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MGS designed the research study and curated, analyzed and validated the data. IKA, SSA, MH, AA, AJK and ZMS performed the research and analyzed the data, MGS wrote the manuscript. DSD conceptualized and supervised the study. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the manuscript.

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Beta-Lactam Efficacy in Hospitalized Patients: A Systematic Review and Evidence Synthesis of Case Studies

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Abstract:

The increasing emergence of antimicrobial resistance continues to compromise the clinical effectiveness of beta-lactam antibiotics, particularly against multidrug-resistant Gram-negative pathogens. An evidence synthesis of published case reports and case series was conducted using PubMed, Google Scholar, and CINAHL databases. Eligible studies published in English between 2018 and 2024 reporting beta-lactam antibiotic use among hospitalized patients were included. Data extracted included patient demographics, infection types, pathogens, antimicrobial therapy, resistance patterns, adverse events, and treatment outcomes. Descriptive and thematic analyses were performed using R-Studio version 2024.09.1+394. A total of 51 publications comprising 75 clinical cases were included. Adults (37.1%) and elderly patients (31.4%) constituted the majority of cases. Sepsis (21.05%), meningitis (13.16%), urinary tract infections (7.89%), and pneumonia (6.58%) were the most frequently reported infections. In this study, Meropenem (58.80%) was the most frequently administered beta-lactam antibiotic, while vancomycin (48.20%) and ceftriaxone (41.20%) were commonly used in combination regimens. *Escherichia coli* (26.32%) and *Klebsiella pneumoniae* (13.16%) were the prevalent organisms. For multidrug-resistant infections, a combination of vancomycin and meropenem was the drug of choice in most cases. Infections associated with Gram-negative organisms like *Aeromonas hydrophila*, *Pseudomonas aeruginosa*, and *Elizabethkingia anophelis* were associated with the highest mortality. This observation likely reflects the limited therapeutic options available for these intrinsically resistant organisms and the severity of infections they cause, rather than differences in antibiotic efficacy. Beta-lactam antibiotics are still very important in patient care, and the rise in drug-resistant bacteria continues to diminish their therapeutic use. AST-guided diagnosis, therapy, and stewardship are important to maintain their effectiveness.

Keywords: Beta-lactam antibiotics; antimicrobial resistance; hospitalized patients; evidence synthesis; case studies; clinical microbiology.

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INTRODUCTION

Beta-lactam antibiotics are broad-spectrum antibiotics that have good pharmacokinetic characteristics with established clinical effectiveness and applications (Pai Mangalore *et al.,* 2022; Suleiman *et al.,* 2022). They are classified as broad-spectrum antibiotics. This category of antibiotics includes penicillins, carbapenems, monobactams, and cephalosporins. These antibiotics exert their bactericidal effects by inhibiting bacterial cell wall synthesis, ultimately leading to cellular lysis and death. However, the increasing emergence of antimicrobial-resistant bacteria has significantly compromised the effectiveness of beta-lactam antibiotics in clinical settings (Hahn *et al*., 2023). Increasing multidrug-resistant Gram-negative infections continue to complicate treatment outcomes in hospitalized patients and frequently limit available therapeutic options, particularly in critically ill individuals (Daccò *et al.,* 2019; Iqbal *et al.,* 2024; Ling *et al.,* 2021). Beta-lactam antibiotics are used or administered differently in hospitals across regions, depending on factors like antibiotic resistance in that region or area, the seriousness of the infection, and the hospital's clinical protocols. While these antibiotics are still effective for many infections, their use is being threatened by the increase in resistant bacteria, like extended-spectrum beta-lactamase (ESBL)-producing *Escherichia coli* and *Klebsiella pneumoniae*. The emergence of extended-spectrum beta-lactamase (ESBL)-producing organisms, particularly *E. coli* and *K. pneumoniae*, has further complicated treatment outcomes by hydrolyzing beta-lactam antibiotics and limiting therapeutic options (Hahn *et al*., 2023). The global increase in multidrug-resistant Gram-negative pathogens, particularly *Pseudomonas aeruginosa* and *K. pneumoniae*, has further complicated the clinical management of severe bacterial infections and contributed to increased morbidity and mortality in healthcare settings (Ríos *et al.,* 2018; Lin *et al.,* 2024).

How well beta-lactam antibiotics work depends on many things, like the patient's other health issues, the type of infection, and whether the treatment is the right one. Occasionally, patients may have problems with their organs, or they may have side effects like allergic reactions (Liu *et al.,* 2024). Long-term and poor use of this class of antibiotics can cause poor patient outcomes, including prolonged hospitalization, which may also lead to the development of resistance within the patient (Bodega-Azuara *et al.,* 2024; Lindemann *et al.,* 2022). Proper use of these drugs may be defined by adequate disease diagnosis, management of antibiotics, and good hospital policies.

Previous case studies have highlighted both the advantages and challenges of beta-lactam antibiotics, including their effectiveness when combined with other antibiotics to treat infections caused by resistant bacteria (Li *et al*., 2024; Siedentop *et al*., 2024). Reports involving extended-spectrum beta-lactamase-producing Enterobacterales have also demonstrated severe invasive infections, septic shock, and limited therapeutic options among hospitalized patients (Altayib *et al.,* 2020; Ling *et al.,* 2021). Now AMR is reported among less commonly encountered bacterial pathogens in surgical infections associated with Salmonella species (Prabhurajan *et al.,* 2019).

Reports involving the importance and challenges of beta-lactam antibiotics, including their strength in combination therapy as it pertains to extended-spectrum beta-lactamase-producing Enterobacterales, are not new (Li *et al.,* 2024; Siedentop *et al.,* 2024). The limiting effect of therapy for severe invasive infections and septic shock in hospitalized patients continues to grow (Altayib *et al.,* 2020; Ling *et al.,* 2021). Literature findings are fragmented in terms of therapeutic strategies and resistance patterns. Pooling case evidence from these reports is important to visualize clinical patterns, repetitive resistance trends, and variables associated with treatment failure or success (Tufa *et al.,* 2020).

