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RESISTANCE OF BACTERIAL MENINGITIS TO ANTIBIOTICS IN CHILDREN AND ADOLESCENTS

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**Abstract.** This literature review provides information on the prevalence and treatment of bacterial meningitis among children and adolescents, the severity of meningitis, and the causes of its occurrence. Bacterial meningitis is most common in infants and children. Because their immune systems are weak, the disease develops very quickly, and the symptoms are hidden. This can lead to severe inflammation of the meninges in a short time. Bacterial meningitis is less common in adolescents than in infants and children. This is due to the maturity of the immune system of adolescents, the rapid recognition of symptoms, and the ability to seek medical attention in a timely manner. Adolescents are mainly infected with Meningococcus (*Neisseria meningitidis*). Some meningitis bacteria are resistant to antibiotics and can cause death. Even in people who recover from it, various neurological complications may remain.

**Keywords:** bacterial meningitis, pathogens, spread, complications, brain tumor, leukocytes.

**Introduction.** Bacterial meningitis is a bacterial infection characterized by inflammation of the protective membranes covering the brain and spinal cord. It is a serious and life-threatening condition that requires prompt diagnosis and treatment [1]. According to WHO data, one in six people with bacterial meningitis (BM) dies, and one in five survivors experiences severe neurological complications [3]. Possible mechanisms of spinal cord dysfunction in bacterial meningitis include spinal cord ischemia due to vasculitis or circulatory shock, post-inflammatory myelitis, and direct infection of the spinal cord [5]. Despite ongoing advances in diagnostic methods and treatment strategies, the mortality rate remains as high as 30% in pneumococcal meningitis and 5–10% in meningococcal meningitis [2]. Among the causative pathogens, *Streptococcus pneumoniae*, *Neisseria meningitidis*, and *Haemophilus influenzae* account for the majority of cases [4]. Group B *Streptococcus* is common in infants younger than 2 months,



whereas *Streptococcus pneumoniae* is the most prevalent pathogen in almost all other age groups, except for those aged 11–17 years, in whom *Neisseria meningitidis* remains the leading cause [1]. In the United States, the annual incidence of meningitis decreased from 2.00 cases per 100,000 population in 1998–1999 to 1.38 cases per 100,000 population in 2006–2007, while the median age of patients increased from 30.3 years in 1998–1999 to 41.9 years in 2006–2007 [1]. The immaturity of the immune system in neonates, especially in preterm infants, places them at a particularly high risk of bacterial meningitis. Their exposure during the perinatal period increases susceptibility to a range of bacterial and viral pathogens. In industrialized countries, the principal pathogens include Group B *Streptococcus*, Gram-negative bacilli—most commonly *Escherichia coli*—and *Listeria monocytogenes*. However, for adequate diagnosis and management of the disease, fungal and viral etiologies must also be considered. Some experts recommend performing a lumbar puncture in all neonates with proven or suspected sepsis in order to exclude neonatal meningitis, with the aim of ensuring early diagnosis and appropriate treatment [7]. In a 2019 multicenter study, the majority of infants younger than 60 days with bacterial meningitis had either positive Gram stain results or corrected cerebrospinal fluid (CSF) pleocytosis, with a sensitivity of 80.3%. The study reported that the specificity of the bacterial meningitis score was low; therefore, the authors recommended against using this predictive tool in infants younger than 60 days. The authors also noted that infants who initially had neither pleocytosis nor positive Gram stain findings but were later diagnosed with bacterial meningitis subsequently developed peripheral leukocytosis or bandemia. Notably, correction of the CSF leukocyte count for red blood cells (RBCs) reduced the sensitivity of pleocytosis for detecting meningitis in this population [6].

**Main part.** *Streptococcus pneumoniae* accounts for approximately 72% of bacterial meningitis cases in individuals older than 16 years, whereas *Neisseria meningitidis* is responsible for about 11% of cases. *Escherichia coli* and *Streptococcus agalactiae* cause nearly 35% of early-onset neonatal meningitis cases [15]. *Streptococcus pneumoniae* is generally considered the most common etiological agent in patients with bacterial meningitis (BM), including the elderly, and is associated with a poorer prognosis compared to other common pathogens [22].

