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Antibiotic Resistance in Cases of Bacterial Meningitis: Literature Review

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ABSTRACT

Background: Meningitis is an infectious disease that attacks the cerebral membrane or swallows. Meningite is among the ten most dangerous diseases in the world. The disease can affect both children and adults. The cause of this disease can be bacteria, viruses, fungi, or aseptic. Most cases of viral meningitis usually heal themselves and are not fatal, but in severe cases, such as bacterial, biased, life-threatening.
Methods: Articles related to bacterial meningitis taken from databases like Google Scholar, Pubmed and Portal Garuda over the last 5 years (2020- 2024). Use keywords: "Bacterial meningitis", "symptoms", "therapy", "antibiotic resistance
Results: Based on studies that have been carried out, antibiotic resistance rates in cases of bacterial meningitis are very high and vary. Streptococcus pneumonia as one of the most common causes has high levels of resistance to antibiotics of the penicillin group.
Conclusion: With the growing number of rapid, reliable and accurate diagnostics and follow-up examinations, it can cope with the incidence of antibiotic resistance in bacterial meningitis.

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INTRODUCTION

Meningitis is an infectious disease that attacks the membranes of the brain or meninges. Meningitis is included in the ten most dangerous types of diseases in the world. This disease can affect children as well as adults. The cause of this disease can be bacterial, viral, fungal, or aseptic. Most cases of viral meningitis usually resolve on their own and are not fatal, but in severe cases, such as bacterial meningitis, it can be dangerous to life-threatening if the right antibiotics are not given appropriately and quickly (1,2).

The incidence of bacterial meningitis is a challenge around the world, especially for developing countries. Worldwide there are 8.7 million cases of bacterial meningitis with the number of deaths reaching 379,000 cases. The incidence rate is particularly high in the so-called "The Meningitis Belt" covering Africa, Dakar, and Senegal. In Indonesia, the incidence of meningitis and death was the highest in Southeast Asia in 2016, the number of cases reached 78,018 cases with 4,313 deaths (3).

Cases of bacteriophageal meningitis are classified into community-acquired meningitis and health-related meningitis, as they have different spectrums of pathogenic bacteria. Patients who have recently undergone neurosurgery (within 1 month of the onset of meningitis) are classified as having healthcare-associated meningitis. Patients without evidence of healthcare-related infection are classified as community-acquired meningitis (4).

Most cases of bacterial meningitis are caused by Streptococcus pneumoniae which often affects people of all ages, then Neisseria meningitidis often affects children aged 11-17 years, and Haemophilus influenzae type B. Other types of bacteria that can cause meningitis, such as Streptococcus suis in Southeast Asia, Listeria monocytogenes, Group B Streptococci, and Gram-negative bacteria such as Escherichia coli and Klebsiella pneumoniae that cause meningitis in certain groups, including neonates, pregnant women, transplant recipients and older adults (5).

Clinical manifestations that appear in patients with meningitis such as lethargy, hyperthermia, anorexia, headache, impaired respiratory frequency and rhythm, the appearance of signs of meningeal stimulation such as stiffness and general rigidity. Meningitis also results in increased intracranial pressure characterized by decreased consciousness, projectile vomiting (squirting), and seizures (6). Children and adults with bacteriophageal meningitis generally present with headache, neck stiffness, fever, and altered mental status, with each of these symptoms occurring in 70-80% of patients (7).

Patients suspected of having bacteriophage meningitis must undergo a lumbar puncture to obtain a sample of cerebrospinal fluid (CSS). The CSS should be sent for Gram staining, culture, complete cell count, and glucose and protein levels checks. Bacteriophrenic meningitis usually results in low glucose levels and high levels of protein in cerebrospinal fluid. Because CSF glucose levels depend on circulating serum glucose levels, the ratio of CSF to serum glucose is considered a more reliable parameter for the diagnosis of acute bacterial meningitis than absolute CSF glucose levels. It is expected that there is a predominance of neutrophils in the number of cells (8).

The diagnosis will be confirmed by the bacteria identified on the gram staining or culture. A CT scan of the head without contrast should be performed before lumbar puncture if the patient is at risk of herniation. Risk factors include papilledema on examination, recently occurring seizures, focal neurological deficits, or immune system disorders. Consider delaying lumbar puncture if the patient has unstable vital signs, coagulation abnormalities, or has recently had a seizure (8).

