

# Bacterial patterns and antibiotic sensitivity in septic patients treated with culture-based antibiotics in intensive care

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## Abstract

**Objective:** This study aims to determine the pattern of germs and antibiotic sensitivity in septic patients treated with culture-based antibiotics.

**Design:** This study was designed for observational-descriptive retrospective.

**Setting:** The medical record of Dr. Wahidin Sudirohusodo Hospital from January 2018 to January 2022.

**Patient and participants:** All patients who were diagnosed with sepsis and had data on bacterial culture and treatment with antibiotics.

**Interventions:** We took blood culture data of patients diagnosed with sepsis from medical records.

**Measurement and results:** The pattern of bacteria

found was Gram-negative bacteria, with the most abundant bacteria being *Burkholderia cepacia* (37.93%), followed by *Acinetobacter baumannii* (24.14%), and *Klebsiella pneumoniae* (10.34%). The highest antibiotic sensitivity was obtained for tigecycline with 88.89% followed by levofloxacin with 78.57%. The lowest antibiotic sensitivity was found in ampicillin, ampicillin/sulbactam, and cefoperazone/sulbactam as much as 0% or all of these antibiotics showed results that were resistant to culture results.

**Conclusions:** Gram-negative bacteria are the main cause of septic patients with varying antibiotic sensitivity depending on the type of antibiotic used.

**Key words:** Antibiotic sensitivity, bacterial patterns, Gram-negative, sepsis.

## Introduction

Sepsis is a clinical condition that can cause mortality due to widespread physiological and biochemical abnormalities. The incidence of sepsis in 2017 was estimated at 48.9 million cases with a

death rate of 11 million deaths. The death rate due to sepsis contributes to 20% of global deaths. (1) Sepsis can progress to septic shock, multiple organ dysfunction syndrome, and severe sepsis which are the main cause of death in critically ill patients. (2) Sepsis generally occurs due to burns, trauma, shock, surgical operations, infections, and other clinically critical illnesses. Various pathogenic microorganisms and toxins from these pathogens in the blood or tissue destroy the normal balance of anti-inflammatory and pro-inflammatory reactions in the body. (2) As many as 40.1% of septic patients are reported to have positive cultures. (3) Several species that are the main etiology of sepsis include *Acinetobacter*, *Klebsiella*, *Pseudomonas*, *Enterobacter*, *S. aureus*, and *E. coli*. (4)

Management of sepsis using antibiotics from the first hour is stated to be able to reduce the death rate in severe sepsis and septic shock. (5) The presence of antibiotic resistance in the treatment of sepsis can

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worsen clinical conditions, increase the length of stay in the hospital, and even cause death. (4) Optimizing the use of antibiotics can reduce the side effects of the antibiotics and prevent drug resistance. Treatment using antibiotics needs to consider all the pathogens involved to provide appropriate antibiotic coverage. (6) Antibiotic stewardship has become an international priority to reduce the risk of antibiotic drug resistance and the rationale for antibiotic use. (5) Therefore, this research was interested in knowing germ patterns and sensitivity of the antibiotics in septic patients treated with antibiotics according to culture.

## Methods

This study was designed for observational-descriptive medical records from January 2018 to January 2022. The sampling technique was total sampling. The inclusion criteria were data on patients over 18 years of age, septic patients who underwent bacterial culture and antibiotic sensitivity, blood procalcitonin examination, and complete and legible medical record data. Exclusion data were septic patients with incomplete or difficult-to-read patient medical record data. The data collected included demographic data such as age, sex, type of disease, disease management, use of invasive devices, antibiotic therapy, and the length of stay in the intensive care unit. Bacterial culture data in the form of bacterial groups, types of bacterial specimens, and types of bacteria based on the specimens cultured. Bacterial sensitivity data to antibiotics based on culture. Data were analyzed descriptively.

