# Susceptibility pattern in bacterial meningitis in patients in Diyala governorate.

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## Abstract

**Aim of study:** To identify the incidence of the antibiotic susceptibility in acute meningitis in Diyala governorate.

**Patients and methods:** This is observational study conducted in the Department of Central laboratories in Al-Batool Teaching Hospital, Diyala Governorate, Iraq in the period from September 2023 to February 2024. This study includes 80 CSF samples with confirmed diagnosis of Bacterial meningitis who were admitted to the infectious diseases ward. Were used the health records to determine the results of their CSF culture and susceptibility tests.

**Results:** *Staphylococcus spp.* as most prevalent pathogen, which was identified in 52.5% of isolates. The most resisted antibiotic group was the penicillin group with ranges that about 90% without the use of beta lactamase inhibitors (Clavulanic acid,

Tazobactam and sulbactam). Cefazoline and cefotaxime was around 85%. Resistant to carbapenems especially to imipenem was high around 65%. Vancomycin resistance was relatively low except in *Enterobacter spp.*

**Conclusion:** Our findings suggest high rate of resistance to multiple antibiotics which is mainly due to excessive usage of antibiotics in unnecessary condition.

## Introduction

Meningitis is a potentially fatal illness mainly brought on by bacteria or viruses, and it has a long history. It used to be always lethal if antibiotics weren't available. With a mortality rate around to 25%, the illness remains dangerous even with major improvements in treatment. Ancient writings have recorded the signs and symptoms of meningeal inflammation, but it was not until surgeon John Abercrombie characterized the condition in 1828 that the name "meningitis" became widely used. Even with advances in diagnosis, treatment, and immunization, the worldwide impact is still substantial. Globally, 8.7 million cases of meningitis were reported in 2015 alone, accounting for 379,000 fatalities. In order to solve the problems caused by meningitis, it is imperative to recognize the continuous efforts being made in research, immunization programs, and healthcare infrastructure development (Chalimou, 2019).

Meningitis is characterized by the inflammation of the meninges, which are the three membranes (dura mater, arachnoid mater, and pia mater) enveloping the brain and spinal cord within the vertebral canal and skull. Conversely, encephalitis specifically involves inflammation of the brain tissue. Meningitis may arise from various causes, including both infectious and non-infectious processes such as autoimmune disorders, cancer or paraneoplastic syndromes, and drug reactions. The infectious agents responsible for meningitis encompass bacteria, viruses, fungi, and, albeit less frequently, parasites (Kasim,2018).

Relying solely on clinical features is insufficient for confirming a meningitis diagnosis. A lumbar puncture (LP) is imperative to validate the diagnosis and determine its specific cause. According to a particular study, 95% of patients with bacterial meningitis exhibited a minimum of two symptoms, including headache, neck stiffness, fever, and altered consciousness. However, the simultaneous presence of fever, neck stiffness, and altered consciousness occurred in only 44% of cases. Neurological deficits were observed in approximately one-third of patients, aligning with similar findings reported in other studies. These results underscore the importance of lumbar puncture in accurately diagnosing meningitis and identifying its causative factors (Stockdale, 2011). A rash in suspected meningitis makes *N meningitidis* more likely. However, 37% of meningococcal meningitis patients have no rash. Varicella and enterovirus can also be associated with a rash.

When a patient displays indications of airway, breathing, or circulatory challenges, particularly in the context of concurrent sepsis, the primary emphasis in management should be on stabilizing these vital systems. It is essential for all patients to undergo evaluation by a senior clinician. The Royal College of Physicians recommends that consultant review be conducted for all acute medical patients within 14 hours of admission. The urgency of this review is determined by assessing

the National Early Warning Score. Recording the Glasgow Coma Scale (GCS) is imperative not only for its prognostic value but also to facilitate the monitoring of any changes. Additionally, documenting the presence of a rash and noting the use of preadmission antibiotics are important components of the comprehensive patient record. These measures collectively contribute to a thorough and effective approach to patient care in cases involving respiratory, circulatory, or septic complications. (Griffithis, 2018).

