Theory Clin Pract Pediatr, 2024, 5: 130-136
DOI: 10.25082/TCPP.2024.01.004

REVIEW

Bacteriological profile of meningitis in children aged 3 months to 15 years in sub-Saharan Africa: About a systematic review and critical reading of the literature

Véronique Vinick Lumaya[1,*] **Tacite Kpanya Mazoba**[2,3,*] **Stéphanie Mikalo Mbambi**[4] **Ariane Mankiele Keto**[1] **Mamy-gloire Manzi Monkoti**[1] **Jennyfer Misengabu Lembalemba**[1] **Joelle Ambis Lumaya**[5] **Irène Kifutu Matula**[1] **Michel Basila Kenye**[6] **Hortense Azama Mumba**[6] **Joseph Mabiala Bodi**[1]

[1] Department of Pediatrics, University Clinics of Kinshasa, Kinshasa, DR Congo
[2] Department of Radiology and Medical Imaging, University Clinics of Kinshasa, Kinshasa, DR Congo
[3] Interdisciplinary Center for Research in Medical Imaging, University Clinics of Kinshasa, University of Kinshasa, DR Congo
[4] Department of Pediatrics, Université Protestante au Congo (UPC), Kinshasa, DR Congo
[5] Department of Gynecology and Obstetrics, Cliniques Universitaires de Kinshasa, Kinshasa, DR Congo
[6] Department of Microbiology, Cliniques Universitaires de Kinshasa, Kinshasa, DR Congo

Correspondence to: Tacite Kpanya Mazoba, Department of Radiology and Medical Imaging, University Clinics of Kinshasa, Kinshasa, DR Congo;
Email: tacitemazoba@gmail.com
Véronique Vinick Lumaya, Department of Pediatrics, University Clinics of Kinshasa, Kinshasa, DR Congo;
Email: vyhnnique7@gmail.com

Received: August 10, 2024;
Accepted: October 13, 2024;
Published: October 18, 2024.

Citation: Lumaya VV, Mazoba TK, Mbambi SM, et al. Bacteriological profile of meningitis in children aged 3 months to 15 years in sub-Saharan Africa: About a systematic review and critical reading of the literature. *Theory and Clinical Practice in Pediatrics*. 2024, 5: 130-136. https://doi.org/10.25082/TCPP.2024.01.004

Abstract: Objective: Bacterial meningitis is a serious, urgent, debilitating and fatal disease. It is therefore necessary to have data on bacterial epidemiology and the profile of sensitivity to antibiotics on which the emergency treatment protocol could be based. This study aimed to identify the bacteriological profile of meningitis in children aged 3 months to 15 years in sub-Saharan Africa by conducting a systematic review of recent literature. **Methods**: This is a systematic review of the literature for which we visited free databases including PubMed, Cochrane, Medline, Google scholar and PMC Free. The key words used were: bacterial meningitis, Sub-Saharan Africa, Acute bacterial meningitis; Culture; Gram stain; Incidence, meningitis; pneumococcus; Haemophilus influenzae. Articles were included from sub-Saharan Africa in any language, and published since 2004. In total, the search generated 48 studies, which after applying the criteria mentioned above, only 7 studies were retained. **Results**: This systematic review showed that the bacterial flora during meningitis in children aged between 3 months to 15 years is essentially dominated by *Streptococcus pneumonia* in the majority with a weighted frequency of 42.9% (35.2–47.4) and significant heterogeneity between different authors ($p < 0.001$). This was followed by *Haemophilus influenzae* with a weighted frequency of 13.8% (11.3–18.1). *Escherichia coli* and *meningococci* were observed in a small proportion. The germs identified were more sensitive to cefotaxime, ceftriaxone, then to amoxicillin, gentamicin and oxacillin. **Conclusion**: Studies are necessary to regularly revisit the bacterial flora during meningitis in children in order to adapt the treatment according to the antibiogram and for probabilistic antibiotic therapy to be based on research results, because this flora bacterial infection varies from one period to another and from one country to another.