## Results

The study found 116 septic patients with a bacterial culture pattern treated at the Intensive Care Installation; all bacteria were Gram-negative. The results of the bacterial cultures of septic patients on 3 culture specimens (blood, sputum, and tissue) showed that all the bacteria found were Gram-negative, namely *Acinetobacter baumannii*, *Acinetobacter lwoffii*, *Klebsiella pneumoniae*, *Pseudomonas putida*, *Pseudomonas aeruginosa*, *Enterobacter cloacae*, *Stenotrophomonas maltophilia*, and *Burkholderia cepacia*. Overall, the most common cultures found were *Burkholderia cepacia*, with 37.93% found in blood specimens, followed by *Acinetobacter baumannii* with 24.14%, which were found in blood and sputum specimens, and *Klebsiella pneumoniae* (Table 1).

From culture, it was found that the highest sensitivity to antibiotics was tigecycline at 88.89%, followed by levofloxacin at 78.57%. The lowest antibiotic sensitivity was found in ampicillin, ampicil-

lin, ampicillin/sulbactam, and cefoperazone/sulbactam as much as 0%. It meant that all of the bacteria were resistant to those antibiotics (Figure 1). Antibiotic sensitivity was also presented based on the findings of each bacteria. It was found that tetracycline had 100% sensitivity against *Acinetobacter baumannii* and 33.33% against *Klebsiella pneumoniae*. Levofloxacin had a sensitivity of 33.33% against *Acinetobacter baumannii*, 7.14% against *Acinetobacter lwoffii*, 7.14% against *Klebsiella pneumoniae*, 7.14% against *Pseudomonas putida*, 7.14% against *Enterobacter cloacae*, 7.14% against *Stenotrophomonas maltophilia*, and 35.71% against *Burkholderia cepacia*. Tigecycline showed 100% sensitivity against *Acinetobacter baumannii* and 66.67% against *Burkholderia cepacia* (Figure 2).

## Discussions

The culture pattern of bacteria in blood, sputum, and tissue specimens from septic patients was found to be all Gram-negative bacteria, where the three most common microorganisms were *Burkholderia cepacia* (37.93%), followed by *Acinetobacter baumannii* (24.14%) and *Klebsiella pneumoniae* (10.34%).

These results were in line with previous research on 14,414 patients in 1,265 intensive care units (ICUs) worldwide showing that as many as 62% of microbial isolates were Gram-negative bacteria. (7) Similar research was reported in a study of patients in the tertiary care ICU at Fatmawati Hospital, Jakarta Indonesia, where *Klebsiella pneumoniae* (15.3%) was found to be the second most common isolate after *Pseudomonas aeruginosa* (26.5%), while the third most common isolate was *Staphylococcus epidermidis* (14.9%). (8) Research on patients treated with ventilators at the ICU of Sanglah General Hospital Denpasar showed that 18 species of the bacteria were *Acinetobacter baumannii* (20%) and *Klebsiella pneumoniae* (17.3%), and the most common bacterial species was *Pseudomonas aeruginosa* (22.2%). (9) Another study on sputum, urine, blood, tissue, and other cultures in severe septic patients obtained Gram-negative cultures in the form of *Klebsiella pneumoniae* (13.1%), *Escherichia coli* (11.7%), *Pseudomonas aeruginosa* (6.2%), *Acinetobacter baumannii* (3.5%), *Burkholderia pseudomallei* (1.3%), and *Enterobacter cloacae* (1.0%). (10) In contrast to this study, it was reported in research during the period 1979 - 2000 in the United States that the germ cultures that grew were mostly Gram-positive bacteria (52.1%), followed by Gram-negative bacteria (37.5%), polymicrobial (4.7%),

4.6% fungi, and 1% anaerobic bacteria. (7,11,12)

The most common bacterial culture found in this study was *Burkholderia cepacia* followed by *Acinetobacter baumannii*. *Burkholderia cepacia* is an aerobic, catalase-producing, Gram-negative bacillus that occurs due to nosocomial transmission such as contaminated drugs, fluids, antiseptics, and medical equipment. (11) Most reports of *Burkholderia cepacia* cultures are due to the use of vascular or Foley catheters. Another cause is the installation of a gastrostomy tube. (13) Meanwhile, *Acinetobacter baumannii* is an aerobic, non-fermenting Gram-negative coccobacillus, which is a nosocomial pathogen that causes urinary tract infections, wounds, meningitis, pneumonia due to mechanical ventilation, and bloodstream infections. *Acinetobacter baumannii* is increasingly showing resistance to the environment and many antibiotics are resistant to this bacterium. (14) Thus, it can be stated that the bacterial infections that occurred in septic patients in this study were mostly bloodstream infections caused by contamination of equipment in patient care in intensive care installations. The cleanliness of medicines, fluids, and equipment that will be used to treat patients in intensive care installations must be strictly considered to prevent ongoing infections that can cause sepsis.

