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Antibiotic Utilization and Patient with Sepsis Characteristics: A Multicenter Retrospective Study in Semarang

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ABSTRACT: Sepsis remains a critical global health challenge requiring prompt and appropriate antimicrobial intervention to reduce mortality. Despite established guidelines recommending early broad-spectrum antibiotic administration, empirical prescribing patterns and their alignment with clinical recommendations remain insufficiently documented in Indonesian multicenter settings, particularly in Central Java. This study addresses the knowledge gap by evaluating antibiotic utilization profiles and patient characteristics among hospitalized sepsis cases in Semarang, with emphasis on empirical therapy practices and stewardship implications. A multicenter retrospective observational study was conducted involving 200 sepsis patients meeting predefined inclusion criteria from two hospitals in Semarang during 2019–2023. Data were extracted from medical records and analyzed descriptively, considering inter-hospital variability in prescribing practices. Results demonstrated male predominance (51.5%), elderly population representation (42.5% aged >60 years), multiple comorbidity burden (50.5% with two comorbidities), and moderate hospitalization duration (36% for 3–7 days). Broad-spectrum agents active against both Gram-positive and Gram-negative organisms dominated prescribing patterns (89.4%), while time-dependent antibiotics represented 10.5% of prescriptions. Meropenem emerged as the most frequently prescribed agent (33.3%), administered exclusively via the intravenous route (100%). These findings underscore the importance of structured antimicrobial management and robust de-escalation strategies in local hospital settings to effectively balance necessary empirical coverage with the prevention of antimicrobial resistance.

Keywords: Antibiotics; Patient characteristics; Sepsis; Utilization

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INTRODUCTION

Sepsis is a life-threatening organ dysfunction caused by an excessive response of the body to infection, also known as Systemic Inflammatory Response Syndrome (SIRS) induced by infection (Singer et al., 2016). Common pathogens responsible for sepsis include Escherichia coli (21.5%), Klebsiella pneumoniae (9.0%), Methicillin-sensitive Staphylococcus aureus (MSSA) (6.5%), and Streptococcus pneumoniae (5.0%) (Abe et al., 2024). Sepsis can be rapidly identified using the Quick Sequential Organ Failure Assessment (QSOFA) with three criteria: respiratory rate >22 breaths per minute, blood pressure <100 mmHg, and altered mental status. According to the Global Report on the, there are 48.9 million cases of sepsis and 11 million sepsis-related deaths worldwide. This data highlights that sepsis remains one of the major challenges in the medical field, requiring prompt and accurate management. In Indonesia, sepsis is also a serious issue, with 14,076 cases recorded in 2016 and a mortality rate of 5,876 (41.7%) patients surviving, while 8,200 (58.3%) patients died. Data from hospitals in Semarang shows 711 cases between 2019 and 2023.

However, comprehensive data regarding antibiotic utilization patterns specifically in Semarang's multicenter hospital settings remain limited, creating a knowledge gap in understanding local prescribing practices, empirical therapy selection, and alignment with international sepsis management guidelines. Furthermore, the extent to which local antibiotic prescribing reflects evidence-based recommendations or institutional antibiogram guidance has not been systematically evaluated. Understanding these patterns is essential for identifying potential areas of antimicrobial overuse, inappropriate spectrum selection, and opportunities for stewardship intervention, particularly given the documented variation in sepsis management practices across Indonesian healthcare facilities. This research gap is especially critical considering Semarang's role as a major urban healthcare center in Central Java, where prescribing patterns may differ significantly from both national trends and international benchmarks due to local pathogen epidemiology, resistance profiles, and institutional resources.

Therefore, this research is important to provide a clearer understanding of the characteristics of sepsis patients and antibiotic usage patterns in hospitals in Semarang. This is especially relevant in the context of the critical importance of timely and appropriate antibiotic administration, considering that delayed or inappropriate antibiotic treatment can increase the risk of patient mortality. The Surviving Sepsis Campaign (SSC) guidelines recommend the administration of broad-spectrum antibiotics within one hour after sepsis diagnosis. Timely and appropriate antibiotic administration is one of the most effective interventions to reduce mortality in sepsis patients. The use of broad-spectrum antibiotics is highly recommended in the initial management of sepsis. We recommend the continuous infusion of beta-lactam antibiotics over a long period for maintenance (after the initial bolus administration) compared to conventional bolus infusions (Evans et al., 2021). Therefore, this study aims not only to identify patient characteristics and antibiotic utilization profiles among sepsis cases in Semarang hospitals but also to evaluate the appropriateness of empirical antibiotic selection, assess the predominance of broad-spectrum therapy, and examine alignment with Surviving Sepsis Campaign guideline recommendations. Additionally, this research seeks to provide baseline data that can inform future antimicrobial stewardship initiatives and optimize empirical therapy protocols in local healthcare settings.

METHODS

This study is categorized as a descriptive observational study with data collected retrospectively. The research was conducted in the medical records department of Sultan Agung Islamic Hospital Semarang and Dr. Kariadi General Hospital Semarang from November 2024 to August 2025.

