

Antibiogram profile of septic meningitis among children in Duhok, Iraq

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ABSTRACT

الأهداف: معرفة انتشار البكتريا المقاومة لعدد من المضادات الحيوية في سائل النخاع الشوكي لدى المرضى المشتبهين بالسحايا.

الطريقة: أجريت دراسة وصفية خلال الفترة من يناير 2014 ويناير 2016 في مستشفى الأطفال التعليمي في داحوك، العراق. تم زرع 432 عينة من سائل النخاع الشوكي وتمت دراسة مقاومتها للمضادات الحيوية.

النتائج: تم عزل 33 بكتريا (7.6%) من العينات المرسله (432) وقد كانت المكورات الرئوية تمثل 18 حالة (54.5%) من هذه البكتريا. وكانت مقاومتها للبنسلين 43%، 87% للسيوفوتاكسيم و0% للفانكوميسين. وكانت هناك 5 حالات للبكتريا السلبية لصبغة الجرام وكانت مقاومتها للامبيينيم والاميكاسين 0% ولكن 100% للسيوفوتاكسيم والفانكوميسين وكانت جميع عزلات المكورات العنقودية حساسة للفانكوميسين والجنتاميسين والكلينداميسين ولكنها كانت مقاومة للبنسلين وسيوفوتاكسيم.

الخاتمة: أشارت الدراسة ان المكورات الرئوية هي أكثر شيوعا بين البكتريا المعزولة. وأن استخدام تلقيحات الهيوفيليس والمينجوكوكس أدى إلى ندرة انتشار هذه البكتريا. جميع المكورات الرئوية كانت حساسة للفانكوميسين وأن جميع البكتريا السلبية لصبغة الجرام كانت حساسة للامبيينيم والاميكاسين ولكن جميعها كانت مقاومة للسيوفوتاكسيم.

Objectives: To determine the prevalence of bacteria in the cerebrospinal fluid (CSF), and the antibiogram profile in pediatric patients with suspected meningitis.

Methods: This descriptive study was conducted between January 2014 and January 2016 in the Hevi Paediatric Teaching Hospital in Duhok, Iraq. The CSF samples were withdrawn from 432 pediatric patients suspected of meningitis. The samples were cultured, and antibiotic sensitivity tests were performed.

Results: There were 33 (7.6%) culture positive cases among 432 CSF samples. Among the positives cases, there were 18 culture positive for *Streptococcus pneumoniae* (*S. pneumoniae*). There were 4 cases of *Viridans streptococci*. In addition, there were 2 cases each of *Escherichia coli* (*E. coli*), *Klebsiella pneumoniae* (*K. pneumoniae*), and Non-coagulase staphylococci. There was only one case each of *Staphylococcus aureus*, *Streptococcus pyogenes*, *Enterococcus species*, *Haemophilus influenzae*, and *Pseudomonas aeruginosa* (*P. aeruginosa*). The isolated *S. pneumoniae* strains showed 47% sensitivity against penicillin, 13% against cefotaxime, but 100% of sensitivity against vancomycin. Isolates of gram-negative bacilli (*E. coli*, *K. pneumoniae*, and *P. aeruginosa*) were 100% sensitive to imipenem and amikacin, but had 0% sensitivity to cefotaxime and vancomycin. All isolates of Staphylococci were sensitive to vancomycin, gentamicin, and clindamycin but were resistant to penicillin and cefotaxime.

Conclusion: *Streptococcus pneumoniae* is currently the leading cause of meningitis among children in Duhok city. The antimicrobial resistance pattern indicates that all isolates of *S. pneumoniae* were sensitive to vancomycin.

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Bacterial meningitis is a life threatening disease that results from infection of the meninges. It is commonly caused by a bacterium or a virus. Bacterial types will depend on age, history of vaccination, and past medical illnesses. Some factors can increase the risk of developing bacterial meningitis, including contact with bacterial meningitis, recent infection (ear or sinus infection), travelling to places where bacterial meningitis is common, serious head injury, and low immunity. Often, differentiating bacterial meningitis from viral and tuberculous meningitis is not easy and it is vital to diagnose viral meningitis, which does not require antibiotic therapy from conditions that can be treated. Acute bacterial meningitis is serious with a high rate of fatality.¹⁻⁴ For this reason bacterial meningitis needs empiric treatment with appropriate potent antibiotics to avoid fatality. The empirical antibiotic regimens should be updated periodically to overcome the development of antimicrobial resistance. The combination of vancomycin with either ceftriaxone for adults or cefotaxime for pediatric ages is given empirically for those with suspected bacterial meningitis, based upon susceptibilities of isolated pathogens.^{1,2} This therapy is to combat against most penicillin-resistant pneumococci and β lactamase resistant *Haemophilus influenzae* (*H. influenzae*).^{1,2,5} Both ceftriaxone and cefotaxime achieve good cerebrospinal fluid (CSF) levels. The etiology of bacterial meningitis and the antibiogram profile is unknown in Duhok City, Iraq. This research was conducted to facilitate the proper judgment regarding the empirical treatment of bacterial meningitis in the city. In addition, ascertaining laboratory-based surveillance regarding the local data will clarify the needs for a vaccination program against *Streptococcus pneumoniae* (*S. pneumoniae*) and *H. influenzae*.⁶

Methods. This study was carried out between January 2014 and January 2016, among pediatrics patients ranging from neonates to 15 years of age admitted to Hevi Paediatric Teaching Hospital, Duhok city, in the Kurdistan Region of Iraq. Samples of CSF were collected by senior doctors who were supervising the patients suspected with meningitis.