Keywords: bacteriological profile, children's meningitis, sub-Saharan Africa

1 Introduction

Meningitis is an inflammatory process of generally infectious origin affecting the meninges. It is a disease present throughout the world with various etiologies: bacterial, viral, fungal or parasitic (1). Meningitis in infants and children poses a serious health problem because it represents a major cause of morbidity and mortality. Clinical signs alone do not make it possible to distinguish viral from bacterial origin. In addition to viral meningitis which has a less severe prognosis, bacterial meningitis remains a frequent and serious problem in pediatrics due to its incidence, mortality and the evolution of resistance [1, 2].

It is estimated that approximately 90% of cases of bacterial meningitis are caused specifically by three pathogens: *Neisseria meningitidis, Streptococcus pneumoniae* and *Haemophilus influenzae type b* [3]. Other germs may be encountered depending on the age (newborn), the terrain (immunosuppression), and particular circumstances (iatrogenic meningitis). Furthermore, we observe constant changes in the epidemiology of meningitis because in particular of vaccination against *Haemophilus influenzae* which has made it possible to considerably reduce the incidence of this germ in Europe. On the other hand, for several years we have been witnessing the

emergence of strains of *pneumococci* with reduced sensitivity to penicillin and there are still epidemics *of meningococcal meningitis*, particularly in Africa [1–3]. Each year, the World Health Organization (WHO) counts one million new cases with a lethality of 10% [4]. In the West, Ramasamy M et al. [5] demonstrated in 2018 that the average age most affected was 2 months and viral meningitis was involved in 26% of cases, the most used antibiotics were ceftriaxone/cefotaxime at 81% for $>$ 1 month.

Bacterial meningitis constitutes a therapeutic emergency. First-line antibiotic therapy is therefore empirical. The choice of antibiotic therapy is therefore based on knowledge of epidemiological data, that of the bacterial agents most often involved and their sensitivity to antibiotics. Although antibiotics have existed for more than 70 years and are effective against this pathology, bacterial meningitis continues to cause significant morbidity and mortality, particularly through diagnostic difficulties and consequently a delay in initiating treatment that is often too long [1–7]. In Mali, Maiga B et *al*. demonstrated in 2019 that the most affected age group was 1-23 months and the germ in question was *pneumococcus* at 27%, the antibiotic used was ceftriaxone at 70% [8].

Bacterial meningitis is a serious, urgent, debilitating and fatal disease [9–14]. This is why it is necessary to have data on the bacterial epidemiology of meningitis in children and on the profile of sensitivity to antibiotics (antibiogram) on which the emergency treatment protocol could be based, which, moreover, has evolved, particularly in the best-equipped countries.

The objective of this study was to identify the bacteriological profile of meningitis in children aged 3 months to 15 years in sub-Saharan Africa by conducting a systematic review of recent literature.

2 Methods

2.1 Study type and procedure

This is a systematic review of the literature for which we visited free databases including PubMed, Cochrane, Medline, Google scholar and PMC. The key words used were: meningitis; bacterial meningitis; Acute bacterial meningitis; Sub-Saharan Africa; Culture; Gram stain; Incidence; pneumococcus; Haemophilus influenzae. Our search considered articles conducted in Sub-Saharan Africa, in all languages, and published since 2004. In total, the search generated 48 studies, of which after applying the criteria mentioned above, only 7 studies were retained. Figure 1 provides information on study recruitment.