The study population comprised 711 patients diagnosed with sepsis between 2019 and 2023 at Rumah Sakit Islam Sultan Agung, Semarang and RSUP Dr. Kariadi, Semarang. Sample size

calculation using Slovin's formula with 95% confidence level yielded a minimum required sample of 256 patients. However, the final analyze sample consisted of 200 patients who fully met all inclusion criteria due to several limiting factors: incomplete or inaccessible medical record documentation, patients receiving combination antibiotic therapy rather than monotherapy, and patients with severely compromised renal function classified as glomerular filtration rate stages 4 and 5. This discrepancy between calculated and actual sample size, while representing a limitation, was addressed through rigorous adherence to predefined eligibility criteria to ensure data quality and analytical validity. Inclusion criteria specified patients diagnosed with sepsis and hospitalized during January 2019 to December 2023, aged ≥18 years, receiving monotherapy with antibiotics from beta-lactam, glycopeptide, or aminoglycoside classes, and possessing complete medical record data. Exclusion criteria encompassed patients with end-stage renal disease and those with chronic liver failure such as cirrhosis. The restriction to monotherapy cases, while limiting real-world representativeness given the common use of combination regimens in severe sepsis, was implemented to enable clear attribution of prescribing patterns to specific antibiotic classes and minimize confounding in utilization analysis. This methodological decision was deemed necessary for achieving the study's descriptive objectives, though it constitutes an important consideration when interpreting findings in the broader context of sepsis management practices. Excel and IBM SPSS were used for data processing. This study obtained ethical approval from Sultan Agung Islamic Hospital Semarang with reference number 46/KEPK-RSISA/III/2025.

Data Analysis

a. The data analysis was conducted descriptively using percentages to present patient characteristics, including:

1. Gender = $\frac{\text{Number of patients with a specific gender}}{\text{Total number of patients}}$ x100% (1)
2. Age = $\frac{\text{Number of patients in a specific age group}}{\text{Total number of patients}}$ x100% (2)
3. Number of Comorbidities= $\frac{\text{Number of patients in a specific category}}{\text{Total number of patients}}$ x100% (3)
4. Length of Hospital Stay= $\frac{\text{Number of patients with a specific length of stay}}{\text{Total number of patients}}$ x100% (4)

b. Analysis of antibiotic utilization profiles was also presented in percentages, including:

1. Bacterial culture results = $\frac{\text{Number of patients in a specific category}}{\text{Total number of patients}}$ x100% (5)
2. Antibiotic class= $\frac{\text{Number of patients receiving a specific class of antibiotics}}{\text{Total number of patients}}$ x100% (6)

   Notes: Mechanism of action, bacterial activity spectrum, and pharmacokinetics
3. Type of antibiotic= $\frac{\text{Number of patients receiving a specific antibiotic}}{\text{Total number of patients}}$ x100% (7)

RESULT AND DISCUSSION

Characteristics of Sepsis Patients

Based on the medical records obtained from Sultan Agung Islamic Hospital and Dr. Kariadi General Hospital between January 2019 and December 2023, a total of 200 respondents diagnosed with sepsis fulfilled all inclusion criteria. The patient characteristics collected included sex, age, number of comorbidities, and length of hospital stay.