The criteria for choosing CSF analysis to diagnose meningitis in this study were mainly the sudden onset of fever, headache, neck stiffness, vomiting, photophobia, and confusion. Irritability and lack of alertness were also considered for neonates. Samples were immediately transported to the Microbiology Laboratory in Hevi

Hospital, where part of it was used for this study. The fluid was inoculated directly onto blood, chocolate, and MacConkey agar plates no later than 2 hours from the time of collection. Gram staining was performed. All isolates were identified based on their colony, morphology, culture characteristics, and biochemical reactions according to the standard microbiological procedures.⁷

The inclusion/exclusion criteria were established to include evaluation of the basic diagnostic bacterial culture of CSF to be the standard diagnosis for bacterial meningitis. The antimicrobial sensitivity testing for the isolates was performed on Muller-Hinton agar by the Kirby-Bauer disk diffusion method based on National Committee for Clinical laboratory standards.⁸ The mean percentage of resistance of isolates was calculated. This study was conducted according to the principles of the Helsinki Declaration with approval of the Research Ethics Committee of Duhok Directorate General of Health.

Results. Among the 432 CSF samples sent to the laboratory for the study, 33 samples were positive (7.6%). The positive bacteria are identified in Table 1. Most of the isolates were *S. pneumoniae* at 18 (54.5%) of the positive bacteria, followed by 4 cases of *Viridans streptococci*. There were 2 isolates for each of *Escherichia coli* (*E. coli*), *Klebsiella pneumoniae* (*K. pneumoniae*), and Non-coagulase staphylococci. There was only one isolate for each of *Staphylococcus aureus*, *Streptococcus pyogenes*, *Enterococcus spp*, *H. influenzae*, and *Pseudomonas aeruginosa* (*P. aeruginosa*).

The antibiogram profile for *S. pneumoniae* is shown in Table 2. All the isolates were sensitive to vancomycin, 47% were sensitive to penicillin, 50% to Augmentin,

Table 1 - Number and percentage of isolated bacteria from suspected meningitis pediatric patients.

Type of bacteria	n	(%)
<i>Streptococcus pneumoniae</i>	18	(54.5)
<i>Viridans streptococci</i>	4	(12.2)
<i>Escherichia coli</i>	2	(6.1)
<i>Klebsiella pneumoniae</i>	2	(6.1)
Non-coagulase staphylococci	2	(6.1)
<i>Staphylococcus aureus</i>	1	(3.0)
<i>Streptococcus pyogenes</i>	1	(3.0)
<i>Enterococcus spp</i>	1	(3.0)
<i>Haemophilus influenzae</i>	1	(3.0)
<i>Pseudomonas aeruginosa</i>	1	(3.0)

Table 2 - Percentage of sensitivity, and resistance to the antibiotic discs used for *Streptococcus pneumoniae*.

Antibiotic	Percentage of sensitivity	Percentage of resistance
Vancomycin	100 (18/18)	00 (0/18)
Pencillin	47 (8/17)	53 (9/17)
Augmentin	50 (8/16)	50 (8/16)
Clindamycin	41 (7/17)	59 (10/17)
Cephalothin	29 (4/14)	71 (10/14)
Gentamicin	24 (4/17)	76 (13/17)
Erythromycin	17 (2/12)	83 (10/12)
Cefotaxime	13 (2/15)	87 (13/15)
Co-trimoxazole	11 (2/18)	89 (16/18)

41% to clindamycin, 29% to cephalothin, 24% to gentamicin, 17% to erythromycin, 13% to cefotaxime, and only 11% to Co-trimoxazole.

The sensitivity for gram-negative bacilli isolates (*E. coli*, *K. pneumoniae*, and *P. aeruginosa*) is shown in Table 3. Vancomycin, Augmentin, clindamycin, cephalothin, cefotaxime, and cotrimoxazole had 0% sensitivity, but for imipenem and amikacin this was 100%. The sensitivity for gentamicin was 60%. All isolates of coagulase negative staphylococci and *S. aureus*, were sensitive to vancomycin, gentamicin, and clindamycin but none were sensitive to penicillin or cefotaxime.