The treatment protocol for bacterial meningitis primarily involves antibiotics, sometimes accompanied by steroids. The selection of antibiotics is a three-step process: an initial empirical decision based on clinical suspicion, a subsequent review following microscopy results, and a final review upon the availability of culture or PCR results. In cases of suspected bacterial meningitis, dexamethasone administration is recommended, either shortly before or simultaneously with antibiotics, at a dosage of 10 mg intravenously (IV) every 6 hours. While dexamethasone can still be initiated up to 12 hours after the commencement of antibiotics, its impact on mortality during this period remains unstudied. In instances where pneumococcal meningitis is likely, it is advised to continue dexamethasone for a duration of 4 days. For suspected tuberculous meningitis, the provision of dexamethasone should align with established guidelines. This comprehensive approach aims to optimize the management of bacterial meningitis, combining timely antibiotic administration with the judicious use of steroids for improved outcomes. (Thwaites, 2009).

Cerebrospinal fluid (CSF) analysis plays a crucial role in suspected meningitis cases, as clinical characteristics alone are insufficient for distinguishing meningitis from other diagnoses and differentiating bacterial from nonbacterial causes. For the majority of patients without a need for a CT scan prior to lumbar puncture (LP) and

lacking other clinical contraindications, CSF analysis should be conducted within 1 hour of presumptive meningitis diagnosis without waiting for additional investigations such as platelet count or coagulation studies. Clinical contraindications to LP encompass anticoagulation, evidence of disseminated intravascular coagulation, and local infection or compromised skin integrity at the puncture site. In patients taking aspirin, LP is considered safe. However, the safety profile is less well-established for those using other antiplatelet agents like clopidogrel or ticagrelor, or those on dual antiplatelet therapy. In such cases, it is recommended to defer LP until further evaluation, ensuring a careful and individualized approach to patient safety. (McGill, 2016).

The sensitivity of culture for cerebrospinal fluid (CSF) is reported to be between 60% and 90% when collected before the initiation of antibiotic treatment, typically providing positive results within 24 to 48 hours. However, the efficacy of culture diminishes significantly in patients who have already received antibiotic therapy. In such cases, alternative tests like polymerase chain reaction (PCR) or bacterial antigen testing (BAT) may become necessary to accurately identify the causative pathogen. In addition to CSF cultures, it is recommended to obtain blood cultures in all suspected cases of bacterial meningitis. This is important because a pathogen may be isolated from blood despite a negative Gram stain and culture of CSF. The combined use of CSF and blood cultures helps enhance the diagnostic accuracy and aids in the identification of the responsible microorganism, even in cases where CSF culture sensitivity is compromised due to prior antibiotic treatment. (van de Beek, 2016).

Beta-lactam antibiotics are the preferred choice for treating meningococcal infections. In developing countries, where cost considerations play a significant role, chloramphenicol is often the standard therapy due to its affordability. For the

chemoprophylaxis of contacts, rifampicin and ciprofloxacin are recommended. Notably, since the early 1980s, isolates with reduced susceptibility to penicillin (PenI) have been identified in various European countries, including England, Spain, Italy, Portugal, Greece, and other Mediterranean nations. This highlights the importance of ongoing surveillance and adaptation of treatment protocols to address emerging challenges, such as antibiotic resistance. The selection of appropriate antibiotics remains crucial in effectively managing meningococcal infections, taking into account both regional considerations and the evolving resistance patterns of the bacteria.s (Fahmizad, 2006). Resistance has not been reported to the extended-spectrum cephalosporins (e.g. cefotaxime or ceftriaxone) that are the most frequently used antibiotics for the treatment of invasive meningococcal disease in most developed countries.

## Aim of study

To identify the incidence of the antibiotic resistance in acute meningitis in Diyala governorate.