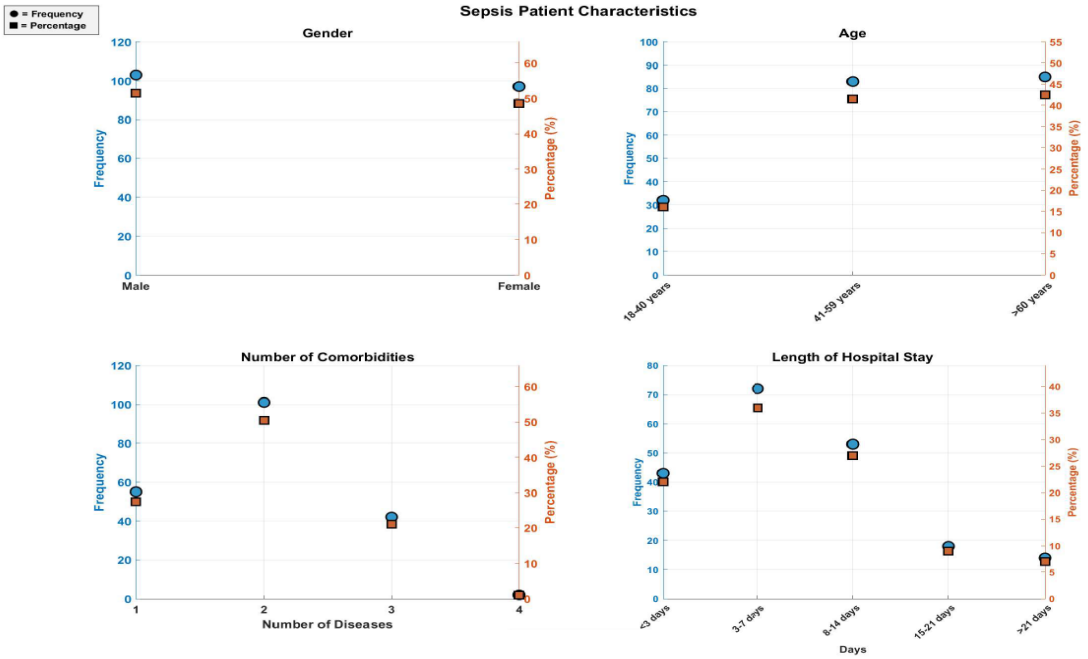


Figure 1. Characteristics of Sepsis Patients

The characteristics of sepsis patients shown in **Figure 1** indicate that the majority of respondents were male, with 103 patients (51.5%), compared to 97 female patients (48.5%). This finding is consistent with the study by Purnamasari et al. (2025), which reported that sepsis occurs more frequently in males than females. This difference is presumed to be related to the relatively stronger immune response in females, influenced by hormonal factors and the activity of pro-inflammatory mechanisms. Additionally, estrogen in females has been shown to enhance immune system function, thereby providing greater protection against infections and the progression of sepsis (Jiang et al., 2024). However, other studies have suggested that sepsis incidence is not significantly influenced by sex, but rather by age and underlying comorbidities (Cory et al., 2024).

Beyond merely confirming demographic patterns observed in prior sepsis literature, critical examination of sex-based differences in this cohort reveals important considerations for antibiotic selection and therapeutic outcomes. The slight male predominance, while consistent with immunological susceptibility patterns, warrants investigation into whether gender-specific differences influenced empirical antibiotic choice, dosing adjustments, or clinical response patterns within this population. Although this descriptive study did not stratify antibiotic utilization by gender, future analyses should explore whether prescribing practices adequately account for pharmacokinetic and pharmacodynamic variations between sexes, particularly given documented differences in drug distribution, metabolism, and immune response modulation that may affect antimicrobial efficacy (Senneville É et.al 2023).

Based on age distribution shown in **Figure 1**, 42.5% of sepsis patients were older than 60 years, and 41.5% were between 41–59 years. According to the Kemenkes RI (2021), individuals over 60 years are categorized as elderly. This group has a higher vulnerability to sepsis, partly due to immunosenescence, or the gradual decline in immune system function with age, which reduces the body's ability to effectively combat infections (Sanjaya et al., 2022). Furthermore, aging is associated with the decline of organ function, increasing the likelihood of comorbidities. Comorbid factors such as diabetes mellitus, renal disorders, and hypertension further elevate the risk of infections progressing into sepsis (Kang et al., 2024).

The analysis presented in **Figure 1** shows that the majority of respondents (50.5%) had two comorbidities. According to Sinapidis et al. (2018), comorbid conditions can significantly increase the likelihood of developing sepsis. Their study highlighted that the severity of infection leading to sepsis varies, and a greater number of comorbidities correlates with higher risks of sepsis and mortality, depending on the underlying infection. In the present study, diabetes mellitus was the most common comorbidity, affecting approximately 27% of patients. Diabetes mellitus has been strongly associated with a higher risk of sepsis, likely due to immunosuppression. Patients with multiple comorbidities, including diabetes, are at greater risk of developing sepsis across nearly all types of infections (Harsini et al., 2024).

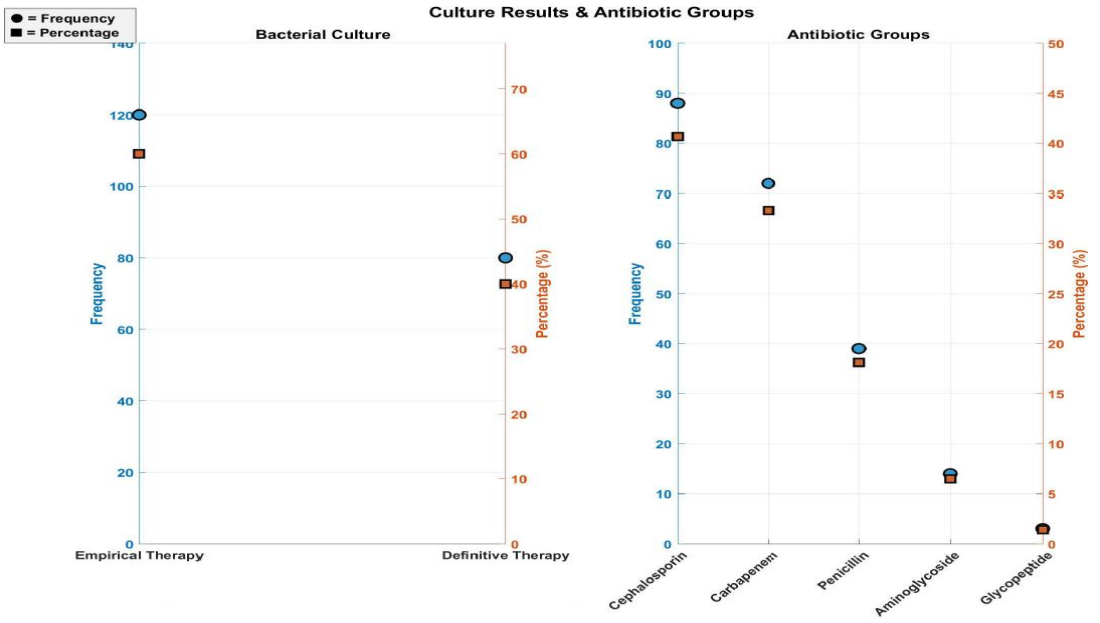
The substantial representation of elderly patients with multiple comorbidities in this cohort provides critical context for interpreting the observed predominance of broad-spectrum antibiotics. Advanced age combined with comorbidity burden creates complex clinical scenarios characterized by altered pharmacokinetics, increased infection severity risk, and compromised immune responses, which collectively may justify aggressive initial empirical therapy. However, this demographic profile simultaneously raises important stewardship concerns regarding prolonged broad-spectrum use without de-escalation. The high comorbidity prevalence with half of patients presenting two concurrent conditions theoretically supports initial broad-spectrum coverage due to unpredictable pathogen profiles and heightened mortality risk. Nevertheless, the appropriateness of sustained carbapenem and third-generation cephalosporin dominance observed in this study must be critically evaluated against whether these patient characteristics genuinely necessitate such extensive broad-spectrum therapy or whether alternative, narrower-spectrum options could have been considered following initial stabilization and diagnostic clarification (Risalati P et al., 2022)