Gram-negative bacteria are frequently involved in the pathogenesis of severe sepsis and septic shock. This can be explained because the bacteria invade through normal or damaged epithelium and enter the bloodstream, inducing a systemic inflammatory response (e.g., increased vascular permeability, leukocyte-endothelial adhesion, and activation of complement and coagulation pathways) and resulting in multiorgan failure. Other theories suggest that multiorgan dysfunction and shock result from neuroendocrine dysregulation and that mediators released into the bloodstream from infected tissues and circulating bacteria or endotoxins are not necessary as direct stimuli for intravascular inflammation. (15) *Pseudomonas aeruginosa* was also found in this study. *Pseudomonas aeruginosa* is a Gram-negative that causes urinary tract, lung, bloodstream, and soft tissue infections. *Pseudomonas aeruginosa* has a type III secretion system where the toxin is also directly injected into the host cell via a macromolecular syringe. (16)

In this study, it was found that *Klebsiella pneumoniae*, *Acinetobacter baumannii*, and *Pseudomonas aeruginosa* were resistant to the carbapenem group. The concern that arose was that the three Gram-negative bacteria had produced carbapenemase. These three bacteria were identi-

fied as the most common microorganisms developing resistance and accounted for two-thirds of healthcare-associated infections. (17) The predominant type of resistance is metallo- $\beta$ -lactamase (MBL). Carbapenemase-producing Enterobacteriales (CPE) strains are invariably multidrug-resistant, thereby significantly limiting treatment options for this type of infection, prolonging patient hospitalization time, and increasing the risk of a more severe and complicated disease course. (18) Therefore, it is important to pay attention to antibiotic resistance in treating septic patients according to the bacterial culture produced.

In this study, overall the highest antibiotic sensitivity was observed for tigecycline at 88.89%, followed by levofloxacin at 78.57%. The lowest antibiotic sensitivity was found in ampicillin, ampicillin/sulbactam, and cefoperazone/sulbactam at 0% (all bacteria were resistant to these antibiotics). Tetracycline had a sensitivity of 100% against *Acinetobacter baumannii* and 33.33% against *Klebsiella pneumoniae*. Levofloxacin had a sensitivity of 33.33% against *Acinetobacter baumannii*, 7.14% against *Acinetobacter lwoffii*, 7.14% against *Klebsiella pneumoniae*, 7.14% against *Pseudomonas putida*, 7.14% against *Enterobacter cloacae*, 7.14% against *Stenotrophomonas maltophilia*, and 35.71% against *Burkholderia cepacia*. Tigecycline had 100% sensitivity against *Acinetobacter baumannii*, 66.67% against *Burkholderia cepacia*, and 11.11% against *Enterobacter cloacae*.

Antibiotics have a rapid and long-lasting effect on the microbiota. (19) Antibiotic sensitivity is the property of microbes that can survive antibiotics. (20) In previous studies it was reported that Gram-negative isolates were sensitive to the following antibiotics: ciprofloxacin (67.46%), levofloxacin (56.35%), gatifloxacin (51.59%), and linezolid (50.79%), and Gram-negative isolates resistant to cefuroxime (24.6%), co-trimoxazole (19.84%), and cefdinir (16.67%). *Pseudomonas aeruginosa* was reported to be sensitive to ciprofloxacin (83.78%), gatifloxacin (51.35%), meropenem (51.35%), ceftazidime (45.95%) and linezolid (43.24%). *Klebsiella pneumoniae* was reported to be sensitive to gatifloxacin (63.16%), levofloxacin (63.16%), ciprofloxacin (63.16%), and linezolid (56.52%). (21) Another study reported that more than 80% of Gram-negative bacterial species in septic patients were sensitive to meropenem and resistant to ampicillin, ceftazidime, ceftriaxone, aztreonam, and trimethoprim. As many as 50% of Gram-negative bacteria form biofilms. (22)