## Patients and methods

This is observational study conducted in the Department of Central laboratories in Al-Batool Teaching Hospital, Diyala Governorate, Iraq in the period from September 2023 to February 2024. This study includes 80 CSF samples with confirmed diagnosis of Bacterial meningitis who were admitted to the infectious diseases ward. Were used the health records to determine the results of their CSF culture and susceptibility tests. We collected the data from the public laboratories in the hospital after taking all the permissions required from the authorities and the administrators. The privacy and confidentiality of the patients was preserved.

## Statistical analysis

Excel 2016 software was used to analysis the data we collected. We expressed the quantitative data by frequencies and percentages.

## Results

The results of the data analysis are demonstrated in table 1.

**Table 1. antibiotic susceptibility results**

| No. | Antibiotic Group | Antibiotic | 18-Isolate *S. aureus* (R. %) | 13- Isolate *S. hemolytica* (R. %) | 3- Isolate *Enterobacter spp.* (R. %) | 3- Isolate *kocuria kristinae* (R. %) | 42- Isolate *Staph. Spp.* (R. %) |
|---|---|---|---|---|---|---|---|
| 1. | Penicillin | Amoxicillin | 100 | 92.3 | 100 | 100 | 97.6 |
| 2. | | Amoxicillin/ Clavulanic acid | 100 | 46.1 | 33.33 | 33.33 | 7.1 |
| 3. | | Ampicillin/Sulba. | 88.8 | 100 | 100 | 100 | 78.5 |
| 4. | | Ticarcillin | 38.8 | 100 | 100 | 100 | 83.3 |
| 5. | | Ticarcillin/ Clavulanic acid | 100 | 92.3 | 100 | 100 | 92.8 |
| 6. | | Piperacillin | 100 | 100 | 100 | 100 | 76.1 |
| 7. | | Piperacillin/ Tazobactam | 94.4 | 13 | 100 | 66.66 | 95.2 |
| 8. | Cephalosporin | Cefuroxime | 88.8 | 92.3 | 66.66 | 66.66 | 80.9 |
| 9. | | Cefazolin | 88.8 | 84.6 | 66.66 | 66.66 | 88.0 |
| 10. | | Cefixime | 94.4 | 84.6 | 66.66 | 66.66 | 85.7 |
| 11. | | Cefotaxime | 83.3 | 100 | 66.66 | 100 | 85.7 |
| 12. | | Ceftazidime | 94.4 | 92.3 | 66.66 | 66.66 | 90.4 |
| 13. | | Ceftriaxone | 16.6 | 46.1 | 66.66 | 0 | 9.5 |
| 14. | | Cefepime | 94.4 | 100 | 100 | 66.66 | 90.4 |
| 15. | Carbapenem | Imipenem | 72.2 | 69.2 | 66.66 | 100 | 95.2 |
| 16. | | Meropenem | 27.7 | 23.0 | 33.33 | 0 | 4.7 |
| 17. | Aminoglycosides | Amikacin | 72.2 | 61.5 | 66.66 | 66.66 | 83.3 |
| 18. | | Tobramycin | 100 | 100 | 100 | 100 | 88.0 |
| 19. | Fluoroquinolones | Ciprofloxacin | 55.5 | 61.5 | 33.33 | 66.66 | 45.2 |
| 20. | | Levofloxacin | 11.11 | 0 | 0 | 0 | 7.1 |
| 21. | | Moxifloxacin | 94.4 | 92.3 | 100 | 100 | 88.0 |
| 22. | Glycylcycline | Tigecycline | 88.8 | 92.3 | 33.33 | 66.66 | 73.8 |
| 23. | Aminopyrimidine, Sulfamethoxazole | Trimethoprim/Sulfactam | 94.4 | 84.6 | 66.66 | 66.66 | 100 |
| 24. | Quinolone | Norofloxacin | 27.7 | 38.4 | 33.33 | 66.66 | 4.7 |
| 25. | Glycopeptide | Vancomycin | 16.6 | 0 | 33.33 | 0 | 0 |

Figure 1 demonstrates the bacterial susceptibility of the isolates in our study.