This paper reviews patient case studies and the use of beta-lactam antibiotics in hospitalized patients, specifically the therapeutic and microbiological trends in patient outcomes, and suggests ways to improve research and treatment in the future.

MATERIALS AND METHODS

Study Design

This was a systematic review of published case reports and case series reporting beta-lactam antibiotic use in hospitalized patients. The study was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, where applicable.

Data sources and searches

Relevant publications were obtained by a systematic search of Cumulative Index to Nursing and Allied Health Literature (CINAHL), PubMed, and Google databases. Case studies published in the English language between January 2018 and December 2024 were included. References of included articles were also searched manually. The search strategy included combinations of keywords and terms such as “beta-lactam antibiotics,” “hospitalized patients,” “antimicrobial resistance,” “case report,” “case series,” “sepsis,” “meningitis,” and “urinary tract infection.” Relevant case reports and clinical studies describing multidrug-resistant Gram-negative infections, antimicrobial susceptibility patterns, extended-spectrum beta-lactamase-producing organisms, and treatment outcomes were also considered during the screening process (Ríos *et al.,* 2018; Altayib *et al.,* 2020; Tufa *et al.,* 2020; Prabhurajan *et al.,* 2019).

The following search strategies were employed:

PubMed:
("beta-lactam antibiotics"[MeSH Terms] OR "beta-lactam"[Title/Abstract] OR "β-lactam"[Title/Abstract] OR "carbapenem"[Title/Abstract] OR "cephalosporin"[Title/Abstract] OR "penicillin"[Title/Abstract] OR "monobactam"[Title/Abstract]) AND ("case reports"[Publication Type] OR "case series"[Title/Abstract] OR "case report"[Title/Abstract]) AND ("hospitalized patients"[Title/Abstract] OR "inpatient"[Title/Abstract] OR "hospital-acquired"[Title/Abstract]) AND ("antimicrobial resistance"[Title/Abstract] OR "drug resistance"[Title/Abstract] OR "multidrug-resistant"[Title/Abstract]) AND ("2018/01/01"[Date - Publication] : "2024/12/31"[Date - Publication]) AND "english"[Language]

CINAHL:
(MH "beta-Lactam Antibiotics+") OR TI (beta-lactam OR β-lactam OR carbapenem* OR cephalosporin* OR penicillin*) OR AB (beta-lactam OR β-lactam OR carbapenem* OR cephalosporin* OR penicillin*) AND (MH "Case Studies+") OR TI ("case report" OR "case series") OR AB ("case report" OR "case series") AND (MH "Hospitalized Patients+") OR TI ("hospitalized" OR inpatient) OR AB ("hospitalized" OR inpatient) AND (MH "Drug Resistance, Microbial+") OR TI ("antimicrobial resistance" OR "drug resistance") OR AB ("antimicrobial resistance" OR "drug resistance") AND (DT 2018-2024) AND LA English

GoogleScholar:
("beta-lactam" OR "β-lactam" OR carbapenem OR cephalosporin) AND ("case report" OR "case series") AND ("hospitalized" OR inpatient) AND ("resistance" OR "multidrug-resistant") AND (2018-2024)

The study selection process was conducted in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, where applicable.

Study selection

The screening of eligible publications was carried out independently by two raters. First, the titles and abstracts of all citations were reviewed. Next, the full text of potentially relevant citations was reviewed. Discrepancies were resolved by consensus. Cases were only included if they reported Case Studies on Beta-Lactam Antibiotic Use in the treatment of Infections Among Hospitalized Patients. To meet inclusion criteria, studies had to focus on patients being treated with beta-lactam antibiotics in hospitals for bacterial infections,

focusing on antibiotic resistance patterns, patient recovery, and clinical outcomes. All infection types associated with an infectious agent were considered. Studies were not included if they were not published in English, focused on non-human subjects, lacked AST data or clinical outcomes, or were published before 2018.

Data extraction, quality assessment, synthesis, and Statistical analysis

Data used in this study were obtained from case reports and case series that met the eligibility criteria. The variables captured were location of the case, infection type, pathogen, gender, age group, medical history, and the World Health Organization (WHO) pathogen category (Wise *et al.,* 2024; Salim *et al.,* 2024). Where possible, details such as the presentation of infection, treatment regimens, adverse events, clinical outcomes, and follow-up duration were recorded. Data extraction was carried out by one reviewer and vetted by another reviewer.

Descriptive statistics were used to summarize demographic characteristics, infection types, pathogen distribution, antimicrobial regimens, and clinical outcomes. Categorical variables were presented as frequencies and percentages. Continuous variables were presented as means with standard deviations where normally distributed, or medians with interquartile ranges where non-normally distributed.

Visual comparison was achieved by showing the data (infection types and medical histories, Clinical outcomes, adverse events, and follow-up periods) in the form of tables and figures. All analyses were conducted using R-studio (Version: 2024.09 1+394). Quality appraisal was performed using the Haneline tool for quality appraisal of case reports (Haneline, 2006). The assessment was performed by one investigator, with a random sample cross-checked by another. We employed four criteria: i) the patient was sufficiently described (including medical history, clinical and laboratory evaluations, and treatments), ii) an accurate diagnosis was provided (with valid and reliable outcome measures used), iii) convincing evidence supporting the diagnosis was presented (based on diagnostic criteria or by describing the evidence for the diagnosis), and iv) alternative explanations were considered and ruled out (differential diagnoses were presented and scientifically excluded, or potential underlying mechanisms were addressed). Each item was rated as yes, partially, or no. Spearman's rank correlation coefficient (ρ) was used to examine associations between variables, as this non-parametric method is appropriate for categorical and ordinal data without assuming normality. P-values were calculated using the cor.test() function in R, and correlations with $p < 0.05$ were considered statistically significant. The correlation matrix was visualized using the corrplot package in R.