The distribution of respondents based on length of hospital stay revealed that the majority of patients (36.0%) were hospitalized for 3–7 days. These demographic and clinical characteristics are comprehensively illustrated in Figure 1, demonstrating the distribution patterns across all analyzed variables. The numerical values presented in the descriptive analysis align consistently with visual representations, ensuring data integrity and interpretability.

This finding aligns with Regulation of Peraturan Mentri Kesehatan Republik Indonesia No. 28 of 2021, which states that the duration of antibiotic therapy is determined by its ability to resolve the infection according to the established diagnosis. In general, antibiotic therapy is administered for 3–7 days. If treatment exceeds seven days, a reassessment is required to ensure the accuracy of the initial diagnosis and to adjust therapy if necessary (Permenkes RI, 2021). Additionally, 21.5% of patients were hospitalized for fewer than three days, which in several cases was due to patient mortality during this periode.

Antibiotic Utilization Profile in Sepsis Patients

Based on medical record data collected from Rumah Sakit Islam Sultan Agung, Semarang and RSUP Dr. Kariadi, Semarang during the period of January 2019 to December 2023, a total of 200 respondents were diagnosed with sepsis and met all inclusion criteria. However, this study found that several patients received more than one type of antibiotic, resulting in a total of 216 recorded antibiotic administrations. This occurred due to changes in antibiotic regimens during hospitalization, which were not consistently accompanied by detailed documentation or clinical justification in the patients' medical records.



Note: Patients may receive more than one type of antibiotic

Figure 2. Results of Culture and Antibiotic Classes in Sepsis Patients

The substantial proportion of culture-negative sepsis cases observed in this cohort represents a critical finding with profound implications for antimicrobial stewardship and empirical therapy practices. As shown in Figure 2, 60% of patients had no bacterial culture results, while 40% had positive culture findings. Culture negativity presents a double-edged clinical dilemma: necessitating continuation of empirical broad-spectrum coverage due to diagnostic uncertainty while simultaneously eliminating opportunities for microbiologically-guided de-escalation a cornerstone stewardship principle. The high culture-negative rate raises important questions regarding appropriateness and duration of broad-spectrum antibiotic use. Specifically, did the observed predominance of carbapenems and third-generation cephalosporins represent appropriate empirical coverage based on local epidemiological patterns, or reflect defensive prescribing driven by diagnostic uncertainty (Thomas, A.P, et al., 2021). Li et al. (2021) reported that globally, approximately 40–60% of sepsis patients present with negative culture results due to early antibiotic administration prior to culture sampling, culture sensitivity limitations, difficult-to-culture pathogens, or non-bacterial infections such as fungal infections (Mellhammar et al., 2021).

Culture-negative status may have hindered timely de-escalation, potentially contributing to unnecessary antimicrobial exposure, increased resistance selection pressure, and elevated healthcare costs. This underscores urgent need for enhanced diagnostic stewardship, including rapid molecular diagnostic techniques, optimized culture collection methodology, and structured protocols for empirical therapy duration. Nevertheless, empirical therapy remains primary in sepsis management, as the Surviving Sepsis Campaign emphasizes broad-spectrum antibiotic administration within one hour after diagnosis (Evans et al., 2021).

The evaluation of antibiotic utilization presented in **Figure 2** shows that cephalosporins were the most frequently used antibiotics, accounting for 40.6%, followed by carbapenems at 33.2%. Among sepsis patients at Sultan Agung Islamic Hospital and Dr. Kariadi General Hospital, third-generation cephalosporins were the most commonly administered agents. This finding is consistent with the study by Abe et al. (2024), which reported that third-generation cephalosporins were the most frequently prescribed antibiotics in hospitals in Japan as empirical therapy for sepsis patients.

Furthermore, this study is supported by Kobayashi et al. (2023), who reported that third-generation cephalosporins were used empirically in 62.3% of cases. The selection of empirical therapy regimens may be influenced by patient risk factors and epidemiological conditions, including clinical signs, symptoms, disease severity, and suspected site of infection (Strich et al., 2021). In addition, the SSC guidelines recommend initiating antibiotic therapy within one hour after the diagnosis of sepsis (Evans et al., 2021). Therefore, empirical therapy plays a crucial role in promptly addressing infections, particularly when the causative pathogen has not yet been identified. Empirical antibiotic administration in sepsis patients is strongly recommended, as it remains one of the most effective interventions for reducing sepsis-related mortality (Abe et al., 2024).