Previous research reported the sensitivity pattern of pathogenic bacteria in a tertiary care ICU at Fatma-

wati Hospital, Jakarta Indonesia, with the results that *Pseudomonas aeruginosa* was sensitive to amikacin (84.4%), imipenem (81.2%), and meropenem (75.0%), and resistant to cephalexin (95.3%), cefotaxime (64.1%), and ceftriaxone (60.9%). Most bacteria are also resistant to third-generation quinolone antibiotics and cephalosporins. (8) Meanwhile, the results showed that *Pseudomonas aeruginosa* was sensitive to ceftazidime (68.3%), gentamicin (68.3%), and amikacin (65.9%). *Acinetobacter baumannii* was sensitive to amikacin (56.8%), gentamicin (32.4%), and tigecycline (32.4%). *Klebsiella pneumoniae* was sensitive to amikacin (83.9%), meropenem (77.4%), and piperacillin/tazobactam (54.8%). (9) In this study, tetracycline and tigecycline were the most sensitive antibiotics, especially against *Acinetobacter baumannii*. Tetracycline antibiotics can block the translation of mitochondria-encoded messenger ribonucleic acid (mRNA) and bind to mitochondrial ribosomes. (23) While tigecycline has structural similarities to tetracycline, tigecycline has a stronger binding affinity, around 5 times greater than tetracycline. Tigecycline and tetracycline also have a similar mechanism of action, namely inhibiting bacterial protein translation through reversible binding to the helical region (H34) on the bacterial 30S ribo subunit. The binding of tigecycline can prevent the incorporation of amino acid residues into the elongation of the peptide chain so that peptides are not formed and bacterial growth stops. Tigecycline can overcome tetracycline resistance through the addition of a

glycylamide moiety to position 9 of minocycline leading to the acquisition of a tetracycline-specific efflux pump (tet(A)) and ribosome protection (tet(M)). (24,25)

In this study, the most resistant antibiotics were ampicillin, ampicillin/sulbactam, and cefoperazone/sulbactam. The increase in antibiotic resistance is related to the ability of bacteria to form biofilms. The existence of antibiotic resistance results in the failure of antibiotic therapy, and the severity and pain of sepsis become worse. (21) Therefore, in septic patients, it is necessary to pay attention when carrying out treatment using ampicillin, ampicillin/sulbactam, and cefoperazone/sulbactam because antibiotic resistance occurs which can worsen the clinical condition.

The limitation of this research was that several samples had incomplete data, thereby slightly reducing the number of research samples. This study looked at all patients with sepsis and various causes and different enteric ports so that patient responded to antibiotic therapy may vary.