Streptococcal meningitis is a life-threatening infection of the central nervous system (CNS) characterized by acute inflammation of the meningeal membranes covering the brain and spinal cord. It is a common form of meningitis, particularly in young children, and is associated with early mortality. This condition is mainly caused by *Streptococcus pneumoniae* and *Streptococcus agalactiae*, which are capable of disrupting the blood–brain barrier under certain pathological conditions. The CNS is normally a sterile environment, and the invasion of bacteria into this compartment triggers a strong inflammatory response that can lead to severe neurological complications and death. The anatomical routes of bacterial entry most often include hematogenous spread or direct extension from adjacent infected sites such as the middle ear or paranasal sinuses [14].

*Neisseria meningitidis* (NM) is a bacterial species belonging to the genus *Neisseria* and is recognized as a strictly human pathogen [18]. NM infections can be caused by different meningococcal serogroups. Five serogroups (A, B, C, W, and Y) account for the majority of cases of invasive meningococcal disease (IMD). Although relatively uncommon, IMD is life-threatening and remains one of the leading causes of bacterial meningitis and septicemia worldwide [19].



The increasing role of Gram-negative bacteria in the etiology of pediatric bacterial meningitis is a matter of concern. It is well established that Gram-negative bacterial meningitis is associated with a poorer prognosis and a higher rate of complications [22].

The clinical symptoms and signs of bacterial meningitis in children are often atypical and may be difficult to distinguish from other diseases [24]. In infants, early-onset meningitis is defined as occurring within the first 7 days of life, whereas late-onset meningitis is identified after 7 days [13]. Within the CHAMPS network, meningitis accounted for 7.0% of deaths among children under five years of age, which is higher than the WHO estimate of 5.1% [20]. This finding suggests that meningitis cases may be underestimated due to the failure to consider all contributing conditions in the chain of causation.

Furthermore, it highlights the high prevalence of resistant organisms such as *Klebsiella pneumoniae* and *Acinetobacter baumannii*. Consequently, without timely lumbar puncture and the administration of appropriate antibiotics, the risk of death from meningitis in children under five years of age remains significant. Although childhood vaccination has reduced the incidence of *Streptococcus pneumoniae* and *Haemophilus influenzae* type b (Hib) meningitis, *S. pneumoniae* remains the leading pathogen in community-acquired meningitis. Therefore, alternative antibiotic therapies should be considered, especially for low-birth-weight infants or children who have been hospitalized for several days [21].

TBM became a treatable disease in the 1940s with the discovery of the first antituberculous drugs—streptomycin and para-aminosalicylic acid. The bactericidal effect produced by these two drugs reduced mortality from nearly 100% to approximately 70% [8].

Capnocytophaga is a rare cause of meningitis. According to Butler et al., the mean age at the time of diagnosis of Capnocytophaga meningitis is 55 years, and males are affected more frequently than females, with a ratio of 3:1 [11]. The mortality rate is about 26% and is most often observed in severe conditions such as severe sepsis, septic shock, gangrene of the fingers, bacteremia, meningitis, endocarditis, neurological abnormalities, and ocular infections. Bites or scratches from cats and dogs are considered the main sources of infection.