Discussion. In this study, *S. pneumoniae* was the most common etiological agent of meningitis (18 cases among 33 cases) in Duhok city, Iraq. *Streptococcus pneumoniae* remains the most frequent cause of bacterial meningitis in children in the USA.⁹ This may be due to many distinct serotypes of pneumococcus that have been identified.⁹ Meningitis caused by *S. pneumoniae* is usually seen during the extremes of age (less than 2 years); in patients with underlying conditions such as splenectomy, hypogammaglobulinemia, chronic liver or kidney disease, malignancy, thalassemia major, diabetes mellitus, skull fracture with leakage of CSF, and in children with cochlear implants.^{10,11} Meningitis due to *Viridans streptococci* or enterococci is seen predominantly in children under the age of one year.¹² In this study, 4 cases of *Viridans streptococci* and one of *Enterococcus spp* were observed. They are probably of oropharyngeal origin, and certain risk factors such as neurosurgical procedures and head trauma are usually present in such patients.^{12,13}

Table 3 - Percentage of sensitivity, and resistance to gram-negative bacilli (*Escherichia coli*, *Klebsiella pneumoniae*, and *Pseudomonas aeruginosa*).

Antibiotic	Percentage of sensitivity	Percentage of resistance
Vancomycin	0 (0/5)	100 (5/5)
Augmentin	0 (0/5)	100 (5/5)
Amikacin	100 (5/5)	0 (0/5)
Clindamycin	0 (0/5)	100 (5/5)
Cephalothin	0 (0/5)	100 (5/5)
Gentamicin	60 (3/5)	40 (2/5)
Cefotaxime	0 (0/5)	100 (5/5)
Co-trimoxazole	0 (0/5)	100 (5/5)
Imipenem	100 (5/5)	0 (0/5)

Since the routine use of the *H. influenzae* type B, conjugate pneumococcal, and conjugate meningococcal vaccine in the United States, the incidence of meningitis due to related bacteria has dramatically decreased. The *H. influenzae* type B conjugate vaccines have led to a profound reduction in the incidence of *H. influenzae* type B meningitis,^{14,15} and this may be attributed to the detection of only one case of *H. influenzae* and none for *Neisseria meningitidis* in this study. Meningococcus is the leading pathogen of meningitis in young adults.¹⁶

Streptococcus pyogenes (group A streptococcus) accounted for only one case in this study. Another study reported a similar rate (0.2-1.2%) among all cases of bacterial meningitis in adults and children, and is community acquired in most cases.¹⁷ The most common predisposing factor is otitis.¹⁸

Meningitis due to *Staphylococcus aureus* (*S. aureus*) and coagulase negative staphylococci is acquired mainly nosocomially, and occurs predominantly after neurosurgical procedures or following the placement of CSF shunts.¹⁹ In this study, there were 2 cases of coagulase negative staphylococci and one of *S. aureus*. In one study, coagulase-negative staphylococcus was reported to make up 52.8% of bacteria of ventriculoperitoneal shunt infections in patients less than 8 years.¹⁸ Community-acquired meningitis due to aerobic gram-negative bacteria (*Klebsiella species*, *E. coli*, and *P. aeruginosa*) are uncommon, but can be found for immuno-compromised patients and neonates.²⁰ In the current study, there were 2 cases for each of *E. coli* and *K. pneumoniae*, and one isolate of *P. aeruginosa*.

The antibacterial susceptibility testing for *S. pneumoniae* isolates showed that penicillin and its derivatives are not very effective (43% resistance against

penicillin and 50% resistance against Augmentin). Both gentamicin and cefotaxime had high levels of resistance (76% and 87%). However, all the isolates were sensitive to vancomycin. Regarding gram-negative bacilli (*E. coli*, *K. pneumoniae*, and *P. aeruginosa*), all the isolates were sensitive to amikacin, but only 60% of the isolates were sensitive to gentamicin. Aminoglycosides achieved marginal levels in the CSF.²¹ Cefotaxime was not effective and should not be used as the single initial drug for these bacteria. These strains are most likely of nosocomial origin possessing extended-spectrum β -lactamases, which renders them resistant to third generation cephalosporin. These isolates were sensitive to Imipenem. It is difficult to estimate the resistance rate of *H. influenzae* meningitis due to the limited number of positive isolates and limited surveillance studies.

Study limitation. The limitation of this study includes delay in culturing few of the CSF samples sent overnight have caused loss of some of the fastidious bacteria. Another limitation of the study was the empirical use of antibiotics prior to presentation in some of the patients.

In conclusion, meningitis due to *S. pneumoniae* is currently the leading cause of meningitis among children in Duhok city. The new and important results of this study compared to other studies worldwide may reflect the differences in vaccination programs, and differences in geographical places. The antimicrobial resistance pattern in this study indicates the emergence of a multidrug resistance pattern among gram-negative bacilli, which could be of hospital-acquired origin. These findings indicate the need for periodic surveillance to select the appropriate antibiotic to be used empirically. It also adds more information on the resistant patterns of the causative bacteria.

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