RESULTS

Publication characteristics

A total of 316 records were identified through database searches and manual reference screening (Figure 1). After removing duplicates, 122 papers were noted as eligible for inclusion. Only 98 full-text papers were eventually checked for eligibility. Studies (27) without clear microbiological evidence of infection were excluded; eight papers could not be downloaded, and 12 focused on non-human subjects. In the end, only 51 papers that reported 75 individual clinical cases were used in the final synthesis (Table 1).

The included cases were geographically diverse, although the majority originated from developed healthcare settings. Cases from the United States accounted for the highest proportion (14.47%), followed by Italy (9.21%), China (7.89%), and Japan (6.58%). Other reports were distributed across Asia, Europe, Africa, and South America, while 18.42% of studies did not clearly specify the geographic location. The study selection process is summarized in figure (1), while demographic and geographic characteristics are presented in table (1).

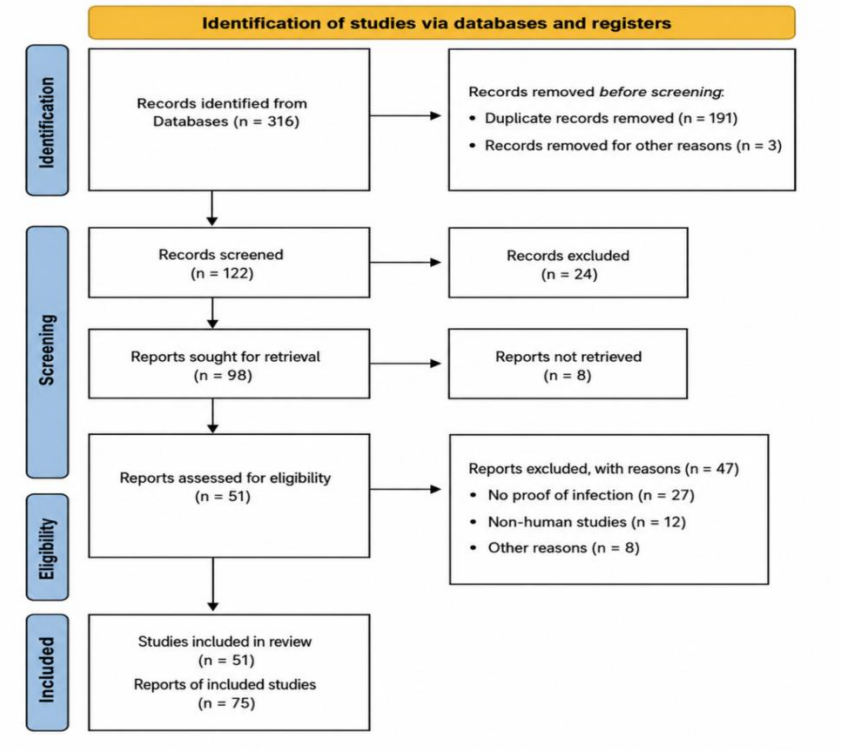


Fig. 1. Study Selection Flow Chart (PRISMA Diagram).

Quality Appraisal

The included case reports and series showed a moderate to good quality of methods. 82.67% of cases provided good clinical descriptions. Reliable outcome measurements were reported in 78.67% of the studies. Good diagnostic evidence accounting for the reported infections was noted in 73.33% of the cases, while alternative diagnoses or differential considerations were addressed in 81.33% of reports.

Demographic and Clinical Characteristics of Patients

A summary of case characteristics by demography is presented in table (2). Females accounted for 42.11% (n = 32), and 50.00% (n = 38) of the total cases were Male patients. In 7.89% of cases, gender information was not reported. The mean patient age was 53.0 ± 26.63 years. Adults were the most populous patient category (37.10%), followed by the elderly group of patients (31.40%). Pediatric populations made up a smaller but clinically significant proportion of the cases: preterm neonates (4.30%), infants (5.70%), and children (8.60%).

Figure (2) shows that the patients' clinical presentations and underlying medical conditions were heterogeneous among the included patients. Fever was the clinical presentation that was the most reported (20.31%), together with dyspnoea, altered consciousness, chills, or systemic signs of infection.

Chronic disorders associated with the kidney (ESRD and PKD) were responsible for 7.81% of cases. Comorbidities for patients with complicated infections were mostly hypertension and diabetes mellitus at 18.75% and 15.63%, respectively. Some other disorders were respiratory (6.25%), cancer-related (4.69%), and prior infectious diseases (6.25%). Disorders of neurological origins, such as hemiparesis, stroke, slurred speech, and change in mental status, were noticed in 9.38% of patients.

Table 1. Included Case Reports and Case Series.