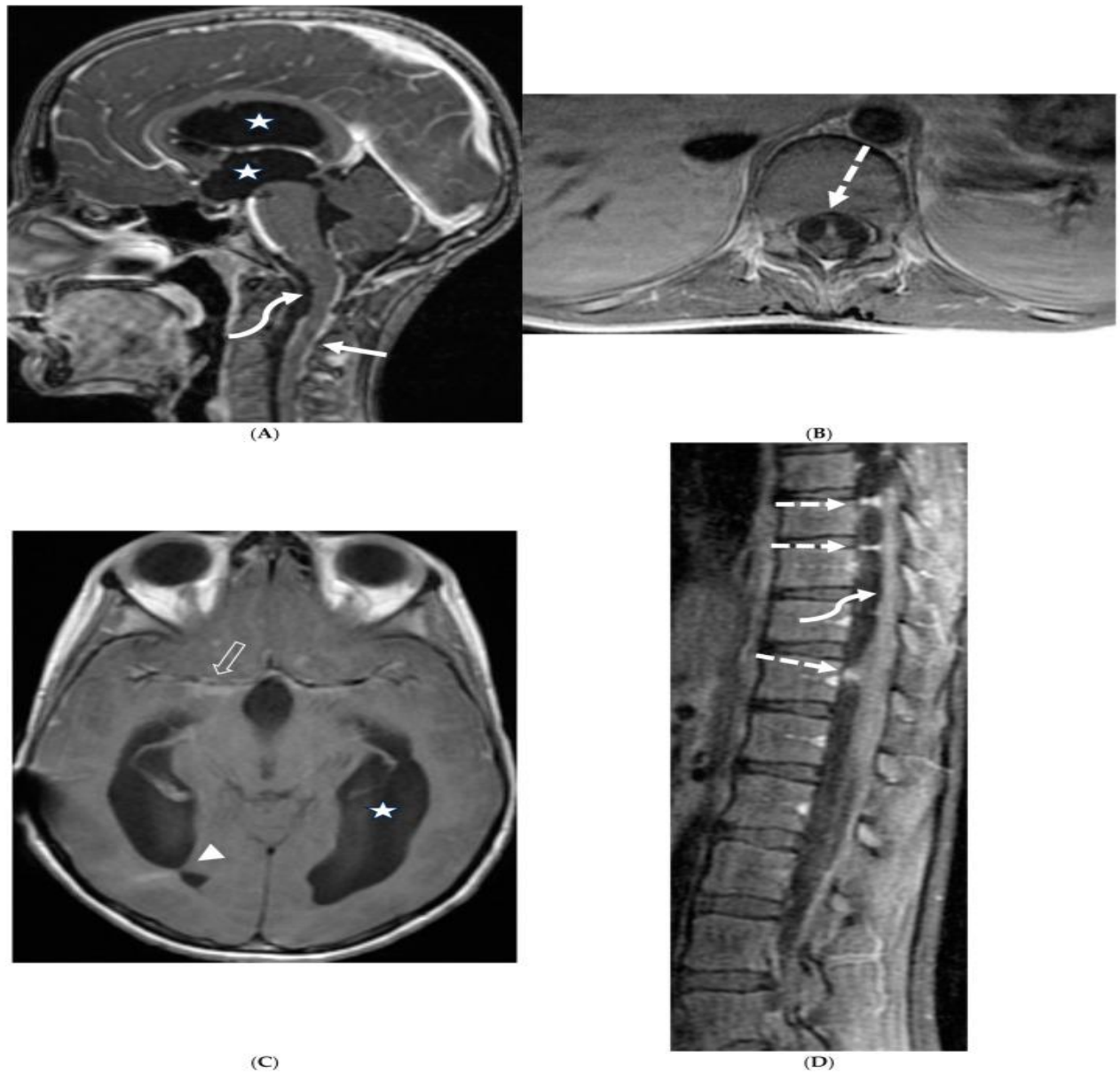
Picture 1. Spinal magnetic resonance imaging (MRI) findings of patients with non-compressive myelopathy secondary to bacterial meningitis.

(a) T2-weighted sagittal spinal MRI shows a hyperintense lesion at T6–T7. The patient was diagnosed with post-inflammatory myelitis.

(b) T2-weighted sagittal spinal MRI demonstrates a longitudinal hyperintense lesion involving a large portion of the thoracic spinal cord. This patient was also diagnosed with post-inflammatory myelitis.

