ISSN: 2588-4115; Infection Epidemiology and Microbiology. 2019;5(4):17-24

A Five-Year Retrospective Multicenter Study on Etiology and Antibiotic Resistance Pattern of Bacterial Meningitis Among Iranian Children

ARTICLE INFO

Article Type
Original Research

Authors
Nahal Hadi, *PhD*[1,2*]
Khosrow Bagheri, *MD* [2]

How to cite this article
Hadi N. Bagheri Kh, A Five-Year Retrospective Multicenter Study on Etiology and Antibiotic Resistance Pattern of Bacterial Meningitis Among Iranian Children. Infection Epidemiology and Microbiology. 2019;5(4): 17-24

[1]Department of Bacteriology and Virology, School of medicine, Shiraz University of Medical Sciences, Shiraz, Iran
[2]Bioinformatics and Computational Biology Research Center, Shiraz University of Medical Sciences, Shiraz, Iran

*** Correspondence***
Address: Department of Bacteriology & Virology, School of Medicine, Shiraz University of Medical Sciences, Zand St, Imam Hossein Sq, Shiraz, Iran.
Phone: +98713 2304356
nahalhadi@gmail.com

Article History
Received: October 21 ,2019
Accepted: December 30 ,2019
Published: January 8 ,2019

ABSTRACT

Background: Bacterial meningitis is a devastating infection associated with significant morbidity and mortality rate among neonates and young children. Early identification and treatment of the causative agents of meningitis is crucial due to high fatality rate in untreated cases. The present study aimed to investigate the common bacterial etiology and occurrence of antimicrobial resistance in patients suspected to meningitis in southwestern Iran.
Materials & Methods: This retrospective cross-sectional study was conducted during a five-year period from January 2011 to January 2016 at two major hospitals in southwestern Iran. CSF samples were aseptically collected in BACTEC™, and conventional methods were used for the bacteria isolation and identification. Antimicrobial susceptibility tests were done using disk diffusion and E-test methods.
Findings: Out of 89 CSF samples collected from children under 17 years, the number of culture positive specimens was 21 (23.6%). The highest number of culture positive cases was observed in patients younger than 5 years (57.1 %). The most frequent pathogens were *Streptococcus pneumonia* (N = 10, 47.6%), followed by *Haemophilus* spp. (N = 3, 14.3%), and *Neisseria meningitidis* (N = 3, 14.3%). Antibacterial susceptibility testing results showed that *S. pneumoniae* isolates were mostly susceptible to vancomycin and chloramphenicol. Moreover, among *N. meningitides* and *Haemophilus* isolates, the most effective in *vitro* drug was ceftriaxone (100%).
Conclusions: These results showed the promising activity of several locally available antibiotics against *S. pneumoniae*, *Haemophilus* spp. and *N. meningitides,* as the most common causative agents of bacterial meningitis in Iranian children. Therefore, such regional studies help prevent and control the burden of infections.

Keywords: Meningitis, Antibiotic resistance, Children, *Neisseria meningitides*, *Streptococcus pneumonia*, *Haemophilus influenzae*

