22.7%)	12 (10.9%)	3 (2.7%)	3 (2.7%)	67 (60.9%)	110 (100%)	
Total	41 (23.2%)	16 (9%)	3 91.7%)	6 (3.4%)	111 (62.7%)	177 (100%)	

* Chi square

Table 3. Seizure characteristics of patients with acute bacterial meningitis

Seizure characteristics	Frequency (n)	Percent (%)
Type of seizure		
Focal	12	17.9
Generalized	53	79.1
Both	2	3
Total	67	100
Number of episodes		
Once	31	46.3
More than once	36	53.7
Total	67	100

Prevalence and risk factors of seizure in children with acute bacterial meningitis

Complication		
Hydrocephaly	20	31.7
Subdural effusion	14	22.2
Hearing impairment	11	17
Hydrocephaly and hearing impairment	7	11.1
Paresis	5	7.9
Cerebritis	2	3.2
Subdural effusion and paresis	1	1.6
Subdural effusion and cerebritis	1	1.6
Visual impairment	1	1.6
Hearing and visual impairment	1	1.6
Total	63	100
Status seizure	17	15.2
No status seizure	50	84.8
Total	67	100
Time of Seizure		
Before the third day	52	77.6
After the third day	15	22.4
Total	67	100

Table 4. Laboratory characteristics in 180 patients with acute bacterial seizure

variable	With seizure	Without seizure	P value
CSF glucose <40 mg/dl	45 (69.2%)	70 (63.1%)	0.4
Leukocyte>1000 cell/mm ³ in CSF sample	30 (44.8%)	63 (56.2%)	0.2
CSF protein > 40 mg/dl	58 (89.2%)	103 (92.8%)	0.41

Table 5. Odds ratio for involved variables in seizure incidence in patients with acute bacterial meningitis

variable	Odds ratio	CI (95%)	P value
Age<1 year	4.33	4.33-42.22	0.0001
Age between 1-5 year	6.54	1.95-21.95	0.002
Leukocytosis<100	1.78	0.6-5.2	0.29
Leukocytosis between 100-1000	1.36	0.64-2.88	0.41
Negative leukocytosis	3.29	0.06-171.35	0.55

Prevalence and risk factors of seizure in children with acute bacterial meningitis

Table 6. Odds ratio for involved variables in complication occurrence in patients with acute bacterial meningitis

Variable	Odds ratio	CI (95%)	P value
Number of seizure	6.33	1.77-22.63	0.005
prolonged seizure	1.43	0.35-5.74	0.6
Gender	2.5	0.73-7.61	0.14

Dissuasion

In the present study, 180 children with acute bacterial meningitis referred to the Imam Reza hospital for the period of 2002 to 2016 were recruited. The prevalence of seizure was 37.4%. Nearly 79% of patients had a generalized seizure and 15.2% had a prolonged seizure. For 34.3% of patients, the seizure occurred before the hospitalization. *S. pneumoniae* was the most common organism detected among the patients with or without seizure. Complication occurred in 35% of patients with the most frequency of hydrocephaly (31.7%). There was a significant difference between patients with and without seizure in the rate of complications. Several studies in different countries have investigated the rate of bacterial meningitis according to CSF cultures and reported that the rate of seizure associated with meningitis and the type of responsible organism depend on geographical area (5, 8-10).

According to the findings, the prevalence of seizure was 37.4%. Unfortunately, the rate of seizure in bacterial meningitis is more in developing countries. In a study in Brazil by Gomes, the rate of seizure in bacterial meningitis is reported at 38.1%. Or another study in Taiwan reported a rate of 47%, while rates of 27% and 31% are reported for the USA in 1985 and 1990 (5, 8, 9, 11). Also, according to the findings, the rate of mortality was 3.3%, which is in line with several studies that reported a prevalence of 3.8 to 12% (12-15).