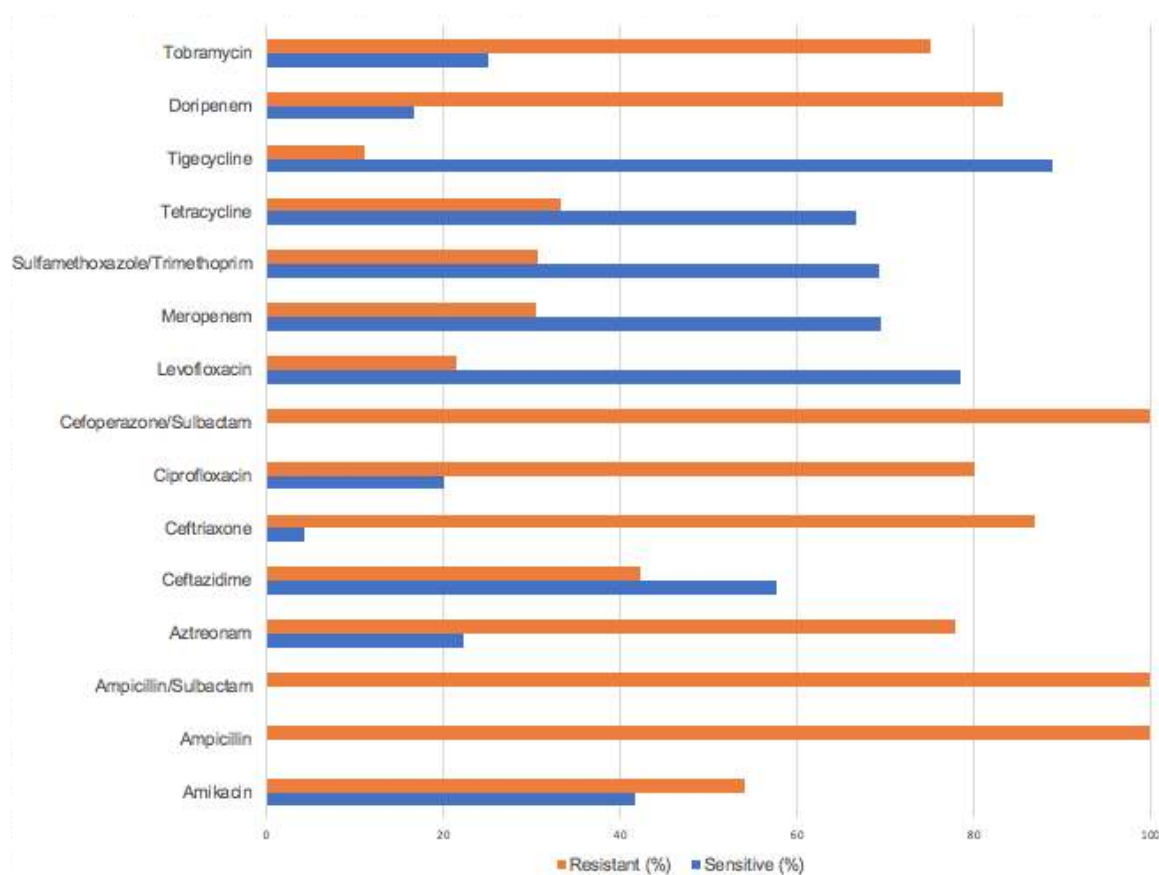
### **Conclusion**

Bacterial patterns from cultures in septic patients treated in the ICU were commonly found in *Burkholderia cepacia* (37.93%) followed by *Acinetobacter baumannii* (24.14%) and *Klebsiella pneumoniae* (10.34%). The sensitivity range of antibiotics varies between 0-100%. The highest antibiotic sensitivity in septic patients was tigecycline followed by levofloxacin.