CITATION LINKS

[1] Ku LC, Boggess KA, Cohen-Wolkowiez M. Bacterial ... [2] Lundbo LF, Benfield T. Risk factors for ... [3] Shrestha RG, Tandukar S, Ansari S, Subedi A, Shrestha A, Poudel R, et al. Bacterial ... [4] Failace L, Wagner M, Chesky M, Scalco R, Jobim LF. Simultaneous... [5] Tunkel AR, Hartman BJ, Kaplan SL, Kaufman BA, Roos KL, Scheld WM, et al. Practice guidelines for... [6] Tacon CL, Flower O. Diagnosis and management of... [7] Aletayeb MH, Ahmad FS, Masood D. Eleven-year study of causes of neonatal bacterial... [8] Brouwer MC, Tunkel AR, van de Beek D. Epidemiology, diagnosis, and antimicrobial... [9] El Bashir H, Laundy M, Booy R. Diagnosis... [10] Tzanakaki G, Mastrantonio P. Aetiology of bacterial meningitis... [11] Mahun C, Manuselis G. Diagnostic... [12] Clinical and Laboratory Standards Institute... [13] Li W, Sun X, Yuan F, Gao Q, Ma Y, Jiang Y, et al. Diagnostic accuracy of... [14] Furyk JS, Swann O, Molyneux E. Systematic review: Neonatal meningitis in... [15] Mahmoudi S, Zandi H, Pourakbari B, Ashtiani MT, Mamishi S. Acute bacterial... [16] Mashouf RY, Hashemi SH, Bijarchi M. Bacterial agents of meningitis in children... [17] Zamani A, Zamani F. Cerebrospinal fluid ... [18] Heydarian F, Ashrafzadeh F, Rostazadeh A. Predicting factors and... [19] Laving AM, Musoke RN, Wasunna AO, Revathi G. Neonatal bacterial... [20] Ahmed R. Cerebro spinal fluid analysis in... [21] May M, Daley AJ, Donath S, Isaacs D. Early onset neonatal... [22] Reta MA, Zeleke TA. Neonatal bacterial meningitis in Tikur Anbessa... [23] Nwadioha SI, Nwokedi EO, Onwuezube I, Egesie JO, Kashibu E. Bacterial isolates ... [24] Abdinia B, Ahangarzadeh Rezaee M, Abdoli Oskouie S. Etiology and antimicrobial... [25] Khan N, Malik A, Rizvi M, Afzal K, Pasha Z. Epidemiology and... [26] Rezaeizadeh G, Pourakbari B, Ashtiani MH, Asgari F, Mahmoudi S, Mamishi S. Antimicrobial... [27] Motamedifar M, Sedigh Ebrahim-Saraie H, Mansury D, Nikokar I, Hashemizadeh Z. Prevalence of etiological... [28] Oordt-Speets AM, Bolijn R, van Hoorn RC, Bhavsar A, Kyaw MH. Global etiology of... [29] Haghi Ashtiani MT, Sadeghian M, Nikmanesh B, Pourakbari B, Mahmoudi S, Mamishi S. Antimicrobial...

Introduction

Bacterial meningitis is a devastating infection associated with significant morbidity and mortality rate among neonates and young children, which is often more prevalent in developing countries [1]. Several risk factors contribute to the development of bacterial meningitis, including socioeconomic status, behavioral risk factors, age-related factors, and immunization [2]. Different types of bacteria could cause bacterial meningitis, depending on patient's age group and geographical area [3]. More than two-thirds of bacterial meningitis cases are caused by *Neisseria meningitidis, Streptococcus pneumoniae*, and *Haemophilus influenza* [4]. Bacterial meningitis is accompanied by several consequences such as increased cost of care, hospital stay, and patient mortality [5].

Early identification and treatment of the causative agents of meningitis is crucial due to high fatality rate in untreated cases [6]. In this regard, cerebrospinal fluid (CSF) culture accompanied by the evaluation of glucose, protein, and leukocyte levels is a proven, rapid, and low-cost test for the diagnosis of bacterial meningitis [7]. Signs of meningitis are often nonspecific, particularly in neonates; thus, immediate empirical therapy should be initiated based on clinical suspicion until meningitis is diagnosed by CSF examination [8]. Empirical antibiotic therapy has a crucial role on the outcomes and adverse effects of bacterial meningitis, but the efficacy of treatment significantly depends on the local resistance pattern [9]. Updated susceptibility patterns toward locally used antibiotics are of utmost priority to overcome serious consequences of bacterial meningitis [8, 10].

Objectives: To the best of our knowledge, there is a lack of published reports available on local etiology and antimicrobial resistance patterns of bacterial meningitis among vulnerable populations, particularly pediatric and neonates. Therefore, the present study aimed to investigate the common bacterial etiology and the occurrence of antimicrobial resistance in patients suspected to meningitis in southwestern Iran.