In our study, being younger than one-year-old and age group of 1 to 5 years were associated with increased risk of seizure incidence in children with ABM; [OR= 4.33; **95% CI:** 4.33-42.22]. For those younger than one-year-old and (OR=6.54; **95% CI:** 1.95-21.95). For those aged one and five years old. In a study on 270 children with confirmed bacterial meningitis in Brazil, Corrêa-Lima et al. investigated the occurrence of in-hospital symptomatic seizures. Age less than 2 years (OR = 0.97; CI: 0.97-0.98), pneumococcal etiology (OR= 4.55; CI: 1.88-11.0), and altered mental status (OR= 3.47; CI=1.66-7.26) were associated with increased risk of seizure (16). The present study showed that patients with meningitis and seizure had significantly higher complications. Also, some other studies reported a significant association between seizure and complications like arthritis, subdural effusion, and hydrocephaly, and hearing impairment, which is in line with the findings of the present results (12, 17, 18). According to the findings of the present, study there was no significant difference concerning the seizure occurrence between boys and girls, while some studies reported a significant difference (19).

In this study, the frequency of seizure episodes was accompanied by experiencing more complications in patients with ABM (OR=6.33; **95% CI:** 1.77-22.63). Corrêa-Lima et al. reported that the mortality rate was higher among patients with intra-hospital epileptic seizures compared to those

without this health problem (25/67 [37.3%] vs 9/203 [4.43%], $P < .001$) (16).

Previous studies suggested that *S. pneumoniae* and *N. meningitidis* are the most common organisms causing ABM. In a study by Chinchankar in India on the common responsible organism for bacterial meningitis, it has been reported that *S. pneumoniae* and *H. influenza* are the most common responsible organisms (39% and 26%, respectively) (20). In another study in Greece (2011), *N. meningitidis* is recognized as a common organism in meningitis, with a rate of 63% (12). The findings of the present study are consistent with previous reports. In Iran, vaccination against *H. influenza* was started in 2014. Our findings indicated that the rate of *H. influenza* infection in children with meningitis was 11.4% before vaccination, which decreased to 3.2% after vaccination, which in turn indicates the critical role of vaccination in the prevention or decrement of bacterial meningitis.

In Conclusion

To conclude, the prevalence of seizure in patients with acute bacterial meningitis was 37.4%. Because of the significant association between seizure and complication, it is necessary to pay more attention to the exact and on-time diagnosis of acute bacterial meningitis, as it can decrease both hospitalization and cost of treatment and is associated with increased quality of life.

According to the findings, we suggest routine administration of *S. pneumoniae* vaccine for children aged 2, 4, and 6 months as well as those aged 12-18 months in Iran.

Acknowledgment

This work was financially supported by Mashhad University of Medical Sciences, Mashhad, Iran

(grant number: 931303).

Author's contribution

Alireza Ataei Nakhaei, Mohammad Hasan Aelami, Malihe Movahed: conception or design

Elham Bakhtiari, Mohammad Saeed Sasan, Javad Akhondian, Sara Ghahremani: acquisition, analysis

Elham Bakhtiari, Alireza Ataei Nakhaei, Mohammad Hasan Aelami, Malihe Movahed, Mohammad Saeed Sasan, Javad Akhondian, Sara Ghahremani: drafting the work

Elham Bakhtiari, Alireza Ataei Nakhaei, Mohammad Hasan Aelami, Malihe Movahed, Mohammad Saeed Sasan, Javad Akhondian, Sara Ghahremani: final approval

Conflict of interest

The authors declare that there is no conflict of interest.