Table 1 Antibiotic Utilization Profile in Sepsis Patients

No	Antibiotic Utilization Profile	Frequency (N=216)	Persentage (%)
1.	Mechanism of Action*		
	a. Antibiotik Targeting the Bacterial Cell Wall	**202**	**93,5**
	1) Cephalosporins	88	40,7
	2) Carbapenems	72	33,3
	3) Penicillins	39	18,1
	4) Glycopeptides	3	1,4
	b. Antibiotic Inhibiting Protein Synthesis	**14**	**6,5**
	1) Aminoglycosides	14	6,5
2.	Spectrum of Antibacterial Activity*		
	a. Gram-Positive	**7**	**3,2**
	1) First-Generation Cephalosporins	4	1,9
	2) Glycopeptides	3	1,4
	b. Gram-Negative	**16**	**7,4**
	1) Aminoglycosides	14	6,5
	2) Second-Generation Cephalosporins	2	0,2
	c. Gram positif & gram negatif	**193**	**89,4**
	1) Carbapenems	72	33,3
	2) Third-Generation Cephalosporins	69	32,0
	3) Penicillins	39	18,1
	4) Fourth-Generation Cephalosporins	13	6,0
3.	Pharmacokinetic Properties*		
	a. Time Dependent	**202**	**93,5**
	1) Cephalosporins	88	40,7
	2) Carbapenems	72	33,3
	3) Penicillins	39	18,1
	4) Glycopeptides	3	1,4
	b. Concentration Dependent	**14**	**6,5**
	1) Aminoglycosides	14	6,5

***Note:** Patients may receive more than one type of antibiotic

The findings presented in **Table 1**, indicate that the most frequently used antibiotics in sepsis patients were cephalosporins (40.7%), followed by carbapenems (33.3%). Both classes belong to the β-lactam group, which act by inhibiting penicillin-binding proteins (PBPs) involved in the synthesis of peptidoglycan, a key component of the bacterial cell wall. Inhibition of PBPs disrupts cell wall formation, leading to bacterial lysis and death (Pandey & Cascella, 2022). β-lactams have a broad antibacterial spectrum, with carbapenems offering the widest coverage among them.

Consequently, β-lactam use is often associated with infections caused by multidrug-resistant organisms (MDROs) (Tamma et al., 2021).

The substantial carbapenem utilization rate (33.3%) documented in this study necessitates critical evaluation regarding appropriateness, potential overuse, and alignment with antimicrobial stewardship principles (Farizi et.al., 2025). Carbapenems, classified as reserve antibiotics in national and international guidelines due to ultra-broad spectrum and resistance development association, should theoretically be reserved for documented multidrug-resistant infections or severely ill patients with high resistant pathogen risk (Peraturan Mentri Kesehatan Republik Indonesia, 2015). The observed carbapenem dominance raises important questions: Does this utilization pattern reflect genuine clinical need based on local antibiogram data demonstrating high extended-spectrum beta-lactamase (ESBL)-producing organism rates, or represent empirical overuse driven by uncertainty, defensive medicine practices, or lack of institutional antimicrobial guidance The absence of local antibiogram data integration in prescribing decisions, coupled with high culture-negative rates, suggests carbapenem selection may not have been consistently guided by microbiological evidence (Farizi et al., 2024). This pattern potentially indicates inappropriate carbapenem overuse, carrying serious implications including accelerated carbapenem-resistant organism development, last-line therapeutic option depletion, increased healthcare expenditure, and adverse hospital microbiome ecological effects (Sultana et al., 2023). Furthermore, lack of documented consideration for narrower-spectrum alternatives such as beta-lactam/beta-lactamase inhibitor combinations or rapid diagnostic-based targeted therapy suggests missed antimicrobial stewardship intervention opportunities. International guidelines, including Surviving Sepsis Campaign recommendations, advocate initial broad-spectrum coverage but emphasize critical importance of early de-escalation based on microbiological results and clinical response. The observed carbapenem utilization pattern appears to prioritize initial empirical breadth without corresponding evidence of systematic de-escalation strategies, highlighting significant gaps between current practice and evidence-based stewardship recommendations.

From a pharmacokinetic perspective, β-lactams exhibit time-dependent activity, where therapeutic effectiveness depends on the duration of drug concentration maintained above the minimum inhibitory concentration (MIC). Sulaiman et al. (2022) reported that the target T>MIC is 40–70%; thus, extended or continuous infusion strategies can improve therapeutic outcomes, particularly in sepsis patients who experience significant pharmacokinetic alterations due to increased volume of distribution or renal replacement therapy.

These findings are consistent with Titiesari & Febriani (2021), who noted that β-lactams are the first-line therapy for sepsis due to their effectiveness in suppressing bacterial growth in severe infections. However, the widespread use of β-lactams also raises the risk of antimicrobial resistance. Therefore, the principles of antibiotic stewardship must be applied, particularly de-escalation of therapy once microbiological culture results are available (Permenkes RI, 2021). Accordingly, the predominant empirical use of β-lactams observed in this study can be regarded as a rational clinical strategy for controlling sepsis infections, but it must be balanced with resistance prevention efforts.