Materials and methods

Study design and subjects: This retrospective cross-sectional study was conducted during a five-year period from January 2011 to January 2016 at two major hospitals of Nemazee and Dastgheib, affiliated to Shiraz University of Medical Sciences, Southwestern Iran. During the study period, demographic and clinical information of children (1 month to 17 years old) suspected to meningitis were recorded based on the compatible clinical manifestations (fever, headache, neck stiffness, etc.) sought by physicians. Patients with incomplete and out-of-range medical records were excluded. This study was in accordance with the declaration of Helsinki and approved by the Ethics Committee of the Shiraz University of Medical Sciences. However, since only medical records were used, and patients were not disturbed, and also as the details were kept strictly confidential, the committee waived the informed consent.

Samples collection and bacteria identification: CSF specimens were aseptically collected by lumbar puncture at the discretion of the attending physicians and transferred into sterile tube. Clinical specimens were immediately transported to the microbiology laboratory in less than 20 minutes. CSF samples were inoculated simultaneously into BACTEC medium and processed using the BACTEC (Model: 9120 and 9050) instrument (Becton Dickinson, NJ, USA). Conventional bacteriological methods were used for the bacteria isolation and identification. CSF specimens were

[DOR: 20.1001.1.25884107.2019.5.4.4.1]

inoculated into culture media containing 5% sheep blood agar, chocolate agar, and enrichment broth thioglycollate (Merck, Germany) and incubated up to 48 hours in humid air with 5-10% CO_2. The grown bacteria were examined for colony morphology as well as Gram-staining characteristics and identified using standard microbiological methods [11].

Antimicrobial susceptibility testing: Antimicrobial susceptibility test was performed for all pathogens, except for *Brucella* isolates, using the disk diffusion method in accordance with the Clinical and Laboratory Standards Institute (CLSI) recommendations [12]. The antimicrobial disks (HiMedia, India) were selected specifically for each pathogen based on CLSI recommendations. Minimum inhibitory concentrations (MICs) were determined for *Brucella* isolates using E-test (Liofilchem, Italy) according to CLSI guidelines.

Pseudomonas aeruginosa ATCC 27853 and *S. aureus* ATCC 25923 were selected for susceptibility testing of each individual bacterium based on CLSI recommendations.

Statistical analysis: The analysis was performed using SPSS™ software, Version 21.0 (IBM Corp., USA). The results were presented as descriptive statistics in terms of relative frequency. Values were expressed as mean ± standard deviation (continuous variables) or the group percentage (categorical variables).

Findings

A total of 89 CSF samples were collected from children under 17 years, suspected to bacterial meningitis during a five-year period at two studied hospitals. Out of 89 CSF samples, the number of culture-positive specimens was 21 (n = 23.6%). Out of 21 (23.6%) culture-positive cases, 71.4 and 28.6% were from boys and girls samples, respectively.

Regarding the patients' age group, the highest number of positive-culture cases were observed in the age group lower than 5 years (57.1 %), and the rest were observed in the age group of 5–17 years. The detailed results of bacterial isolation rate according to the pathogen type and patient's age group are shown in Table 1. The most frequent Gram-positive bacteria were *S. pneumonia* (N = 10, 47.6%) and coagulase-negative *Staphylococci* (N = 2, 9.4%), while the most frequent Gram-negative bacteria were *N. meningitidis* (N = 3, 14.3%), followed by *Haemophilus* (N = 3, 14.3%).

Antibacterial susceptibility testing results showed that among Gram-positive bacteria, *S. pneumoniae* showed a high resistance against co-trimoxazole (90%) and penicillin (70%), while the highest resistance of coagulase-negative *Staphylococci* was observed toward tetracycline (100%) and erythromycin (100%). Furthermore, all of the *S. pneumonia* and coagulase-negative *Staphylococci* isolates were susceptible to vancomycin, gentamicin, and rifampin. For *N. meningitides* and *Haemophilus* isolates, the most effective *in vitro* antibiotic was ceftriaxone (100%), whereas all of the *N. meningitides* and *Haemophilus* isolates were resistant against co-trimoxazole and ciprofloxacin, respectively. A single isolate of *Escherichia coli* was found to be resistant to all antibiotics tested, except for ciprofloxacin, amikacin, cefoxitin, and imipenem. Based on the MIC test results, a single isolate of *Brucella* spp. was susceptible to all tested antibiotics. The full antimicrobial susceptibility patterns of bacterial pathogens isolated from CSF samples are shown in Table 2.