Antibiotic therapy and supportive care are essential in all cases of bacterial meningitis, airway management, maintaining oxygenation, providing adequate intravenous fluids, as well as providing fever control are part of the basics of meningitis management, the type of antibiotics based on the organism suspected of causing the infection. (9).

METHOD

All articles related to the incidence of bacterial meningitis were taken from databases such as Google Scholar, PubMed, Scopus and the Garuda Portal in the last 5 years (2020-2024). Search strategies included prospective studies, retrospective cohorts, mixed methods, experimental, cross-section, case-control, delphi techniques, and reviews using keywords: "bacterial meningitis", "outpatient", "inpatient", "symptoms", "risk factors", "therapy", "antibiotic resistance". During article review, articles related to the subject are also reviewed. Research articles that cannot be accessed in full text will then be excluded.

RESULTS

Table 1. Article search results

NO	Author, Year	Study	Pathogens	Result
1.	(Peng, et all, 2021)	Retrospective	S. epidermidis, E. coli and S. pneumoniae are the main pathogens that cause pediatric bacterial meningitis in Chinese patients. The distribution of the organisms that cause pediatric bacterial meningitis varies by age.	Methisillin-resistant coagulase-negative staphylococcus (MRCoNS) decreased from 80.5% to 72.3%. Penicillin-resistant S. pneumoniae isolate increased from 75.0 % to 87.5%. The proportion of broad-spectrum β-lactamase (ESBL)-producing E. coli fluctuated between 44.4% and 49.2%, and the detection rate of ESBL production

				in Klebsiella pneumoniae ranged from 55.6% to 88.9%. The resistance of E. coli strains to carbapenems was 5.0%, but the prevalence of carbapenem-resistant K. pneumoniae (CRKP) was high overall (54.5%).
2.	(Rostamian, et all, 2022)	Systematic review and analysis methodology	Neisseria meningitidis	However, non-sensitivity to penicillin, as a first-line antibiotic to N. meningitis, was higher (27.2%).
3.	(Okparasta, et all, 2020)	Retrospective	The pathogen found based on the results of the culture is Staphylococcus sp. (69%), Acinetobacter baumanii (5.3%), Klebsiella pneumonie (15%), Shigella somnei, and E. coli (5.3%).	Antibiotic resistance to Staphylococcus sp. are also quite high, namely Erythromycin and Oxacillin reaching 77%, Trimetoprim/Sulfametoxazone 55%, Ciprofloxacin, Clidemomycin, Levofloxacin reaching 33%. Higher mortality is found in patients who develop drug resistance.
4.	(Namale, et all, 2020)	Systematic review	Streptococcal pneumoniae was found to be the most common cause of disease at 12.4% (CI 11.1%-13.6%), Neisseria meningitidis at 8.1% (CI 7.1%-9.2%) and Hemophilus influenza at 4.0% (CI 3.6%-4.3%)	Of the 64 studies reviewed, 29 (45%) reported on antimicrobial resistance. Resistance was found to be highest in ampicillin 2.7% (CI 2.1%-3.3%) and gentamicin 2.75% (2.09-3.40).
5.	(Cabellos, et all, 2022)	Cohort studies	Streptococcal pneumoniae	Penicillin-susceptible strains accounted for 246 (73%), penicillin-resistant strains accounted for 93 (27%), Cefotaxime susceptible to 58, and Cefotaxim-resistant 35. Nine patients failed or relapsed and 69 died (20%), 22% of which were vulnerable cases and 17% were resistant cases.
6.	(Ali, et all, 2021)	Cross-sectional	Steptococcus pneumoniae, Staphylococcus aureus, Neisseria meningitidis, Haemophilus influenzae, Escherichia coli and Klebsiella pneumonia.	S. aureus isolate showed the highest resistance to erythromycin 90.2% (55/61) and oxytetracycline 65.6% (40/61), S. pneumoniae isolate showed the highest resistance to amoxicillin 100% (130/130) and rifampicin 59% (77/130). E. coli isolate showed a high level of resistance to amoxicillin 80% (32/40) and rifampicin 77.5%