Furthermore, **Table 1** shows that all antibiotics inhibiting protein synthesis in this study belonged to the aminoglycoside class. Aminoglycosides act by binding to the 30S ribosomal subunit, leading to codon misreading of mRNA and inhibition of ribosomal translocation. These disruptions result in the production of abnormal proteins and a halt in overall protein synthesis, ultimately impairing cell function and causing bacterial death, making aminoglycosides bactericidal agents (Thy et al., 2023).

Aminoglycosides are commonly used as adjunctive therapy against Gram-negative bacteria, particularly in severe infections or when MDROs are suspected (Peraturan Mentri Kesehatan Republik Indonesia, 2021). Pharmacokinetically, aminoglycosides are concentration-dependent, where efficacy relies on achieving a peak concentration (Cmax) relative to the MIC. The optimal therapeutic target is a Cmax-to-MIC ratio of 8–10. Therefore, once-daily high-dose regimens are

frequently recommended to achieve maximal bactericidal activity while reducing the risk of toxicity (Titiesari & Febriani, 2021).

While aminoglycosides demonstrate favorable concentration-dependent bactericidal activity and synergistic potential with beta-lactams in severe gram-negative infections, their clinical utilization in sepsis management requires careful consideration of nephrotoxicity risk a critical safety concern inadequately addressed in the current analysis. Aminoglycoside-associated nephrotoxicity occurs in 10-25% of patients depending on duration, dosing strategy, and patient-specific risk factors including advanced age, pre-existing renal impairment, concurrent nephrotoxic agents, and hypovolemia characteristics notably prevalent in the elderly, comorbidity-burdened population comprising this cohort. Although this study excluded patients with advanced chronic kidney disease (stages 4-5), the inclusion of elderly patients with multiple comorbidities and potential baseline renal dysfunction (stages 1-3) raises important questions regarding aminoglycoside safety and appropriateness (Pacifi GM et al. 2017)

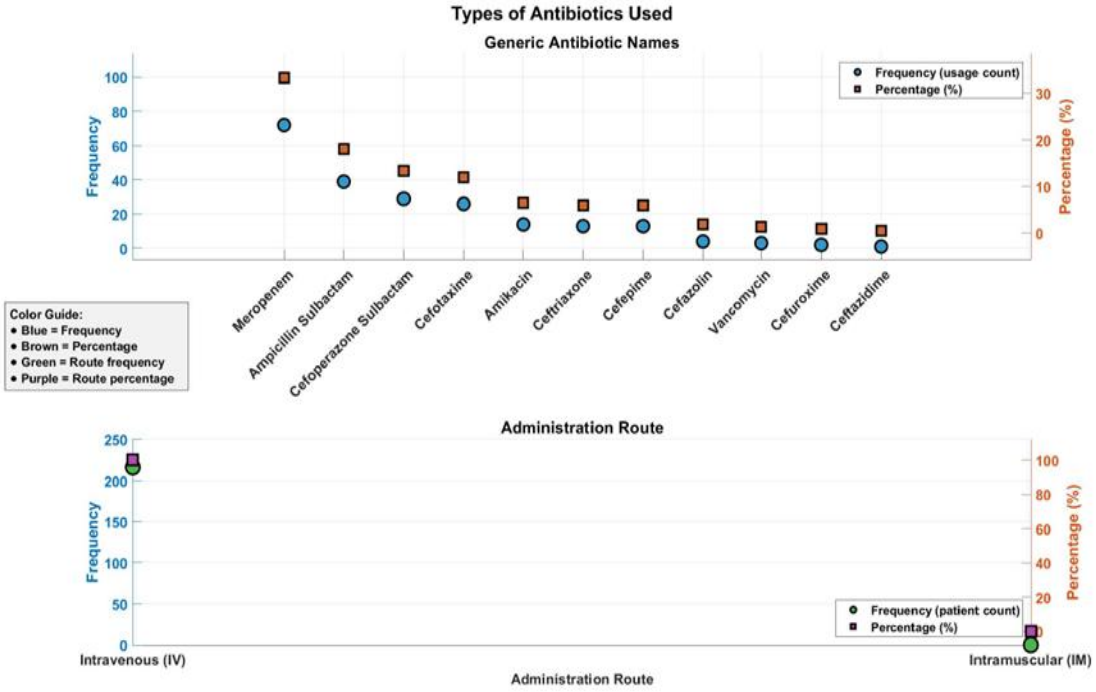
The absence of renal function monitoring data, therapeutic drug monitoring practices, and documentation of dose adjustments based on pharmacokinetic principles represents a significant limitation preventing evaluation of whether aminoglycoside use in this population adhered to evidence-based dosing strategies designed to maximize efficacy while minimizing toxicity. Contemporary guidelines recommend once-daily aminoglycoside dosing in hemodynamically stable patients to optimize pharmacodynamic parameters and potentially reduce nephrotoxicity, yet whether this approach was systematically implemented in the study cohort remains unknown. Furthermore, the duration of aminoglycoside therapy a critical determinant of nephrotoxicity risk was not analyzed, preventing assessment of whether prescribing practices aligned with recommendations for short-course therapy (typically ≤ 5-7 days) in empirical sepsis management (Bowen D et al., 2024)

The evaluation presented in **Figure 3** shows that meropenem was the most frequently used antibiotic, accounting for 33.2% of prescriptions. This finding is consistent with a study by Rohman et al. (2023), which reported that meropenem was the most commonly administered antibiotic in the ICU of Fatmawati Hospital, Jakarta. The high rate of use can be attributed to the fact that meropenem belongs to the carbapenem class, a broad-spectrum antibiotic effective against both Gram-positive and Gram-negative bacteria. This makes meropenem a frequent recommendation for empirical therapy in sepsis patients, particularly when culture results are not yet available.