Supplementary ID	Citation
S1	Ojdana *et al.,* 2020
S2	Xu *et al.,* 2018
S3	Park *et al.,* 2019
S4	Sakai *et al.,* 2019
S5	Kitaoka *et al.,* 2020
S6	Aarab *et al.,* 2021
S7	Ugarte-Torres *et al.,* 2018
S8	Parruti *et al.,* 2019
S9	Stein *et al.,* 2023
S10	Sah *et al.,* 2019
S11	Loconsole *et al.,* 2020
S12	Saboe *et al.,* 2021
S13	Maniara and Wells, 2021
S14	Zhang *et al.,* 2021
S15	Saraca *et al.,* 2019
S16	Lo *et al.,* 2021
S17	Jacobo-Pinelli *et al.,* 2022
S18	Singh *et al.,* 2022
S19	Pandey *et al.,* 2023
S20	Ziegler *et al.,* 2020
S21	Ren *et al.,* 2023
S22	Mc Gann *et al.,* 2021
S23	Miranda *et al.,* 2023
S24	Mirzamidinov *et al.,* 2023
S25	Mutoh *et al.,* 2019
S26	Kim *et al.,* 2018
S27	Yang *et al.,* 2019
S28	Fernández-Bravo *et al.,* 2020
S29	DeFilipp *et al.,* 2019
S30	Procaccianti *et al.,* 2020
S31	Ziga *et al.,* 2021
S32	Shah *et al.,* 2021
S33	Iwazawa *et al.,* 2021
S34	Tosa *et al.,* 2018
S35	Sakamoto and Sakamoto, 2019
S36	Patrial *et al.,* 2019
S37	Ahmad *et al.,* 2021
S38	Sood *et al.,* 2023
S39	Oh *et al.,* 2023
S40	Ra *et al.,* 2018
S41	Merticariu *et al.,* 2022
S42	Shittu *et al.,* 2021
S43	Wang *et al.,* 2022
S44	Lestari *et al.,* 2020
S45	Killington *et al.,* 2023
S46	Bouazra *et al.,* 2024
S47	Nakamura *et al.,* 2024
S48	Shen, 2024
S49	Vy *et al.,* 2024
S50	Sun *et al.,* 2023

Table 2. Demographic and Geographic Characteristics of Included Cases.

Category	Subcategory	n (%)
Gender	Male	38 (50.0%)
	Female	32 (42.1%)
	Not Reported	6 (7.9%)
Age Category	Adult	26 (37.1%)
	Elderly	22 (31.4%)
	Child	6 (8.6%)
	Infant	4 (5.7%)
	Preterm	3 (4.3%)
	Adolescent	3 (4.3%)
	Not Reported	4 (5.7%)
Location	USA	11 (14.5%)
	Italy	7 (9.2%)
	China	6 (7.9%)
	Japan	5 (6.6%)
	India	4 (5.3%)
	South Korea	3 (4.0%)
	Indonesia	2 (2.6%)
	Brazil	2 (2.6%)
	Canada	2 (2.6%)
	Vietnam	2 (2.6%)
	Other Locations	24 (31.6%)
	Not Reported	14 (18.4%)

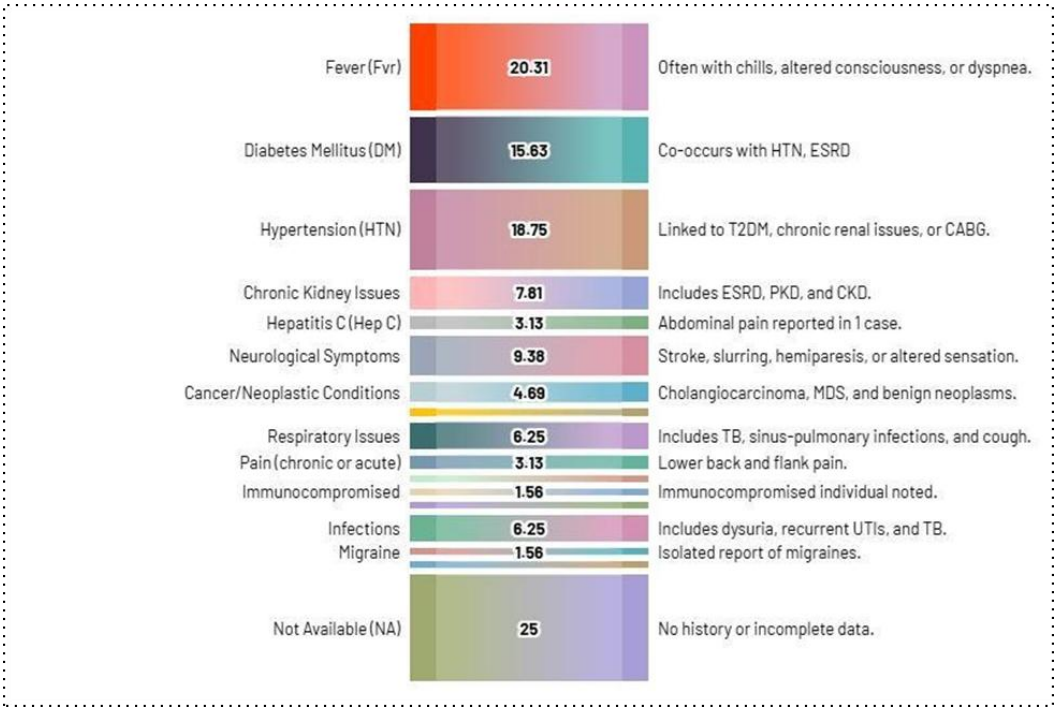


Fig. 2. Summary of patient medical history.

Infection Types and Pathogen Distribution

Sepsis was the most reported infection type of all cases at 21.05% (Table 3). All forms of meningitis (neonatal, bacterial, and post-neurosurgical) made up 13.16% of infections. Febrile UTIs and pyelonephritis made up 7.89%, while pneumonia-related infections contributed 6.58% of the total cases. Between 2.63% and 1.32% of the cases reported were each contributed by post-neurosurgical infections, endogenous endophthalmitis, bacteremia, endocarditis, typhoid fever, and pyelonephritis. Some studies reported mixed or co-existing infections. Also captured were surgical site infections, Necrotizing fasciitis, emphysematous aortitis, and empyema necessitans.

Table 3. Distribution of reported infections among included cases.