				(31/40). K. pneumoniae isolate is 100% (17/17) resistant to amoxicillin, while 88.2% (15/17) is resistant to erythromycin and oxytetracycline.
7.	(Zheng, et all, 2022)	Retrospective	Klebsiella pneumoniae	Ninety patients with Multidrug-Resistant Enterobacteriaceae were included in this study. Klebsiella pneumoniae accounted for the highest proportion of causative pathogens (46/90, 51.1%), and 40 causative pathogens (44.4%) were resistant to meropenem. blaKPC (27/40, 67.5%) is the dominant carbapenem resistance gene.
8.	(Ishikawa, et all, 2022)	Systematic review	Steptococcus Pneumoniae	Identified 18 papers describing thirty-five cases of penicillin- and cephalosporin-resistant S. pneumoniae meningitis
9.	(Willerton, et all, 2021)	Retrospective	Neisseria meningitidis	Of the 4,122 IMD isolates, 113 isolates were resistant to penicillin, five were resistant to ciprofloxacin, two were resistant to rifampicin, and one was resistant to sephthachim.
10.	(Henny, et all, 2020)	Retrospective	The most common gram-negative bacteria are Pseudomonas sp, and Pseudomonas stutzeri. The most commonly found gram-positive bacteria is Staphylococcus sp, with Staphylococcus hemolyscus.	About 26.9% of bacteria are drug-resistant organisms and the vast majority (78.6%) are gram positive. Ceftriaxone as our empirical therapy has low sensitivity (30%) to gram-positive bacteria and moderate sensitivity to gram-negative bacteria (53.57%). Resistance to cephalosporins may be quite high in this particular clinical setting due to the high number of drug-resistant organisms.
11.	(Kumar, et all, 2024)	Prospective	Escherichia coli, pseudomonas sp.	E. coli is highly resistant to Cefixime and Ampicillin. Pseudomonas sp. is relatively sensitive to all antibiotics tested with varying resistance patterns.

DISCUSSION

Bacterial meningitis has become a challenge for the whole world, including Indonesia. In 2016 Indonesia had the highest number of meningitis cases in Southeast Asia. Based on 11 recent studies on bacteriological meningitis, it was found that there is a pattern of bacterial resistance to the antibiotic treatment that has been given.

In the Peng, et all 2021 study, it was found that the three main pathogens that cause bacterial meningitis in children are Staphylococcus epidermidis (16.5%), Escherichia coli (12.4%) and Streptococcus pneumoniae (10.6%). Resistance in infants under 3 months of age, the 3 most common pathogens are E. coli (116/523; 22.2%), Enterococcus faecium (75/523; 14.3%), and S. epidermidis (57/523; 10.9%). However, in children older than 3 months, the 3 causative pathogens are S. epidermidis (140/670; 20.9%), S. pneumoniae (117/670; 17.5%), and S staphylococcus hominis (57/670; 8.5%). More than 93.0% of E. coli isolates were sensitive to cefoxitin, piperacillin or tazobactam, etoperidone or sulbactam, amicicide and carbapenem, and the levels of resistance to ceftriaxone, cefotaxime and ceftazidime were 49.4%, 49.2% and 26.4%, respectively. From 2016 to 2018, the proportion of coagulase-Negative Staphylococcus Resistant Methicillin isolates (MRSnK) decreased from 80.5% to 72.3%, and the frequency of penicillin-resistant S. pneumoniae isolates increased from 75.0% to 87.5%. The proportion of broad-spectrum β-lactamase producing E. coli (ESBL) fluctuated between 44.4% and 49.2%, and the detection rate of ESBL production in Klebsiella pneumoniae ranged from 55.6% to 88.9%. The resistance of E. coli strains to carbapenems was 5.0%, but the prevalence of K. pneumoniae (Carbapenem Resistant Pneumonia) overall had high resistance (54.5%) (10).

Other studies show overall resistance to the most commonly used antibiotics such as ceftriaxone, velotaxis, ciprofloxacin, and revamping is low, ranging from 1% to 3.4%. However, insensitivity to penicillin, as a first-line antibiotic against N. meningitis, was higher (27.2%). Overall, resistance to first-line antibiotics (except penicillin) is still low, suggesting that these drugs are effective against meningococcal meningitis. In the review literature we also found a significant gap between MIC and disc diffusion to evaluate resistance to antibiotics where disc diffusion exaggerates the degree of resistance.US$ 11

Supporting previous research, antibiotic resistance to Staphylococcus sp. is quite high, namely Erythromycin and Oxacillin reaching 77%, Trimethoprim or Sulfamethoxazole 55%, Ciprofloxacin, Clindamycin, Levofloxacin reaching 33%. Higher mortality is found in patients who develop drug resistance.US$ 12

Another study, which specifically examined Streptococcus pneumonia resistance also found that of the 64 studies reviewed, 29 (45%) reported on antimicrobial resistance. Resistance was found to be highest in ampicillin 2.7% (CI 2.1%-3.3%) and gentamicin 2.75% (2.09-3.40).US$ 13

Based on the results of the study, it was found that Streptococcus pneumonia as the main cause of bacterial meningitis, this bacterium has a high level of resistance, especially the penicillin group. The consequences of this incident affect the treatment results and the selection of the right antibiotics for the patient. On average, patients who have resistance have a high recurrence rate and a higher mortality rate than others.