The emergence of meropenem as the single most frequently prescribed antibiotic (33.3%) warrants careful examination regarding alignment with Surviving Sepsis Campaign (SSC) guidelines and evidence-based antimicrobial stewardship principles. While SSC guidelines recommend early administration of broad-spectrum antibiotics in sepsis management, they do not uniformly endorse carbapenems as first-line empirical therapy across all sepsis presentations. The appropriateness of meropenem dominance depends critically on several factors not systematically evaluated in this study: local antimicrobial resistance patterns, documented prevalence of ESBL-producing Enterobacterales, institutional antibiogram data, and patient-specific risk factors for multidrug-resistant infections (Lipsky, B.A et al., 2020).

The observed meropenem utilization rate in this cohort may suggest either (1) high local prevalence of resistant pathogens justifying empirical carbapenem use, which would align with guideline recommendations but remains unverified due to absent resistance surveillance data, or (2) empirical prescribing patterns driven by factors other than microbiological evidence, potentially representing deviation from evidence-based practice. Furthermore, SSC guidelines emphasize the importance of antimicrobial de-escalation within 48-72 hours based on microbiological results and clinical response. The absence of temporal prescribing data in this study prevents evaluation of whether meropenem initiation was appropriately followed by de-escalation to narrower-spectrum agents when clinically indicated. This represents a critical knowledge gap, as sustained meropenem use without reassessment contradicts fundamental stewardship principles and may indicate prescriber preference or institutional culture rather than guideline-concordant care.

Furthermore, this study aligns with Subhan et al. (2024), who reported that meropenem had the highest utilization rate among ICU patients, reaching 83.71%. This reflects the strong clinical confidence in meropenem's effectiveness in managing severe infections, including sepsis. In addition, a study by Anggraeni et al. (2024) at Gatot Soebroto Army Hospital, Jakarta, found that meropenem had the highest total antibiotic use, with 97.75 DDD per patient-days. These findings confirm that the use of meropenem as a first-line therapy for sepsis is not confined to a single hospital but is consistently observed across various referral healthcare facilities.



Note: *Patients may receive more than one type of antibiotic*

Figure 3. Antibiotic Types Administered to Sepsis Patients

In this study, most of patients received antibiotics via the intravenous (IV) route. This choice was based on the characteristics of sepsis as a medical emergency, marked by infection accompanied by organ dysfunction due to an excessive systemic immune response. Delayed administration of antibiotics has been proven to increase mortality rates; therefore, IV administration is considered a critical initial step. The IV route ensures rapid and stable achievement of plasma antibiotic concentrations. Moreover, sepsis patients often experience impaired gastrointestinal perfusion, making oral absorption unreliable. Additionally, intravenous administration, particularly of beta-lactam antibiotics through prolonged infusion, can enhance therapeutic effectiveness. This finding is consistent with a study conducted by Roberts et al. (2023), which demonstrated that prolonged infusion strategies improve target antibiotic concentrations in critically ill patients, although their effect on mortality remains variable. These findings highlight that IV administration is not only essential for ensuring rapid drug onset but also provides flexibility in adjusting dosing regimens according to the clinical needs of sepsis patients.

While the exclusive intravenous administration observed in this cohort aligns with evidence-based recommendations for initial sepsis management, the absence of data regarding early intravenous-to-oral (IV-to-oral) switch strategies represents a missed antimicrobial stewardship opportunity. Contemporary stewardship frameworks increasingly emphasize early transition from intravenous to oral therapy in clinically stable patients meeting specific criteria: hemodynamic stability, resolving fever, improving inflammatory markers, tolerating oral intake, and adequate

gastrointestinal absorption (Low DE., 1993). IV-to-oral conversion offers multiple benefits including reduced hospitalization duration, decreased catheter-related complications, lower healthcare costs, improved patient mobility, and facilitation of early discharge. The universal intravenous administration raises important questions regarding whether early switch criteria were systematically evaluated during hospitalization. For antibiotics with excellent oral bioavailability—fluoroquinolones, linezolid, metronidazole, and certain beta-lactams—early oral conversion may have been feasible in patients demonstrating clinical improvement, yet this analysis provides no insight into whether such opportunities were recognized. The observed length of stay distribution, with 36% hospitalized for 3-7 days, suggests potential timeframes for IV-to-oral switch evaluation (Lakoh S et al., 2023). However, without temporal prescribing data documenting route changes, we cannot determine whether prescribers implemented switch strategies or patients remained on intravenous therapy despite clinical improvement justifying oral transition. This knowledge gap highlights the need for future prospective studies incorporating daily IV-to-oral switch eligibility assessment using validated criteria and evaluation of associated clinical outcomes.