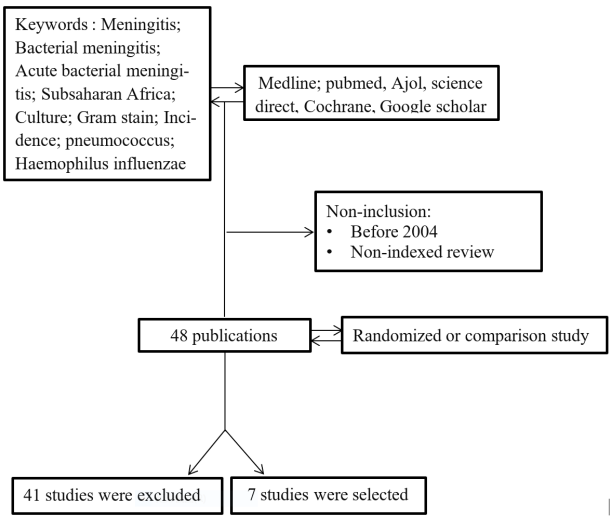

Figure 1 Study selection flow

2.2 Data processing and analysis

The weighted frequency of germs was estimated by the random method with SPSS 26.0 software (Statistical Package of Social Sciences), globally stratified for each type of germ found, with a confidence interval estimated at 95% (95% CI). The estimate of the common effect was obtained using the mean of the estimates from each trial, weighted by the inverse of their variance. The statistical significance threshold was $p<0.05$ (95% CI). The linear results

provided in the form of tables by SPSS were then transported to Excel 2016 which allowed us to generate forest plots for better presentation.

3 Results

3.1 General characteristics

Table 1 shows the general characteristics of the studies selected.

Table 1 General characteristics of the studies selected

Authors	Country	Nature of the study	Year	Sample size
Doumbia AK, et al.	Mali	Transverse	2020	120
Nhantumbo AA, et al.	Mozambique	-	2015	369
Sigauque B, et al.	Mozambique	Analytical prospective	2008	475
Boni-Cisse C, et al.	Ivory Coast	Longitudinal	2019	2762
Tagbo BN, et al.	Nigeria	Longitudinal	2019	5134
Kwambana-Adams BA, et al.	Senegal, Ghana, Togo, – Nigeria, Niger	Longitudinal	2020	1535
Maiga B, et al.	Mali	Retrospective description	2019	100

3.2 Microbiological characteristics of the studies selected

Overall, *Streptococcus pneumonia* predominates, followed by *Haemophilus influenzae*. *Escherichia coli* and *meningococci* were observed in a small proportion. The germs identified were more sensitive to cefotaxime, ceftriaxone, then to amoxicillin and gentamicin finally to oxacillin. (Table 2)

Table 2 Microbiological characteristics of the studies selected

Authors	Diagnostic methods	Superiority	Antibiogram	Pathogens isolated	Remarks
Doumbia AK, et al.	Direct examination, Gram Stain and culture	-	Ceftriaxon/cefotaxim + Gentamicin	*S. pneumoniae* : 57%	Fatality rate: 1% - After-effects: 8%
Nhantumbo AA, et al.	qPCR, Culture, Macroscopic examination, cytochemical study	qPCR >Culture (52.3% vs 7.3%)	-	*S..pneumoniae* : 32.8% *H. influenzae* : 12.2%	-
Sigauque B, et al.	Culture	-	- Oxacillin - Chloraphenicol	*S. pneumniae* : 43.7% *H. influenzae* : 18.3%	Fatality rate: 36%
Boni-Cisse C, et al.	Microbiology, PCR	-	10-valent pneumococcal conjugate vacin	*S. pneumoniae* : 69.5% - *H. influenzae* : 15.8%	- Sequels: 7.4% Lethality rate: 6.2%
Tagbo BN, et al.	Microbiology, latex agglutination techniques, serotyping, PCR	-	10-valent pneumococcal conjugate vacin	*S. pneumoniae* : 46.4% - Meningococcus: 34.6%	- Sequels: 2% Case fatality rate: 15.0%
Kwambana-Adams BA, et al.	Bacteriologic culture, PCR, TAC (TaqMan Array Card)	TAC: 20% PCR: 2.4% Culture:2.0%	Conjugate Vaccines	- Escherichia coli: 4.8% - *S. pneumoniae* : 3.5%	- Lethality: 9.8%
Maiga B, et al.	Direct examination	-	- Ceftriaxone: 70% - Amoxicillin: 20% Gentamycin: 10%	*S. pneumoniae* : 27% *H. influenzae* : 9%	- Lethality: 18% - After-effects: 9%

Among the studies identified, *Streptococcus pneumonia* had, in the majority, a weighted frequency of 42.9%, a confidence interval ranging from 35.2 to 47.4 and significant heterogeneity between different authors ($p < 0.001$) (Figure 1a). Next came Haemophilus influenzae with a weighted frequency of 13.8% (11.3–18.1) (Figure 2b). Escherichia coli and meningococci were observed in a small proportion (Figure 2).