References

1. Kim KS. Acute bacterial meningitis in infants and children. *The Lancet infectious diseases*. 2010;10(1):32-42.
2. Alsaeed G, Alsaeed I, Alsaeed M. Recurrent Bacterial Meningitis in Paediatrics. *American Journal of Pediatrics*. 2019;5(3):98-103.
3. Ceyhan M, Yildirim I, Balmer P, Borrow R, Dikici B, Turgut M, et al. A prospective study of etiology of childhood acute bacterial meningitis, Turkey. *Emerging infectious diseases*. 2008;14(7):1089.
4. Brouwer MC, Tunkel AR, van de Beek D. Epidemiology, diagnosis, and antimicrobial treatment of acute bacterial meningitis. *Clinical microbiology reviews*. 2010;23(3):467-92.
5. Chang C-J, Chang H-W, Chang W-N, Huang L-T, Huang S-C, Chang Y-C, et al. Seizures

- complicating infantile and childhood bacterial meningitis. *Pediatric neurology*. 2004;31(3):165-71.
6. Murthy JMK, Prabhakar S. Bacterial meningitis and epilepsy. *Epilepsia*. 2008;49:8-12.
 7. Zoons E, Weisfelt M, De Gans J, Spanjaard L, Koelman J, Reitsma J, et al. Seizures in adults with bacterial meningitis. *Neurology*. 2008;70(22 Part 2):2109-15.
 8. Rosman NP, Peterson DB, Kaye EM, Colton T. Seizures in bacterial meningitis: prevalence, patterns, pathogenesis, and prognosis. *Pediatric neurology*. 1985;1(5):278-85.
 9. Gomes I, Melo A, Lucena R, Cunha-Nascimento MH, Ferreira A, Góes J, et al. Prognosis of bacterial meningitis in children. *Arquivos de neuro-psiquiatria*. 1996;54(3):407-11.
 10. Mehrdadi S. Acute Bacterial Meningitis: Diagnosis, Treatment and Prevention. *Journal of Archives in Military Medicine*. 2019(In Press).
 11. Pomeroy SL, Holmes SJ, Dodge PR, Feigin RD. Seizures and other neurologic sequelae of bacterial meningitis in children. *New England journal of medicine*. 1990;323(24):1651-7.
 12. Vasilopoulou VA, Karanika M, Theodoridou K, Katsioulis AT, Theodoridou MN, Hadjichristodoulou CS. Prognostic factors related to sequelae in childhood bacterial meningitis: data from a Greek meningitis registry. *BMC infectious diseases*. 2011;11(1):214.
 13. Kaaresen P, Flaegstad T. Prognostic factors in childhood bacterial meningitis. *Acta Paediatrica*. 1995;84(8):873-8.
 14. Daoud A, Al-Sheyyab M, Batchoun R, Rawashdeh M, Nussair M, Pugh R. Bacterial meningitis: still a cause of high mortality and severe neurological morbidity in childhood. *Journal of tropical pediatrics*. 1995;41(5):308-10.
 15. Bundy LM, Noor A. Neonatal Meningitis. *StatPearls [Internet]: StatPearls Publishing*; 2019.
 16. Corrêa-Lima ARM, de Barros Miranda-Filho D, Valença MM, Andrade-Valença L. Risk factors for acute symptomatic seizure in bacterial meningitis in children. *Journal of child neurology*. 2015;30(9):1182-5.
 17. Pelkonen T, Roine I, Monteiro L, Correia M, Pitkäranta A, Bernardino L, et al. Risk factors for death and severe neurological sequelae in childhood bacterial meningitis in sub-Saharan Africa. *Clinical infectious diseases*. 2009;48(8):1107-10.
 18. Singhi P, Bansal A, Geeta P, Singhi S. Predictors of long term neurological outcome in bacterial meningitis. *Indian journal of pediatrics*. 2007;74(4):369-74.
 19. Kazemi A, Pormansury L. the Study of Early Complications of the Bacterial Meningitis in Admitted Children Patients in the Years. 2001.
 20. Chinchankar N, Mane M, Bhav S, Bapat S, Bavdekar A, Pandit A, et al. Diagnosis and outcome of acute bacterial meningitis in early childhood. *Indian pediatrics*. 2002;39(10):914-21.