Discussion

The primary treatment of meningitis is usually empirical, since rapid and accurate identification of etiological agents could be time-consuming and expensive to improve

[DOR: 20.1001.1.25884107.2019.5.4.4.1]

Table 1) The detailed results of bacterial isolation rate in relation to the type of pathogens and age groups

Bacteria	Frequency	Male	Female	Age ≤ 5 Year	Age≥ 5 Year	2011-2012	2012-2013	2013-2014	2014-2015	2015-2016
S. pneumoniae	10	7	3	5	5	3	2	1	2	2
Haemophilus spp.	3	3	-	3	-	2	1	-		-
N. meningitidis	3	2	1	1	2	1	-	1	1	-
Coagulase-negative *Staphylococci*	2	1	1	1	1	-	1	-	1	-
E. coli	1	1	-	1	-	-	-	1	-	-
P. aeruginosa	1	1	-	1	-	-	-	-	1	-
Brucella spp.	1	-	1	-	1	-	-	-	-	1

patient health [13].

Since age group and geographical variation influence the etiology of bacterial meningitis, they also significantly influence the choice of appropriate therapy [2]. Measures to reduce high morbidity and mortality rate, especially in neonatal meningitis, demand for information based on periodic surveillance in order for reducing the risk of complications in such critically ill patients [14].

In the present study, the rate of bacterial isolation from the examined CSF samples was 23.6%. Compared to the previous studies in Iran, the isolation rate in this study was lower than those reported in Mahmoudi et al.'s (2013) study among 5-month to 10-year-old children suspected to invasive bacterial infection (64.5%) [15] and in Yousefi-Mashouf et al.'s (2006) study among children under 10 years (21.5%) [16]. However, the isolation rate in this study was higher than those reported in Zamani et al.'s (2005) study among newborns less than 28 days (5.1%) [17] and in Heydarian et al.'s (2014) study among 6-18 month old children (6.25%) [18]. At global scale, the isolation rate in children suspected to meningitis was reported as 17.9% in Kenya [19], 10.6% in Oman [20], 9.2% in Australia [21], 4.7% in Ethiopia [22], and 3.3% in Nigeria [23]. The observed discrepancy in bacterial isolation rate may be due to differences in geographical distribution, infection control policies, diagnostic methods, and samples size.

In the present study, the most common bacterial agent of meningitis was *S. pneumoniae,* followed by *Haemophilus* spp. and *N. meningitides*. Previously, several authors from different parts of Iran introduced *S. pneumoniae*, *H. influenza*, and *N. meningitides* as the most prevalent pathogens among Iranian children suffering from meningitis, consistent with the present

[DOR: 20.1001.1.25884107.2019.5.4.4.1]

Table 2) Antimicrobial susceptibility patterns of pathogens isolated from CSF cultures