4 Discussion

Bacterial meningitis constitutes a therapeutic emergency worldwide and particularly in sub-Saharan Africa in children aged 3 months to 15 years. Its management requires protocolized, aggressive actions and good knowledge of the bacteriological profile present.

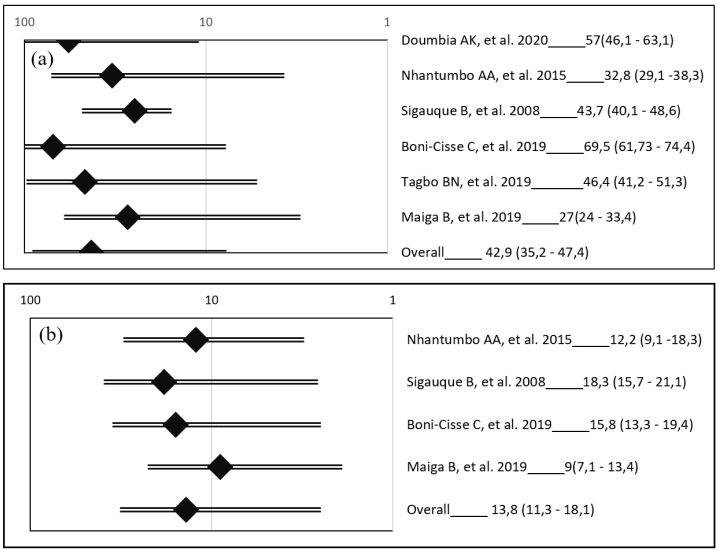

Figure 2 Weighted frequency

4.1 Diagnostic means

The studies included in this systematic literature review report that meningitis was laboratory confirmed in cerebrospinal fluid (CSF), by bacteriological culture, Gram stain, Direct examination, Polymerase Chain Reaction (PCR), latex agglutination techniques and TaqMan Array Card (TAC) with notably higher specificity of the TAC on the PCR and of the PCR on the culture [15, 16]. Gram stain and bacteriological culture, analyzed by an experienced reader, generally help to detect the germs in question, however previous antibiotic therapy can significantly reduce this perfomance [17]. In this specific case, PCR may be more sensitive for diagnosis despite previous antibiotic therapy [15] and the TAC test has the advantage of simultaneously and accurately detecting multiple pathogens [16].

4.2 Incriminated germs

The most common pathogen encountered in the majority of included studies was *Streptococcus pneumoniae*, followed by *Haemophilus influenza*. This finding is consistent with those reported in previous reviews in Africa and globally [18–20]. Indeed, despite the introduction of vaccination against these germs, *Streptococcus pneumoniae* and *Haemophilus influenza,* remain the main bacterial pathogens causing meningitis in the pediatric environment and beyond the neonatal period [20, 21]. However, one of the studies recorded in the journal reported *Escherichia coli* as the pathogen most implicated in meningitis in West Africa. The bacterial pathogen *Escherichia coli* is well known to be the common cause of neonatal meningitis and this high rate in older children may be associated with the presence of comorbidities such as malnutrition as prominent in these settings in this study [22, 23].