Infection Type	n (%)
Sepsis (all mentions)	16 (21.1%)
Meningitis (all types)	10 (13.2%)
Urinary Tract Infection (UTI)	6 (7.9%)
Pneumonia (all mentions)	5 (6.6%)
Endogenous Endophthalmitis	2 (2.6%)
Typhoid Fever	2 (2.6%)
Bacteremia	2 (2.6%)
Post-neurosurgical Meningitis	2 (2.6%)
Endocarditis (all types)	2 (2.6%)
Pyelonephritis (all types)	2 (2.6%)
Bacterial Meningitis	2 (2.6%)
Other individual infections	1 (1.3%) each

As mentioned in figure (3), 26.32% of all reported organisms were *E. coli*. Mostly multidrug-resistant and carbapenem-resistant infections associated with *K. pneumoniae* made up 13.16% of isolates. *Elizabethkingia anophelis*, *P. aeruginosa*, and *Acinetobacter baumannii* were also reported at 3.95%, 5.26%, and 3.95%, respectively. Other noted organisms were *Haemophilus influenzae*, *Capnocytophaga canimorsus*, *Salmonella* species, *Proteus mirabilis*, *Raoultella planticola*, and *Providencia* species.

The studied dosing schedules mirror individualized therapeutic approaches according to how severe an infection is renal function, AST patterns, and patient-specific clinical conditions. The six-hourly dosing schedule was the most reported regimen in 22.4% of cases, then 8-hour (q8h) dosing schedules at 17.6%, Once-daily (q24h) at 14.10%, and every 12-hour (q12h) at 12.9% treatments. Less frequently reported dosing schedules included every 48 hours (q48h), every 3 hours (q3h), and twice- daily (BID) regimens.

Although Vancomycin (48.20%) and ceftriaxone (41.20%) were used frequently, Beta-lactam antibiotics were the foundation of treatment in the majority of the studied cases (Table 4). Meropenem appeared in 58.80% of treatment regimens and was the most administered antibiotic, especially for infections involving CNS infections and suspected multidrug-resistant infections. In the management of carbapenem-resistant Gram-negative pathogens, Colistin was used in 14.10% of cases. The study also spotted the usage of other agents in antibacterial therapy, including tigecycline, polymyxin B, amikacin, linezolid, ceftazidime-avibactam, and ciprofloxacin. Combination therapy of meropenem plus vancomycin (in 21.20% of cases) was employed in infections involving resistant pathogens.

Antimicrobial Therapy and Dosing Patterns

All patients included in the review received antimicrobial therapy, with beta-lactam antibiotics forming the foundation of treatment in most cases. As seen in Table 3, Meropenem was the most frequently administered antibiotic, appearing in 58.80% of treatment regimens. Vancomycin (48.20%) and ceftriaxone (41.20%) were also commonly used, particularly in severe infections, central nervous system infections, and suspected multidrug-resistant infections.

Colistin was utilized in 14.10% of cases, mainly in the management of carbapenem-resistant Gram-negative pathogens. Other commonly administered agents included tigecycline, polymyxin B, amikacin, linezolid, ciprofloxacin, and ceftazidime-avibactam. Combination antimicrobial therapy was frequently employed,

particularly in critically ill patients or infections involving resistant pathogens. The most commonly reported combination regimen was meropenem plus vancomycin (21.20%), followed by ceftriaxone plus metronidazole and ceftazidime-avibactam-based combinations.

Considerable variability was observed in dosing schedules across the included cases. Every 6-hour (q6h) dosing was the most frequently reported regimen (22.40%), followed by every 8-hour (q8h) dosing schedules (17.60%). Once-daily (q24h) and every 12-hour (q12h) regimens accounted for 14.10% and 12.90% of treatments, respectively. Less frequently reported dosing schedules included every 48 hours (q48h), every 3 hours (q3h), and twice-daily (BID) regimens. The diversity of dosing schedules reflected individualized therapeutic approaches based on infection severity, renal function, antimicrobial susceptibility patterns, and patient-specific clinical conditions.

Clinical outcomes and follow-up

Clinical outcomes following beta-lactam antibiotic therapy were generally favorable. Resolution of symptoms was reported in 73.68% of cases, indicating substantial clinical improvement after treatment. Mortality occurred in 13.16% of patients, while 7.89% experienced persistent or unresolved infection despite therapy. A small proportion of cases (1.32%) reported complete microbiological resolution of infection without further complications. In 3.95% of cases, outcomes were not clearly categorized due to incomplete documentation.