Study Limitations

This study acknowledges several methodological limitations substantially affecting interpretability and generalizability. First, the absence of sepsis severity scoring—particularly qSOFA or SOFA scores—prevents stratification by illness severity, essential for determining whether broad-spectrum antibiotic dominance reflects appropriate escalation for critically ill patients or indiscriminate prescribing. Without severity adjustment, we cannot definitively assess carbapenem and third-generation cephalosporin utilization appropriateness. Second, complete absence of local antimicrobial resistance surveillance data and institutional antibiogram integration prevents evaluation of whether empirical prescribing aligned with microbiological evidence. Antibiotic utilization patterns cannot be assessed as appropriate or excessive without understanding local prevalence of ESBL-producing organisms, carbapenem-resistant Enterobacterales, or MRSA—all influencing rational therapy selection. This limitation is particularly consequential given high culture-negative rates, amplifying the importance of epidemiologically-guided empirical therapy. Third, the purely descriptive design precluded outcome analysis, preventing assessment of whether utilization patterns correlated with mortality, microbiological cure rates, adverse events, or treatment failure. Fourth, despite the multicenter design, absence of inter-hospital comparative analysis limits understanding of institutional variability in prescribing practices, formulary influences, and stewardship program implementation. Fifth, excluding combination therapy patients—while necessary methodologically—significantly limits real-world representativeness, as combination regimens are frequently employed in severe sepsis per SSC recommendations, potentially creating selection bias toward less severely ill patients. Sixth, the 2019-2023 study period encompassed COVID-19 pandemic disruptions, yet temporal trend analysis was not performed, preventing identification of pandemic-associated shifts in antibiotic utilization. Finally, retrospective methodology inherently depends on documentation completeness, with potential information bias regarding dosing, timing, duration, and de-escalation practices.

Comparative Evaluation with Indonesian and Regional Studies

Contextualizing observed patterns within Indonesian and regional sepsis management reveals important insights regarding prescribing variability and stewardship challenges. Purnamasari et al. (2025) at RSUD Dr. H. Abdul Moeloek, Lampung, reported similar broad-spectrum predominance with notable drug selection differences. Our carbapenem utilization (33.3%) contrasts with varying Lampung patterns, potentially reflecting regional resistance epidemiology, formulary restrictions, or prescriber preferences. Similarly, Anggraeni et al. (2024) at RSPAD Gatot Soebroto identified comparable broad-spectrum trends yet highlighted different de-escalation practices and culture utilization rates. Higher culture-negative rates in our cohort suggest variability in diagnostic practices and microbiological laboratory capabilities across facilities. Internationally,

the Japan Sepsis Alliance study by Abe et al. (2024) revealed markedly different practices with greater anti-MRSA coverage and lower carbapenem utilization, reflecting differences in pathogens, resistance patterns, healthcare systems, and stewardship program maturity between Indonesia and developed Asian nations. Our meropenem dominance (33.3%) appears higher than similar resource settings, potentially indicating appropriate response to unverified local resistance pressures or empirical overuse requiring intervention. Broad-spectrum preference consistency across Indonesian studies suggests systemic challenges in implementing de-escalation strategies, possibly reflecting diagnostic limitations, prescriber uncertainty, medicolegal concerns, and insufficient stewardship infrastructure. These observations underscore that while certain patterns appear universal across Indonesian sepsis management, significant inter-regional variability exists in agent selection and carbapenem intensity, highlighting critical need for national antimicrobial resistance surveillance and standardized protocols adapted to local contexts.

CONCLUSION

This multicenter retrospective study provides critical baseline data characterizing antibiotic utilization patterns in sepsis management across Semarang hospitals, revealing predominant broad-spectrum use with notable carbapenem dominance (33.3%) and exclusive intravenous administration. These findings carry important implications for antimicrobial stewardship program development and empirical therapy optimization in Indonesian healthcare settings. The observed patterns substantial carbapenem utilization, high culture-negative rates (60%), and absence of documented de-escalation strategies—highlight critical stewardship intervention opportunities including local antimicrobial resistance surveillance implementation, evidence-based empirical therapy algorithms, enhanced diagnostic stewardship, and structured antibiotic review processes. Future research priorities include prospective evaluation using severity-adjusted analyses, outcome studies examining mortality associations, carbapenem-sparing strategies evaluation, and implementation science assessing stewardship program barriers. Ultimately, optimizing antibiotic utilization requires multifaceted interventions addressing diagnostic limitations, prescriber education, institutional culture change, and rigorous local research.

AUTHOR CONTRIBUTION

GRA and TS were responsible for supervision, conceptualization, methodology design, and provided the final approval of the manuscript. LDS contributed to the data collection, data analysis, and preparation of the manuscript draft. YDA contributed to data validation. RBS and SAS were involved in data processing and visualization.

ETHICS APPROVAL

This study has been approved and declared ethically feasible by the Ethics Committee of Sultan Agung Islamic Hospital Semarang with the ethical approval code No. 46/KEPK-RSISA/III/2025.

CONFLICT OF INTEREST

The authors declare that this study was conducted without any commercial or financial relationships that could be construed as a potential conflict of interest.

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