4.3 Curative therapeutic means

Among the studies visited, apart from the established vaccination, the most used molecules were third generation cephalosporins (cefotaxime, ceftriaxone) associated with an aminoglycoside specifically Gentamicin. Currently, dual therapy based on high doses of third-generation cephalosporins combined with either vancomycin or gentamicin is proposed as optimal empirical treatment in cases of presumed meningitis or while awaiting antibiogram [24]. Several reports worldwide have noted therapeutic failures using meningitic doses of third-generation cephalosporins as monotherapy [25–27]. Although in adults a high dose of cefotaxime may have good results [28], in children a high dose of cefotaxime has been shown to be insufficient to achieve the necessary bactericidal activity [29]. Hence the need for children aged 3 months to 15 years to introduce dual therapy in the treatment of bacterial meningitis which has effective results even on resistant strains of *streptococcus pneumoniae* [30]. The recommended dose of Cefotaxime remains 200 mg/kg/day and that of ceftriaxone 100 mg/kg/day [24, 25]. In our review, an article that used chloramphenicol combined with a penicillin (oxacillin) reported an overall lethality of 36%, generally in the presence of *S. pneumoniae* (45%) and *H. influenza*

(55%). The growing resistance to penicillin and chloramphenicol among strains of pneumococcus may justify in particular this significant therapeutic failure and the need to use dual therapy based on high doses of third generation cephalosporins associated with either vancomycin or gentamicin against bacterial meningitis in Africa. Concerning the use of corticosteroid therapy, no study in our review mentioned it as an adjunctive treatment, however it has been proven that the use of corticosteroid therapy, in particular Dexamethasone, was necessary to reduce the inflammatory reaction of the CSF and prevent the after-effects (neurological and auditory) of meningitis [18, 31].

4.4 Evolution

Studies included in the review reported up to 36% deaths among children affected by bacterial meningitis and almost 10% clinically evident sequelae. These figures are still high despite the use of appropriate antibiotic therapy and the implementation of a vaccination policy using conjugate vaccines effective against the three main bacterial pathogens responsible for bacterial meningitis, Streptococcus *pneumoniae, Haemophilus influenzae type b (Hib) and Neisseria meningitifis serogroup A*. Another review conducted in Africa in 2009 also reported similar results [18]. It turns out that several protocols are necessary in the treatment of meningitis in children aged 3 months to 15 years in Sub-Saharan Africa, depending on the country and the bacterial epidemiology observed in the environment. These protocols should be updated regularly to adapt them to the bacterial ecology which varies from one period to another. For prevention, mass vaccination of children against *Haemophilus* represents a major means of reducing the frequency of meningitis caused by these germs, even if all serotypes are not covered by these vaccines.

5 Conclusion

This study revealed that the bacterial flora during meningitis in children aged 3 months to 15 years is essentially dominated by *Streptococcus pneumoniae* in the majority, followed by *Haemophilus influenzae*. *Escherichia coli* and *meningococci* were observed in a small proportion. The identified germs were more sensitive to cefotaxime, ceftriaxone, then to amoxicillin, gentamicin and finally to oxacillin. In view of this results, we believe that studies are necessary to regularly revisit the bacterial flora during meningitis in children in order to adapt the treatment according to the antibiogram and for probabilistic antibiotic therapy to be based on the research results, because this bacterial flora varies from one period to another and from one country to another.

Conflicts of interest

The authors declare that they have no conflict of interest.

References

[1] Bourillon A, Brigen E. Méningites purulentes du nouveau-né, du nourrisson et de l'enfant. In: EMC pédiatrie et maladies infectieuses. Paris: Elsevier Masson, 2013. https://doi.org/10.1016/S1637-5017(13)59621-9

[2] Bosdure E., Méningites bactériennes de l'enfant et complications,Flammarion, Neurologie Pédiatrique (3ème editions). 2010: 403-17

[3] Lafolie J, Labbé A, L'Honneur AS, et al. Assessment of blood enterovirus PCR testing in paediatric populations with fever without source, sepsis-like disease, or suspected meningitis: a prospective, multicentre, observational cohort study. The Lancet Infectious Diseases. 2018, 18(12): 1385-1396. https://doi.org/10.1016/s1473-3099(18)30479-1

[4] World Health Organization. New and Under-utilized Vaccines Implementation (NUVI). Bacterial meningitis. Geneva: WHO; August 2010. https://www.who.int