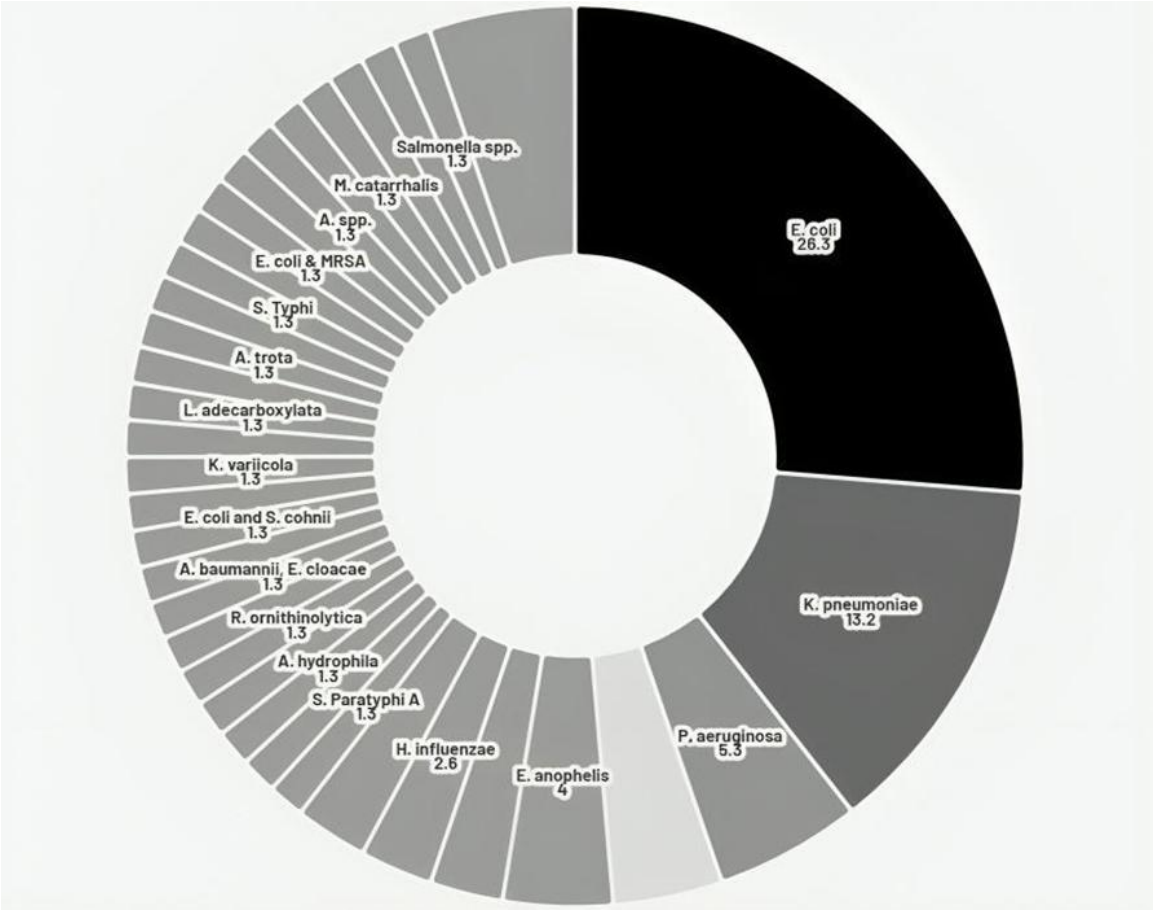


Fig. 3. Most frequently isolated pathogen.

Table 4. Frequently used antibiotics and regimens with dosing frequencies

Category	Antibiotic/Regimen	Count (%)
Antibiotics used overall	Meropenem	50 (58.80%)
	Vancomycin	41 (48.20%)
	Ceftriaxone	35 (41.20%)
	Piperacillin/Tazobactam	15 (17.60%)
	Amikacin	12 (14.10%)
	Colistin	11 (12.90%)
	Ciprofloxacin	9 (10.60%)
	Linezolid	8 (9.40%)
	Clindamycin	7 (8.20%)
	Gentamicin	6 (7.10%)
	Ampicillin/Sulbactam	5 (5.90%)
Combination Regimens	Meropenem + Vancomycin	18 (21.20%)
	Ceftriaxone + Metronidazole	7 (8.20%)
	Piperacillin/Tazobactam + Vancomycin	6 (7.10%)
	Ceftriaxone + Amikacin	5 (5.90%)
	Meropenem + Colistin	4 (4.70%)
	Meropenem + Linezolid	3 (3.50%)
Monotherapies	Meropenem	7 (8.20%)
	Ceftriaxone	6 (7.10%)
	Vancomycin	5 (5.90%)
Dosing frequency	Treatment	
q6h	IV Amk, IV Cipro, IV Mero, Col, Cefotax, Gent, Tig, Ceftaz	19 (22.4%)
q8h	Mero, Vanco, Ceftriax, IV Levo, Cefep, Metro, Amp-Sulb, Poly-B	15 (17.6%)
q24h	Ceftriax, Vanco, Mero, Ceftaz, Linez, Erta, Cipro	12 (14.1%)
q12h	Ceftriax, Mero, Levo, Tig, Metro, Linez, Poly-B, Amp-Sulb	11 (12.9%)
BID	Oral Cipro, Clinda, IV Mero, Erta	8 (9.4%)
Other	Aug, Cotrim, Clinda, Amp-Sulb	7 (8.2%)
q48h	IV Levo, Ceftaz/Avib, Ceftriax, Mero	4 (4.7%)
q3h	Col, Fosfo, Cefop-Sulb, Imp/Cil	3 (3.5%)
q14d	IV Mero, Cefop-Sulb	2 (2.4%)

Key: Amk: Amikacin, Cipro: Ciprofloxacin, Mero: Meropenem, Col: Colistin, Cefotax: Cefotaxime, Gent: Gentamicin, Tig: Tigecycline, Ceftaz: Ceftazidime, Vanco: Vancomycin, Ceftriax: Ceftriaxone, Levo: Levofloxacin, Cefep: Cefepime, Metro: Metronidazole, Amp-Sulb: Ampicillin-Sulbactam, Poly-B: Polymyxin B, Linez: Linezolid, Erta: Ertapenem, Clinda: Clindamycin, Aug: Augmentin, Cotrim: Cotrimoxazole, Ceftaz/Avib: Ceftazidime/Avibactam, Fosfo: Fosfomycin, Cefop-Sulb: Cefoperazone-Sulbactam, Imp/Cil: Imipenem/Cilastatin.
Dosing Frequency: q6h: Every 6 hours, q8h: Every 8 hours, q24h: Once daily (Every 24 hours), q12h: Every 12 hours, BID: Twice daily, Other: No specified time, q48h: Every 48 hours, q3h: Every 3 hours, q14d: Every 14 days.

Most patients (90.79%) did not experience documented adverse drug reactions or treatment-related complications. However, rare adverse events were reported, including agranulocytosis, hemolytic anemia, drug-related fever, and eosinophilia with drug reaction and systemic symptoms (DRESS syndrome), each accounting for 1.32% of cases. Follow-up duration varied considerably among studies. The majority of documented follow-up periods ranged between 8 and 30 days, although some reports documented extended monitoring periods exceeding 120 days. In approximately 39.47% of cases, follow-up duration was not clearly

reported. Clinical outcomes, adverse events, and follow-up periods are listed in Table 5.