Bacteria	Antimicrobial agent	Resistant No. (%)	Susceptible No. (%)
S. pneumonia (N = 10)	Erythromycin	3 (30)	7 (70)
	Ceftriaxone	4 (40)	6 (60)
	Clindamycin	3 (30)	7 (70)
	Chloramphenicol	1 (10)	9 (90)
	Penicillin	7 (70)	3 (30)
	Co-trimoxazole	9 (90)	1 (10)
	Vancomycin	0	10 (100)
N. meningitides (N = 3)	Ceftriaxone	0	3 (100)
	Chloramphenicol	0	3 (100)
	Co-trimoxazole	3 (100)	0
	Amikacin	0	3 (100)
Haemophilus spp. (N = 3)	Ceftriaxone	0	3 (100)
	Ampicillin	2 (66.7)	1 (33.3)
	Tetracycline	1 (33.3)	2 (66.7)
	Azithromycin	0	3 (100)
	Chloramphenicol	0	3 (100)
	Ciprofloxacin	3 (100)	0
	Co-trimoxazole	2 (66.7)	1 (33.3)
Coagulase negative *Staphylococci* (N = 2)	Ciprofloxacin	1 (50)	1 (50)
	Tetracycline	2 (100)	0
	Rifampin	0	2 (100)
	Erythromycin	2 (100)	0
	Chloramphenicol	0	2 (100)
	Gentamicin	0	2 (100)
	Penicillin	1 (50)	1 (50)
	Cefoxitin	1 (50)	1 50)
	Co-trimoxazole	1 (50)	1 (50)
E. coli (N =1)	Ciprofloxacin	0	1 (100)
	Ampicillin	1 (100)	0
	Ceftazidim	1 (100)	0
	Cefoxitin	0	1 (100)
	Ceftriaxone	1 (100)	0
	Cefexim	1 (100)	0
	Amikacin	0	1 (100)
	Imipenem	0	1 (100)
	Cephalotin	1 (100)	0
	Co-trimoxazole	1 (100)	0
P. aeruginosa (N =1)	Ciprofloxacin	0	1 (100)
	Amikacin	0	1 (100)
	Ceftazidime	1 (100)	0
	Aztreonam	1 (100)	0
	Imipenem	0	1 (100)
	Tobramycin	0	1 (100)
Brucella spp. (N =1)	Co-trimoxazole	0	1 (100)
	Ciprofloxacin	0	1 (100)
	Gentamicin	0	1 (100)
	Rifampicin	0	1 (100)
	Doxycycline	0	1 (100)

study results [15, 16, 24].

In a study in India, the etiology of acute bacterial meningitis in children was investigated. *Pneumococcus* and Gram-negative isolates were identified as the most common pathogens. In their study, the prevalence rate of *Pneumococcus* was in line with the present study result [25].

Moreover, there are several comparable reports showing that coagulase-negative *Staphylococci* strains are one the most common causative agents of bacterial meningitis in Iranian children [26-27]. Moreover, despite high geographical diversity, reports about *S. pneumoniae*, *N. meningitides, H. influenza*, and Gram-negative rods, as the leading causes of bacterial meningitis, are almost the same in pediatric and neonatal population globally [21-23, 28]. Early antibiotic treatment prevents true identification of bacterial agents widespread in the region, which could be the reason for low or no detection of other agents by culture method. Moreover, the sensitivity and specificity of used diagnostic methods could be effective in detecting the etiologic agents of meningitis [25].

In the present study, *S. pneumoniae* isolates as the prevalent agents of meningitis showed high susceptibility toward vancomycin, chloramphenicol, and third generation cephalosporins. In agreement with the present study findings, Haghi Ashtiani et al. (2014) in a study conducted in an Iranian referral children hospital during an 11-year period, showed that a total of 194 *S. pneumoniae* isolates were mostly susceptible to vancomycin, followed by cephalosporins, ampicillin, and chloramphenicol [29].

Despite the increasing trend of penicillin-insusceptible *N. meningitides* strains, the isolates in this study were fully susceptible to third-generation cephalosporins; therefore, this antibiotic could currently be considered as a drug of choice for empirical therapy of related infections. Meanwhile, Abdinia et al. (2014) showed complete susceptibility of *N. meningitides* isolates obtained from Iranian children with acute bacterial meningitis to ceftriaxone, chloramphenicol, and amikacin, consistent with the present study results [24].

Haemophilus isolates in the present study were fully susceptible to ceftriaxone, azithromycin, and chloramphenicol. The closest results to the present study results were the results of Abdinia et al.'s (2014) study that showed the susceptibility of *H. influenza* isolates to chloramphenicol and ceftriaxone as 100 and 80%, respectively [24].