[5] Ramasamy R, Willis L, Kadambari S, et al. Management of suspected paediatric meningitis: a multicentre prospective cohort study. Archives of Disease in Childhood. 2018, 103(12): 1114-1118. https://doi.org/10.1136/archdischild-2017-313913

[6] Levy C, Varon E, Bingen E, et al. Épidémiologie nouvelle des méningites bactériennes sous l'effet des vaccinations. Archives de Pédiatrie. 2011, 18(5): H91-H93. https://doi.org/10.1016/s0929-693x(11)70982-4

[7] Le Saux N. Lignes directrices pour la prise en charge de la méningite bactérienne présumée ou confirmée chez les enfants canadiens de plus d'un mois. Paediatrics & Child Health. 2014, 19(3): 147-152.
https://doi.org/10.1093/pch/19.3.147

[8] Maiga B, Sacko K, Diakité F, et al. Méningites bactériennes chez l'enfant au service de Pédiatrie du CHU Gabriel Toure. Health Sciences and Disease. 2019, 20(4).
https://doi.org/10.5281/hsd.v20i4.1515

[9] Doumbia AK, Togo P, Konaté D, et al. La Méningite Infectieuse chez les Enfants de Moins de 5 Ans en Milieu Hospitalier Bamakois. Health Science and Disease. 2020, 21(10). doi: 10.5281/hsd.v21i10.2346

[10] Nhantumbo AA, Cantarelli VV, Caireão J, et al. Frequency of Pathogenic Paediatric Bacterial Meningitis in Mozambique: The Critical Role of Multiplex Real-Time Polymerase Chain Reaction to Estimate the Burden of Disease. Griffiths UK, ed. PLOS ONE. 2015, 10(9): e0138249.
https://doi.org/10.1371/journal.pone.0138249

[11] Sigaúque B, Roca A, Sanz S, et al. Acute bacterial meningitis among children, in Manhiça, a rural area in Southern Mozambique. Acta Tropica. 2008, 105(1): 21-27.
https://doi.org/10.1016/j.actatropica.2007.01.006

[12] Boni-Cisse C, Jarju S, Bancroft RE, et al. Etiology of Bacterial Meningitis Among Children $<$ 5 Years Old in Côte d'Ivoire: Findings of Hospital-based Surveillance Before and After Pneumococcal Conjugate Vaccine Introduction. Clinical Infectious Diseases. 2019, 69(S2): S114-S120.
https://doi.org/10.1093/cid/ciz475

[13] Tagbo BN, Bancroft RE, Fajolu I, et al. Pediatric Bacterial Meningitis Surveillance in Nigeria From 2010 to 2016, Prior to and During the Phased Introduction of the 10-Valent Pneumococcal Conjugate Vaccine. Clinical Infectious Diseases. 2019, 69(S2): S81-S88.
https://doi.org/10.1093/cid/ciz474

[14] Kwambana-Adams BA, Liu J, Okoi C, et al. Etiology of Pediatric Meningitis in West Africa Using Molecular Methods in the Era of Conjugate Vaccines against Pneumococcus, Meningococcus, and Haemophilus influenzae Type b. The American Journal of Tropical Medicine and Hygiene. 2020, 103(2): 696-703.
https://doi.org/10.4269/ajtmh.19-0566

[15] NESHER L, HADI CM, SALAZAR L, et al. Epidemiology of meningitis with a negative CSF Gram stain: under-utilization of available diagnostic tests. Epidemiology and Infection. 2015, 144(1): 189-197.
https://doi.org/10.1017/s0950268815000850

[16] Abade A, Eidex RB, Maro A, et al. Use of TaqMan Array Cards to Screen Outbreak Specimens for Causes of Febrile Illness in Tanzania. The American Journal of Tropical Medicine and Hygiene. 2018, 98(6): 1640-1642.
https://doi.org/10.4269/ajtmh.18-0071

[17] Therapy of suspected bacterial meningitis in Canadian children six weeks of age and older. Paediatrics & Child Health. 2001, 6(3): 147-152.
https://doi.org/10.1093/pch/6.3.147

[18] Ramakrishnan M, Ulland AJ, Steinhardt LC, et al. Sequelae due to bacterial meningitis among African children: a systematic literature review. BMC Medicine. 2009, 7(1).
https://doi.org/10.1186/1741-7015-7-47

[19] Knoll MD, O'Brien KL, Henklle E, et al. Revue de la littérature mondiale sur les maladies invasives à Haemophilus influenza de type b et à streptococcus pneumoniae chez les enfants de moins de cinq ans. 1980-2005. Genève, Suisse: Organisation mondiale de la Santé, 2009.