Clinical outcomes by patient category and pathogen

Clinical outcomes according to the WHO age category and pathogen are presented in Table 6. Clinical outcomes differed across patient age groups and infecting pathogens. Adolescents, children, infants, and preterm patients demonstrated the highest rates of symptom resolution, with no reported mortality within these categories. In contrast, adults and elderly patients experienced lower rates of recovery and higher mortality. Mortality rates were 14.6% among adults and 22.6% among elderly patients.

The highest number of deaths was associated with Aeromonas hydrophila and Elizabethkingia anophelis infections, while infections caused by *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, and *Klebsiella pneumoniae* demonstrated comparatively lower rates of symptom resolution. Infections involving E. coli generally turned out to be favorable except in severe multidrug-resistant cases, where mortality still occurred in a proportion.

Correlation Analysis

Figure 4 shows that links were noticeable between the demographic, microbiological, and treatment-related variables by correlation analysis. At r = 0.796 and r = 0.735. The medical history of a patient and infection types had a strong positive correlation with the treatment regimen, respectively, unlike the moderate positive correlation of r = 0.590, r = 0.528, and r = 0.537 observed with pathogen type, infection type, and pathogen distribution, and Geographic location, respectively. The year the documented cases were reported had a moderate likelihood with how the pathogens were distributed (r = 0.457) and an even weaker one with treatment regimen (r = 0.345). There were weak correlations between the duration of follow-up, gender, and the year in which the included cases were published. Adverse events had very little to do with geographic location (r = –0.110), as well as WHO patient categorization (r = –0.108). These correlations should be interpreted cautiously, as they represent associations rather than causal relationships, and are derived from case report data with inherent limitations.

Table 5. Summary of clinical outcomes, adverse events, and follow-up periods.

Category	Subcategory	Count (%)
Clinical Outcomes	Resolution of symptoms	56 (73.68%)
	Death	10 (13.16%)
	No resolution of symptoms	6 (7.89%)
	Resolution of infection	1 (1.32%)
	Uncategorized	3 (3.95%)
Adverse Events	No adverse event reported	69 (90.79%)
	Agranulocytosis	1 (1.32%)
	Fever	1 (1.32%)
	Hemolytic anemia	1 (1.32%)
	EoDRESS	1 (1.32%)
Follow-up (Days)	≤7 days	7 (9.21%)
	8–14 days	11 (14.47%)
	15–30 days	12 (15.79%)
	31–60 days	8 (10.53%)
	61–120 days	6 (7.89%)
	>120 days	2 (2.63%)
	Uncategorized	30 (39.47%)

Keys: EoDRESS = Eosinophilia and drug reaction with systemic symptoms.

Table 6. Clinical outcomes by WHO category and pathogen.

WHO Category	Resolution (%) (n)	No Resolution (%) (n)	Death (%) (n)	Total (n)
Clinical Outcomes by WHO age Category				
Adult	73.2% (30)	9.8% (4)	14.6% (6)	41
Elderly	67.7% (21)	9.7% (3)	22.6% (7)	31
Child	100.0% (6)	0.0% (0)	0.0% (0)	6
Infant	100.0% (5)	0.0% (0)	0.0% (0)	5
Preterm	100.0% (4)	0.0% (0)	0.0% (0)	4
Adolescent	100.0% (3)	0.0% (0)	0.0% (0)	3
NA	75.0% (3)	0.0% (0)	25.0% (1)	4
Clinical Outcomes by Pathogen				
Escherichia coli	72% (18)	8% (2)	20% (5)	25
Klebsiella pneumoniae	54.6% (6)	18.2% (2)	18.2% (2)	11
Acinetobacter baumannii	66.7% (2)	0% (0)	33.3% (1)	3
Pseudomonas aeruginosa	55.6% (5)	11.1% (1)	33.3% (3)	9
Aeromonas hydrophila	0% (0)	0% (0)	100% (1)	1
Elizabethkingia anophelis	0% (0)	33.3% (1)	66.7% (2)	3
Proteus mirabilis	66.7% (2)	0% (0)	33.3% (1)	3
Haemophilus influenzae	50% (1)	0% (0)	50% (1)	2
others(*Salmonella* spp., *R. planticola*)	Mixed (0–100%)	0–33% (varied)	0–66.7% (varied)	Varied

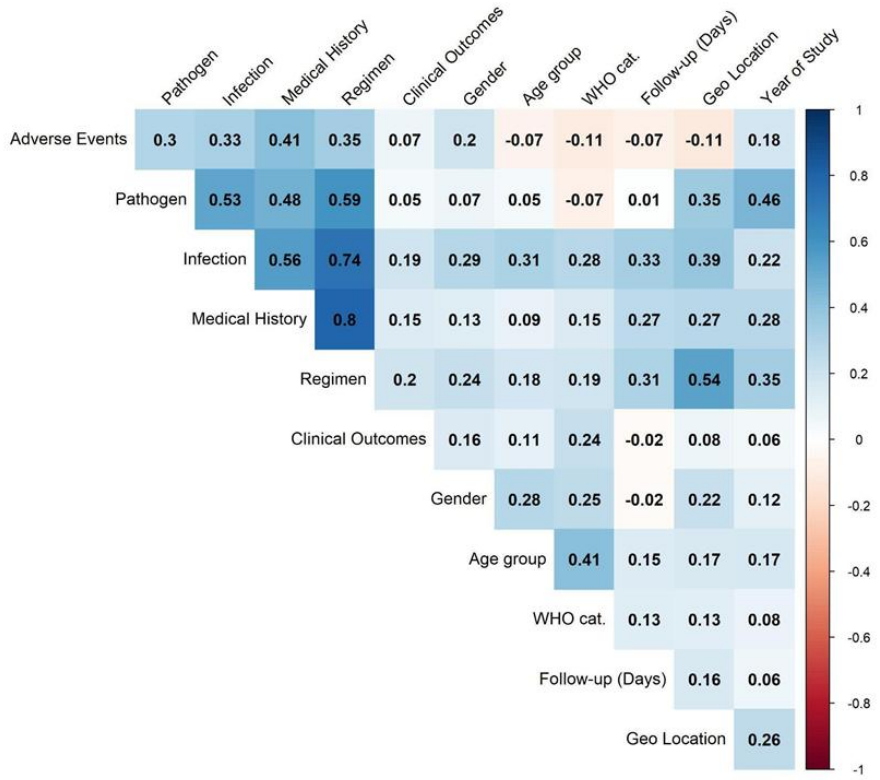


Fig. 4. Pairwise Correlation Matrix of Clinical and Demographic Variables.