Finally, the limitation of this study was that due to lack of access to patients, it was not possible to investigate further aspects of infections. Also, due to lack of patients' follow-up, it was not possible to evaluate the effectiveness of targeted antibiotic therapy based on the antimicrobial susceptibility testing results.

Conclusion

This study results introduced *S. pneumoniae*, *Haemophilus* spp., and *N. meningitides* as the most common causative agents of bacterial meningitis in children less than 17 years in this. Hopefully, several locally available antibiotics showed promising activity against these pathogens. Managing meningitis among pediatric and neonatal population requires comprehensive regional specific investigations on the current etiology and risk factors of this complication. Therefore, such regional studies would help prevent and control the burden of infections and also could be useful for comparing the status of the study area with other areas.

Acknowledgements: We are thankful to all Members of the Department of Bacteriology and Virology and Shiraz University of Medical Sciences.

Ethical Permissions: The study protocol

[DOR: 20.1001.1.25884107.2019.5.4.4.1]

was approved by the Ethics Committee of Shiraz University of Medical Sciences.

Conflict of interests: The authors declare that they have no comp eting interests.

Authors ' Contribution: NH, KB: Designed, and supervised the study and revised the manuscript.

Fundings: This study was supported by Shiraz University of Medical Sciences with grant No. 94-9702.

References:

1. Ku LC, Boggess KA, Cohen-Wolkowiez M. Bacterial meningitis in infants. Clin Perinatol. 2015;42(1):29-45.
2. Lundbo LF, Benfield T. Risk factors for community-acquired bacterial meningitis. Infect Dis. 2017;49(6):433-44.
3. Shrestha RG, Tandukar S, Ansari S, Subedi A, Shrestha A, Poudel R, et al. Bacterial meningitis in children under 15 years of age in Nepal. BMC Pediatr. 2015;15(1):94.
4. Failace L, Wagner M, Chesky M, Scalco R, Jobim LF. Simultaneous detection of Neisseria meningitidis, Haemophilus influenzae and Streptococcus sp. by polymerase chain reaction for the diagnosis of bacterial meningits. Arq Neuro-Psiquiat. 2005;63(4):920-4.
5. Tunkel AR, Hartman BJ, Kaplan SL, Kaufman BA, Roos KL, Scheld WM, et al. Practice guidelines for the management of bacterial meningitis. Clin Infect Dis. 2004;39(9):1267-84.
6. Tacon CL, Flower O. Diagnosis and management of bacterial meningitis in the paediatric population: A review. Emerg Med Int. 2012;2012:320309.
7. Aletayeb MH, Ahmad FS, Masood D. Eleven-year study of causes of neonatal bacterial meningitis in Ahvaz, Iran. Pediatr Int. 2010;52(3):463-6.
8. Brouwer MC, Tunkel AR, van de Beek D. Epidemiology, diagnosis, and antimicrobial treatment of acute bacterial meningitis. Clin Microbiol Rev. 2010;23(3):467-92.
9. El Bashir H, Laundy M, Booy R. Diagnosis and treatment of bacterial meningitis. Arch Dis Child. 2003;88(7):615-20.
10. Tzanakaki G, Mastrantonio P. Aetiology of bacterial meningitis and resistance to antibiotics of causative pathogens in Europe and in the Mediterranean region. Int J Antimicrob Agents. 2007;29(6):621-9.
11. Mahun C, Manuselis G. Diagnostic microbiology. Londen: WB Saunderes Company; 1995, 58-96.
12. Clinical and Laboratory Standards Institute (CLSI). M100S: Performance standards for antimicrobial susceptibility esting; Informational supplement. 26 Edition. Wayne, PA: Clinical and Laboratory Standards Institute; 2016.
13. Li W, Sun X, Yuan F, Gao Q, Ma Y, Jiang Y, et al. Diagnostic accuracy of cerebrospinal fluid procalcitonin in bacterial meningitis patients with empiric antibiotic pretreatment. J Clin Microbiol. 2017;55(4):1193-204.
14. Furyk JS, Swann O, Molyneux E. Systematic review: Neonatal meningitis in the developing world. Trop Med Int Health. 2011;16(6):672-9.
15. Mahmoudi S, Zandi H, Pourakbari B, Ashtiani MT, Mamishi S. Acute bacterial meningitis among children admitted into an Iranian referral children's hospital. Jpn J Infect Dis. 2013;66(6):503-6.
16. Mashouf RY, Hashemi SH, Bijarchi M. Bacterial agents of meningitis in children and detection of their antibiotic resistance patterns in Hamadan, Western Iran. Pak J Bio Sci. 2006;9(7):1293-8.
17. Zamani A, Zamani F. Cerebrospinal fluid findings in neonatal bacterial meningitis. Med J Islam Repub Iran (MJIRI).