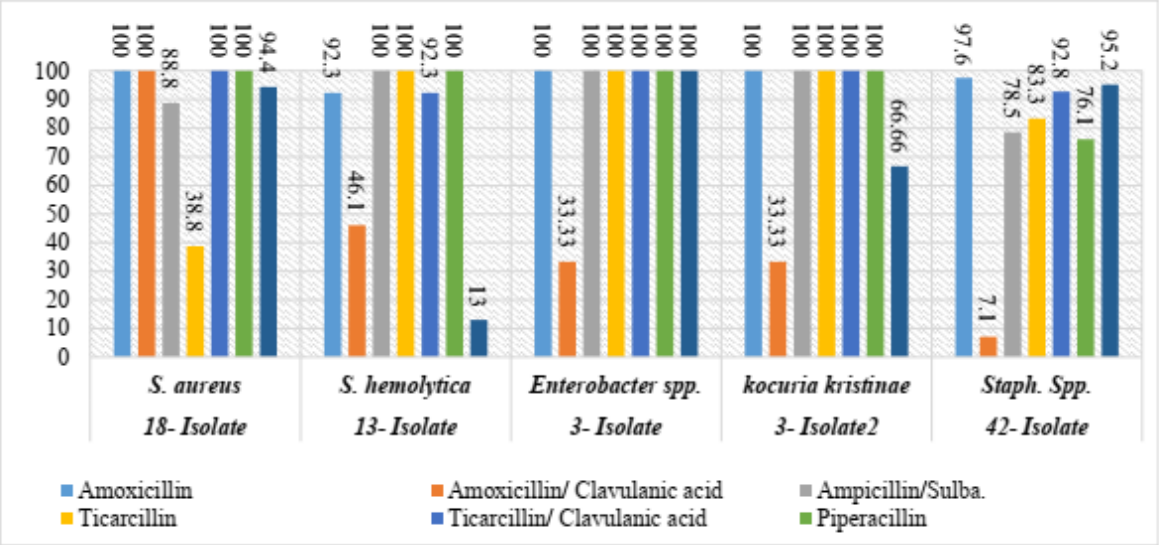


**Figure 1. the bacterial susceptibility of the isolates**

Figure 2 demonstrate the percentages of resistance in Cephalosporins group.