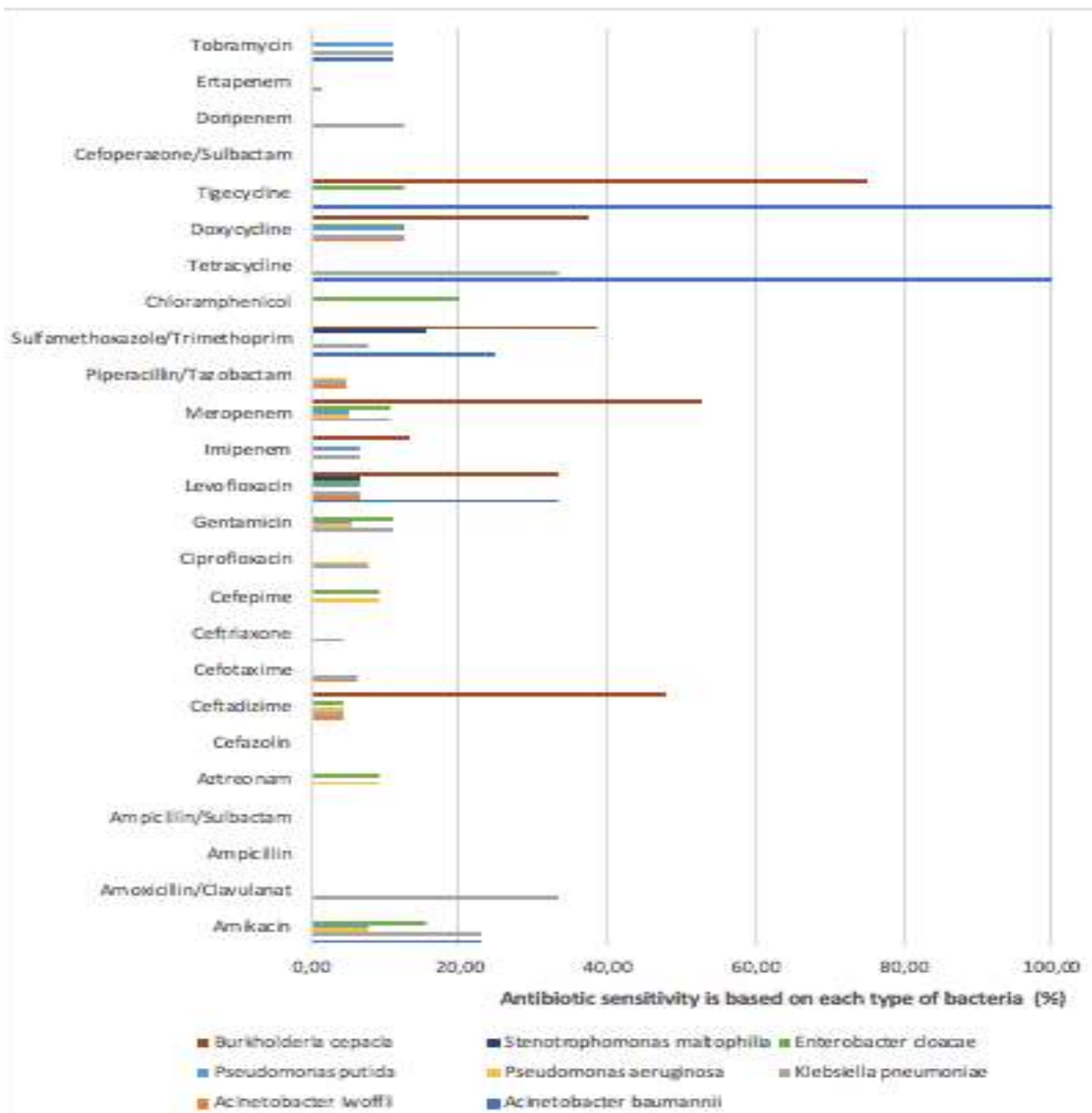
**Table 1.** Bacterial culture patterns of septic patients

| Bacteria                     | Blood |       | Sputum |       | Tissue |        | Total |       |
|------------------------------|-------|-------|--------|-------|--------|--------|-------|-------|
|                              | n     | %     | n      | %     | n      | %      | n     | %     |
| Acinetobacter baumannii      | 12    | 14.29 | 16     | 57.14 | 0      | 0.00   | 28    | 24.14 |
| Acinetobacter lwoffii        | 4     | 4.76  | 0      | 0.00  | 0      | 0.00   | 4     | 3.45  |
| Klebsiella pneumoniae        | 8     | 9.52  | 0      | 0.00  | 4      | 100.00 | 12    | 10.34 |
| Pseudomonas putida           | 4     | 4.76  | 0      | 0.00  | 0      | 0.00   | 4     | 3.45  |
| Pseudomonas aeruginosa       | 0     | 0.00  | 4      | 14.29 | 0      | 0.00   | 4     | 3.45  |
| Enterobacter cloacae         | 8     | 9.52  | 0      | 0.00  | 0      | 0.00   | 8     | 6.90  |
| Stenotrophomonas maltophilia | 4     | 4.76  | 8      | 28.57 | 0      | 0.00   | 12    | 10.34 |
| Burkholderia cepacia         | 44    | 52.38 | 0      | 0.00  | 0      | 0.00   | 44    | 37.93 |
| Total                        | 84    | 100   | 28     | 100   | 4      | 100    | 116   | 100   |

**Figure 1.** Antibiotics' sensitivity and resistance in septic patients



**Figure 2.** Antibiotics' sensitivity based on each type of bacteria in septic patients



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