2005;19(3):241-5.
18. Heydarian F, Ashrafzadeh F, Rostazadeh A. Predicting factors and prevalence of meningitis in patients with first seizure and fever aged 6 to 18 months. Neurosciences (Riyadh). 2014;19(4):297-300.
19. Laving AM, Musoke RN, Wasunna AO, Revathi G. Neonatal bacterial meningitis at the newborn unit of Kenyatta National Hospital. East Afr Med J. 2003;80(9):456-62.
20. Ahmed R. Cerebro spinal fluid analysis in childhood bacterial meningitis. Oman Med J. 2008;23(1):32-3.
21. May M, Daley AJ, Donath S, Isaacs D. Early onset neonatal meningitis in Australia and New Zealand, 1992-2002. Arch Dis Child Fetal Neonatal Ed. 2005;90(4):F324-7.
22. Reta MA, Zeleke TA. Neonatal bacterial meningitis in Tikur Anbessa specialized hospital, Ethiopia: A 10-year retrospective review. Springerplus. 2016;5(1):1971.
23. Nwadioha SI, Nwokedi EO, Onwuezube I, Egesie JO, Kashibu E. Bacterial isolates from cerebrospinal fluid of children with suspected acute meningitis in a Nigerian tertiary hospital. Niger Postgrad Med J. 2013;20(1):9-13.
24. Abdinia B, Ahangarzadeh Rezaee M, Abdoli Oskouie S. Etiology and antimicrobial resistance patterns of acute bacterial meningitis in children: A 10-year referral hospital-based study in northwest Iran. Iran Red Crescent Med J. 2014;16(7):e17616.
25. Khan N, Malik A, Rizvi M, Afzal K, Pasha Z. Epidemiology and drug resistance profile of acute bacterial meningitis in children in Northern India: A university hospital perspective. Asian Pac J Trop Dis. 2014;4:S818-S23.
26. Rezaeizadeh G, Pourakbari B, Ashtiani MH, Asgari F, Mahmoudi S, Mamishi S. Antimicrobial susceptibility of bacteria isolated from cerebrospinal fluids in an Iranian referral pediatric center, 1998-2008. Maedica (Buchar). 2012;7(2):131-7.
27. Motamedifar M, Sedigh Ebrahim-Saraie H, Mansury D, Nikokar I, Hashemizadeh Z. Prevalence of etiological agents and antimicrobial resistance patterns of bacterial meningitis in Nemazee hospital, Shiraz, Iran. Arch Clin Infect Dis. 2015;10(2):e22703.
28. Oordt-Speets AM, Bolijn R, van Hoorn RC, Bhavsar A, Kyaw MH. Global etiology of bacterial meningitis: A systematic review and meta-analysis. PLoS One. 2018;13(6):e0198772.
29. Haghi Ashtiani MT, Sadeghian M, Nikmanesh B, Pourakbari B, Mahmoudi S, Mamishi S. Antimicrobial susceptibility trends among Streptococcus pneumoniae over an 11-year period in an Iranian referral children hospital. Iran J Microbiol. 2014;6(6):382-6.