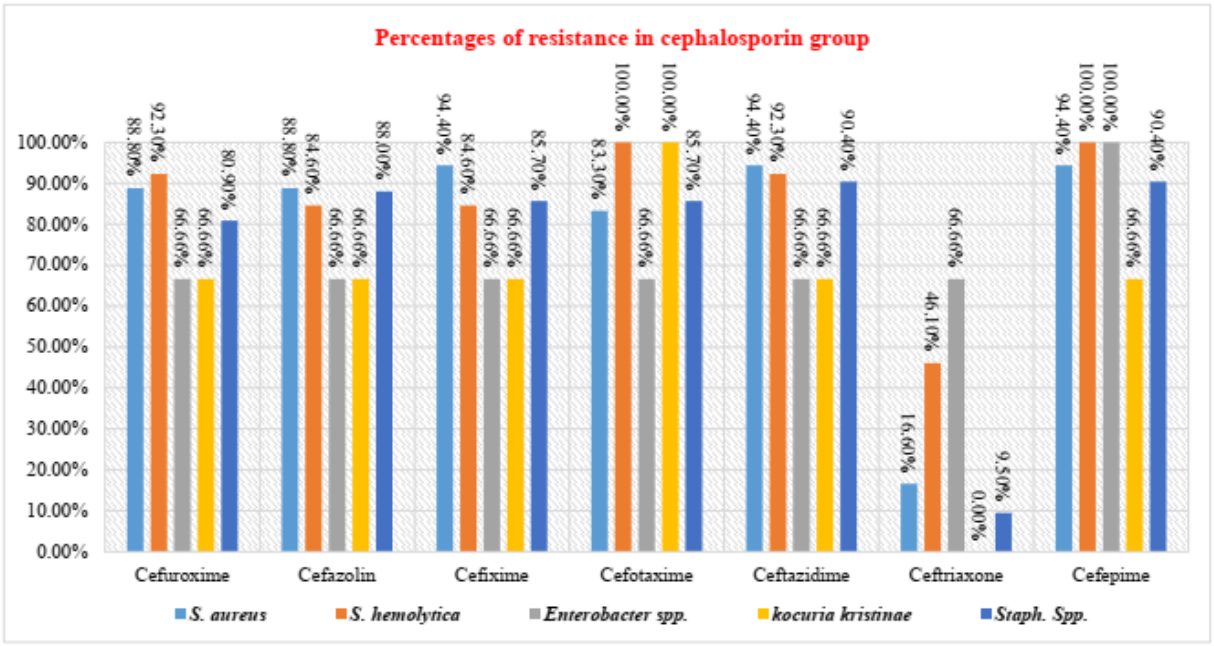


**Figure 2.**

Figure 3 demonstrate the percentages of resistance to carbapenem and aminoglycoside groups.

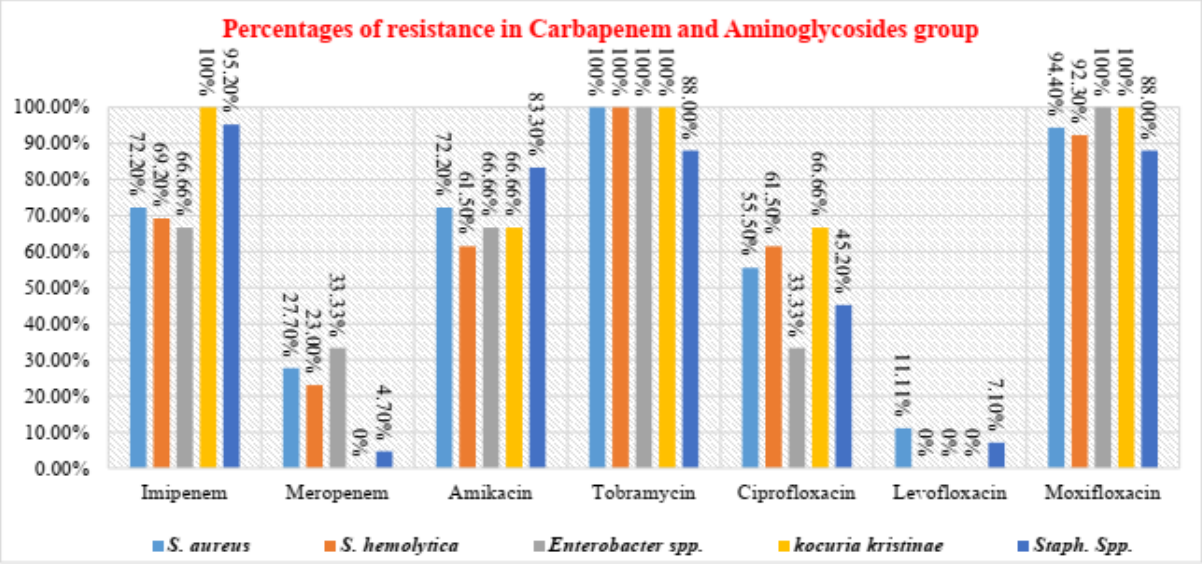


**Figure 3.**

Figure 4 demonstrate the resistance to miscellaneous antibiotics.