[20] Peltola H. Burden of Meningitis and Other Severe Bacterial Infections of Children in Africa: Implications for Prevention. Clinical Infectious Diseases. 2001, 32(1): 64-75.
https://doi.org/10.1086/317534

[21] Johnson HL, Deloria-Knoll M, Levine OS, et al. Systematic Evaluation of Serotypes Causing Invasive Pneumococcal Disease among Children Under Five: The Pneumococcal Global Serotype Project. Cohen J, ed. PLoS Medicine. 2010, 7(10): e1000348.
https://doi.org/10.1371/journal.pmed.1000348

[22] Roine I, Weisstaub G, Peltola H. Influence of Malnutrition on the Course of Childhood Bacterial Meningitis. Pediatric Infectious Disease Journal. 2010, 29(2): 122-125.
https://doi.org/10.1097/inf.0b013e3181b6e7d3

[23] Kuti BP, Bello EO, Jegede TO, et al. Epidemiological, clinical and prognostic profile of childhood acute bacterial meningitis in a resource poor setting. Journal of Neurosciences in Rural Practice. 2015, 06(04): 549-557.
https://doi.org/10.4103/0976-3147.165424

[24] Wubbel L, McCracken GH. Management of Bacterial Meningitis: 1998. Pediatrics In Review. 1998, 19(3): 78-84.
https://doi.org/10.1542/pir.19.3.78

[25] París MM, Ramilo O, McCracken GH. Management of meningitis caused by penicillin-resistant Streptococcus pneumoniae. Antimicrobial Agents and Chemotherapy. 1995, 39(10): 2171-2175.
https://doi.org/10.1128/aac.39.10.2171

[26] John CC. Treatment Failure with Use of a Third-Generation Cephalosporin for Penicillin-Resistant Pneumococcal Meningitis: Case Report and Review. Clinical Infectious Diseases. 1994, 18(2): 188-193.
https://doi.org/10.1093/clinids/18.2.188

[27] Sloas MM, Barrett FF, Chesney PJ, et al. Cephalosporin treatment failure in penicillin and cephalosporin-resistant Streptococcus pneumoniae meningitis.

[28] Viladrich PF, Cabellos C, Pallares R, et al. High doses of cefotaxime in treatment of adult meningitis due to Streptococcus pneumoniae with decreased susceptibilities to broad-spectrum cephalosporins. Antimicrobial Agents and Chemotherapy. 1996, 40(1): 218-220. https://doi.org/10.1128/aac.40.1.218

[29] Friedland IR, Klugman KP. Cerebrospinal fluid bactericidal activity against cephalosporin-resistant Streptococcus pneumoniae in children with meningitis treated with high-dosage cefotaxime. Antimicrobial Agents and Chemotherapy. 1997, 41(9): 1888-1891. https://doi.org/10.1128/aac.41.9.1888

[30] Klugman KP, Friedland IR, Bradley JS. Bactericidal activity against cephalosporin-resistant Streptococcus pneumoniae in cerebrospinal fluid of children with acute bacterial meningitis. Antimicrobial Agents and Chemotherapy. 1995, 39(9): 1988-1992. https://doi.org/10.1128/aac.39.9.1988

[31] Brouwer MC, Heckenberg SGB, de Gans J, et al. Nationwide implementation of adjunctive dexamethasone therapy for pneumococcal meningitis. Neurology. 2010, 75(17): 1533-1539. https://doi.org/10.1212/wnl.0b013e3181f96297