Limitations and Cautions

Quality and Heterogeneity of Studies: The literature on antibiotic resistance in bacterial meningitis often includes studies with diverse methodologies, populations, and geographical settings. This heterogeneity can complicate the synthesis of findings and limit the generalizability of conclusions.

Limited Regional Data: Many studies on antibiotic resistance focus on high-income countries, with limited data available from low- and middle-income regions where resistance patterns may differ significantly. This imbalance restricts the applicability of findings to global settings.

Temporal Changes in Resistance: Antibiotic resistance patterns are dynamic and can change over time due to evolving bacterial strains and varying antibiotic usage practices. Some reviewed studies may use outdated data, limiting their relevance to current clinical scenarios.

Variability in Diagnostic Accuracy: The accuracy of bacterial identification and antibiotic susceptibility testing may vary across studies due to differences in laboratory techniques and diagnostic technologies, potentially leading to inconsistencies in reported resistance rates.

Lack of Comprehensive Mechanism Analysis: While many studies report resistance patterns, fewer focus on the underlying genetic and molecular mechanisms driving resistance in bacterial meningitis pathogens. This gap hinders a deeper understanding of resistance development.

Recommendations for Future Research

Enhance Regional Data Collection: Future research should prioritize studies in low- and middle-income countries where data on antibiotic resistance in bacterial meningitis is limited. This will provide a more comprehensive understanding of global resistance patterns.

Longitudinal Studies: Conduct long-term studies to monitor the evolution of antibiotic resistance over time. These studies should consider changes in resistance due to regional antibiotic stewardship programs and emerging pathogens.

Focus on Multidrug-Resistant Strains: Research should specifically address the prevalence, mechanisms, and clinical management of multidrug-resistant (MDR) bacterial strains in meningitis cases to develop targeted treatment protocols.

Standardization of Methodologies: Develop and adopt standardized methods for diagnosing bacterial meningitis and testing antibiotic susceptibility. Consistent methodologies will improve the comparability and reliability of research findings across studies.

Molecular and Genetic Analysis: Increase focus on genetic and molecular mechanisms underlying resistance in key pathogens such as Streptococcus pneumoniae and Neisseria meningitidis. Understanding these mechanisms can aid in developing novel therapeutic strategies.

Evaluate Novel Antibiotics: Conduct clinical trials on the efficacy of new and alternative antibiotics in treating bacterial meningitis, especially against resistant strains. Exploring combination therapies and adjunctive treatments should also be prioritized.

Role of Vaccination Programs: Investigate the impact of vaccination programs on reducing the prevalence of resistant bacterial strains, particularly for pathogens like Haemophilus influenzae type b (Hib) and Streptococcus pneumoniae.

Contextual Resistance Studies: Examine how local healthcare practices, antibiotic usage patterns, and infection control measures influence resistance in bacterial meningitis to inform region-specific treatment guidelines.

Research in Vulnerable Populations: Emphasize studies on resistance in vulnerable groups such as neonates, immunocompromised individuals, and populations in conflict zones where bacterial meningitis is prevalent.

Integration of One Health Approach: Incorporate the One Health framework in studying antibiotic resistance, linking human, animal, and environmental health to understand the broader context of resistance emergence and dissemination.

CONCLUSION

The level of antibiotic resistance in bacterial meningitis patients is very high and also varies. The average patient is resistant to antibiotics first-line antibiotic treatment. It is necessary to make efforts to conduct a complete examination to find out the exact cause of the bacteria that cause meningitis so that appropriate and fast treatment steps are taken to prevent unexpected complications.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest regarding the publication of this literature review on antibiotic resistance in cases of bacterial meningitis. All opinions and conclusions presented in this review are solely based on the analysis of the existing literature and have not been influenced by any external financial or personal interests.

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