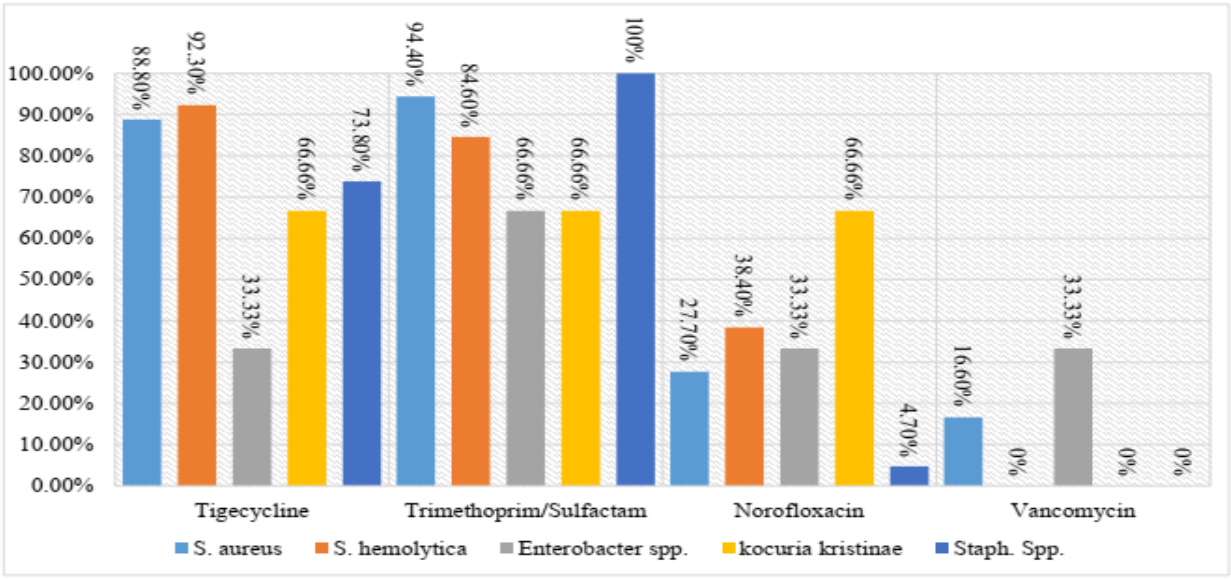


**Figure 4. the resistance to miscellaneous antibiotics.**

## Discussion

Acute bacterial meningitis continues to pose a significant health challenge among children and newborn infants globally, necessitating prompt diagnosis and aggressive treatment. Despite the presence of potent newer antibiotics, the mortality rate linked to acute bacterial meningitis remains alarmingly high in certain developing countries. Rates of mortality in these regions can range from 16% to 32%, underscoring the persistent severity of the condition and the urgent need for improved healthcare infrastructure, early detection, and access to effective therapeutic interventions to address this critical public health concern (Al Jarousha, 2014).

Our study identified *Staphylococcus spp.* as most prevalent pathogen, which was identified in 52.5% of isolates obtained from the patients included in this study; which is higher than the results have been reported in developed countries (Furyk, 2011).

The most resisted antibiotic group was the penicillin group with ranges that about 90% without the use of beta lactamase inhibitors (Clavulanic acid, Tazobactam and sulbactam) which is similar to the findings of Paris et al (Paris, 1995).

Cephalosporins resistance in our study is of worry, as the resistant of Cefazoline and cefotaxime was around 85% as a range which is higher than the findings of Chang et al (Chang, 2010) and this due to resistant strains and the massive use of empiric therapy before the confirmation of the culture and the susceptibility.

Resistant to carbapenems especially to imipenem was high around 65% from all isolates and was much lower to meropenem and this could be due to restricted

use of meropenem in Iraqi hospitals and not being the empiric agent of choice in most hospitals.

Vancomycin resistance was relatively low except in *Enterobacter spp*. And this due to the fact the most isolate are gram-positive which are vancomycin sensitive antibiotics (Knoll, 2013).

## Conclusion and recommendation

Antibiotic resistance in high mortality infection like meningitis should be red flag in Iraqi health ministry. Our findings suggest high rate of resistance to multiple antibiotics which is mainly due to excessive usage of antibiotics in unnecessary condition. We recommend more lights to put on this spot and to enact major action against the rubbish use of antibiotics and more restriction on their trade in private pharmacies.