(c, d) T2-weighted sagittal spinal MRI shows a longitudinal hyperintense lesion in the lower cervical spinal cord [c] and an epidural abscess at C1–C2 on T1-weighted images (d). The patient was diagnosed with infectious myelitis

[10].



Picture 2. Post-contrast sagittal T1 brain (A), T1 spine (B), axial T1 brain (C), and spine (D): a 17-year-old girl with a several-year history of fatigue, gait disturbance, and back/lower limb pain. Moderate ventriculomegaly (white star) is present. Meningeal enhancement around the cervical region (white arrow) is observed. The thecal sac shows a flattened and deformed conus medullaris and diffusely affected spinal cord (curved arrows), along with enhancing septations (dashed arrows), likely secondary to chronic meningitis. Basal cisternal enhancement in the lateral ventricles (open arrow) and septations (arrowhead) probably reflect the sequelae of chronic inflammation/infection. Pathology: *Prototheca zopfi* [23].

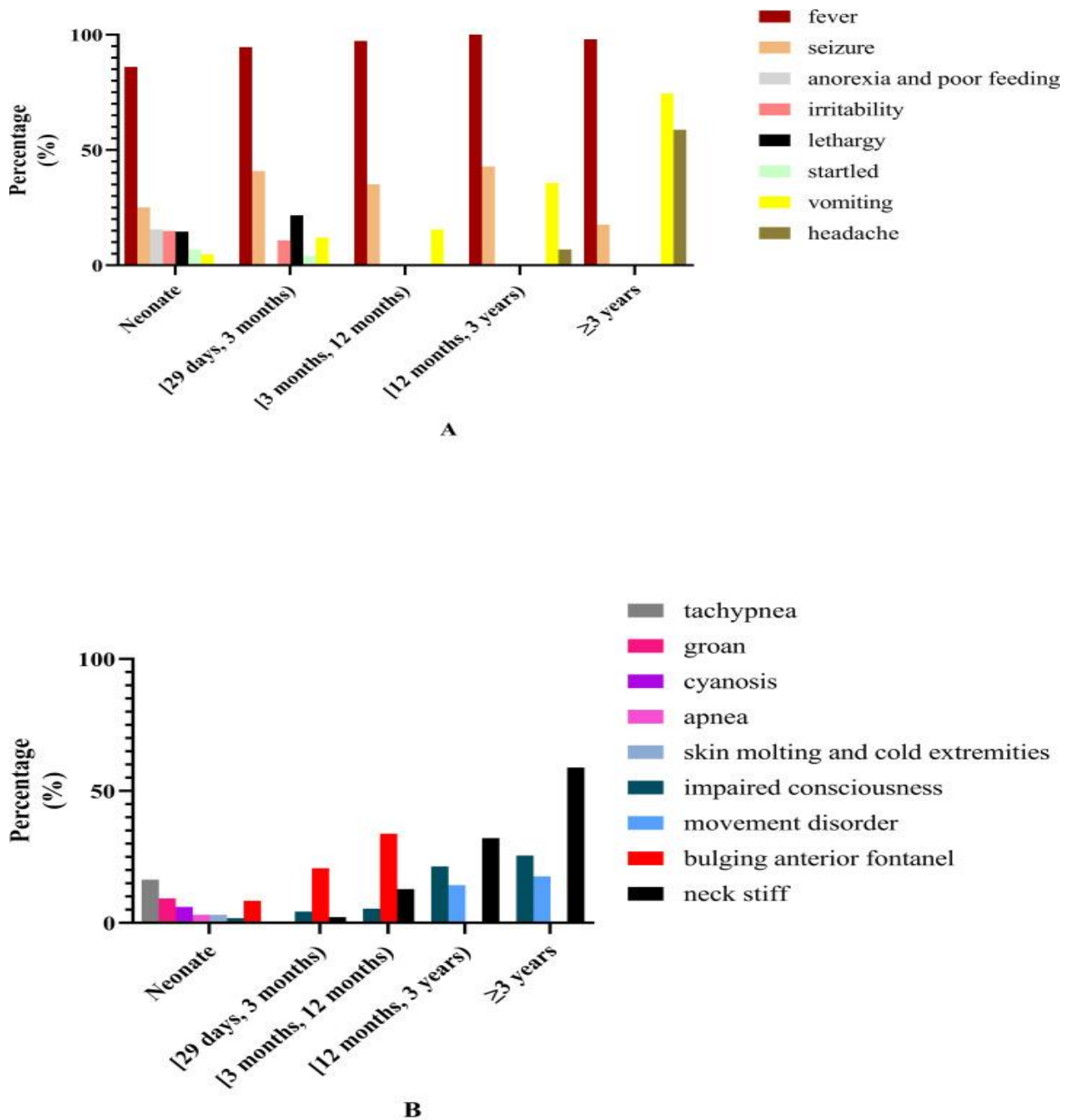


Figure 3. Common and less common symptoms and clinical signs in patients of different age groups.

(A) Common and less common symptoms in patients of different age groups.

(B) Common and less common clinical signs in patients of different age groups.

Clinical symptoms and signs: The most common symptoms were fever [92.0%], seizures [32.2%], fatigue [18.3%], vomiting [14.3%], anorexia and poor feeding [12.1%], and irritability [11.8%]. Less common symptoms included tachypnea [8.6%], startle response [6.1%], impaired consciousness [5.5%], grunting [5.4%], headache [3.8%], cyanosis [2.9%], apnea [2.1%], skin



mottling and cold extremities [1.9%], and movement disorders [paralysis and/or dystonia, 1.8%]. The most frequent clinical signs were bulging of the anterior fontanelle [16.1%] and neck stiffness [7.6%].

Clinical presentation in patients of different age groups: The common and less common symptoms in patients of different age groups are shown. Fever was the most frequent symptom across all age groups. In patients <3 years of age, the second most common symptom was seizures, whereas in patients ≥3 years old it was vomiting. The frequency of vomiting increased with age. Dyspnea was observed more frequently in neonates compared to older infants (26.1% vs 7.0%, chi-square test,  $\chi^2 = 59.873$ ,  $P < 0.0001$ ) [9]. The study evaluated biochemical and hematological parameters in patients with different outcomes and found that although hemoglobin levels, platelet counts, calcium, urea, and creatinine levels were similar between the groups, the total leukocyte count (TLC) was significantly higher in the poor outcome group, with slightly higher sodium levels and lower potassium levels. The percentages of neutrophils and lymphocytes were similar between the groups. Serum albumin levels were significantly higher in the good outcome group [25].

All patients received empirical antibiotic therapy before the identification of the causative bacteria, and if a pathogen was identified, the antimicrobial treatment was adjusted according to the results of antimicrobial susceptibility testing. Dexamethasone (0.15 mg/kg every 6 hours for 4 days or 0.4 mg/kg every 12 hours for 2 days) was administered to patients in the early severe stage. After consultation with neurosurgeons, neurosurgical intervention was performed in patients with subdural effusion, subdural empyema, brain abscess, hydrocephalus, or structural abnormalities of the brain or spinal cord [9].

The most commonly used treatment approach for all pathogens was combination therapy, which shifted during the study period from third-generation cephalosporin (3GC)-based regimens to meropenem-based therapies due to increasing antibiotic resistance [16]. *Acinetobacter* species showed moderate susceptibility to penicillins and cephalosporins, and resistance to carbapenems reached approximately 40–45%. Although this indicates that carbapenems remain a useful treatment option, their declining efficacy is consistent with the global trend of increasing carbapenem-resistant *Acinetobacter* infections [17].

**Conclusion.** Bacterial meningitis continues to pose a serious threat to human life and can affect individuals of all ages. Despite the aggressive implementation of modern therapeutic strategies in the contemporary medical era, mortality remains considerable. One of the main reasons for this is the increasing antibiotic resistance associated with bacterial meningitis. Even in cases of recovery, patients may develop various long-term neurological sequelae.

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