DISCUSSION

The clinical effectiveness of beta-lactam antibiotics is influenced by complex interactions among the patient, pathogen, and infection characteristics, highlighting the need for a comprehensive understanding of these dynamics in clinical practice. This review provides a comprehensive synthesis of beta-lactam antibiotic use across a diverse range of clinical case reports.

The included studies covered a wide range of cases across both high- and middle-income countries. This is typical of this kind of review article. The poorest clinical outcomes, including deaths, were largely associated with cases involving multidrug-resistant Gram-negative organisms, chiefly including *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, and *Elizabethkingia anophelis*. Early pathogen detection, identification, and profiling are important for susceptibility-guided therapy to curb death rates and improve patient outcomes.

No significant gender- or age-related differences in beta-lactam antibiotic utilization patterns were observed in this study, which aligns with previous reports (Abdel-Wahab *et al.,* 2016). The higher mortality observed in elderly patients (22.6%) compared to other age groups likely reflects the greater burden of comorbidities and age-related physiological changes that affect drug pharmacokinetics and pharmacodynamics, rather than direct effects of antibiotic selection. The frequent use of meropenem and vancomycin in this study is consistent with reports from other studies (Niederman *et al.,* 2021; Rhee *et al.,* 2024) because of their broad action and effectiveness against resistant Gram-negative and Gram-positive bacteria. However, infections required a combination of both drugs. This high repetitiveness of resistance to therapy observed and its consequent use of broad-spectrum agents aligns with the intrinsic multidrug resistance nature of *Elizabethkingia* species and several Gram-negative pathogens. As reported by previous studies, these resistance profiles hamper treatment options and often necessitate combination therapy or prolonged treatment regimens (Alkattan *et al.,* 2022; Woicka-Kolejwa *et al.,* 2018; Ahamed Riyaaz *et al.,* 2018; Rehman *et al.,* 2021). This style is similar to other studies where such combinations were used in MDR bacterial therapy (Monti *et al.,* 2023; Umemura *et al.,* 2022).

Switchable dosing plans, including every 6-hour regimen, showed the importance of tailoring treatments to individual patients in this study, which is in tandem with the reports of Chua and Tam (2022). This shows how important the role of antimicrobial stewardship and continued monitoring of AST patterns in admitted patients with infections involving multidrug-resistant organisms. While earlier studies focused on specific infections or bacteria, our review covers a wide range of conditions and treatments. However, the high levels of resistant bacteria like *K. pneumoniae* and *A. baumannii* are troublesome and point to the growing problem of AMR (Shelenkov *et al.,* 2025). The use of colistin to treat MDRGNB indicates its importance as a reserve antibiotic (Mondal *et al.,* 2024).

It is crucial to track AMR trends and create clear guidelines to ensure these antibiotics are used properly. Poor infection prevention practices and inadequate AMR management add to the spread of resistant pathogens in clinical settings, where HA bacterial contamination remains an issue (Shuaibu *et al.,* 2026; Gastmeier *et al.,* 2024). Paying attention to how hospitals and their healthcare providers handle and monitor AMR stewardship programs may help reduce the transmission of multidrug-resistant organisms and improve patient outcomes.

This systematic review has several important limitations that should be considered when interpreting the findings: Case reports and case series represent selected patient experiences and are not designed to establish causal relationships. Findings should be interpreted as descriptive observations rather than definitive evidence of treatment effectiveness. The absence of comparator groups prevents any assessment of comparative effectiveness

between different treatment regimens or approaches. There is a well-documented tendency to publish cases with unusual or successful outcomes, while cases with poor outcomes or "routine" presentations may be underrepresented. This may bias the observed outcomes toward resolution (73.68%) and away from poor outcomes, potentially overestimating treatment success rates. A substantial proportion of included studies lacked complete documentation of key variables. Follow-up duration was not clearly reported in approximately 39.47% of cases, and some studies lacked comprehensive demographic or clinical outcome data. Incomplete data may limit the generalizability of findings. The predominance of cases from developed healthcare settings (especially the United States, Italy, China, and Japan) may limit generalizability to resource-limited settings where infection patterns, antimicrobial resistance profiles, diagnostic capabilities, and treatment options may differ substantially. The included cases encompassed diverse infection types, pathogens, patient populations, and treatment regimens. While this enhances the scope of the review, it limits the ability to draw specific conclusions about optimal treatment for particular clinical scenarios. Correlation analyses using Spearman's rank correlation are appropriate for the categorical nature of the data, but the sample size (n=75) limits statistical power. Correlations should be interpreted as exploratory rather than confirmatory, and they represent associations rather than causal relationships. Restriction to English-language publications may have introduced language bias, excluding relevant cases published in other languages. This may affect the comprehensiveness of the evidence synthesis. Quality assessment using the Haneline tool indicated that 64.7% of included studies were of good quality, 29.4% were of moderate quality, and 5.9% were of poor quality. The inclusion of lower-quality studies may introduce methodological limitations that affect the reliability of synthesized findings.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

GENERATIVE AI STATEMENT

The author(s) declare that no Generative AI was used for the writing of this manuscript, nor for the creation of images, graphics, tables, or their corresponding captions.

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