

Original Article

Open Access



A PROSPECTIVE EVALUATION OF RESERVE ANTIBIOTICS UTILIZATION USING DAILY DEFINED DOSE IN HICU OF A TERTIARY CARE HOSPITAL

Nisha Jose^{1*}, Athira Krishnan¹, Balakeshwa Ramaiah¹, Banjara Raju Prabhudev¹

ARTICLE INFO

Article history:

Received 6 October 2025

Received in revised form

1 November 2025

Accepted 6 November 2025

Available online 15 November 2025

Keywords:

Defined Daily Dose

Reserve antibiotics

Hospital-acquired infections

Antimicrobial resistance

ABSTRACT

Background: Monitoring antimicrobial consumption is essential for evaluating the effectiveness of antimicrobial stewardship programs. This study aimed to analyze the utilization pattern of reserve antibiotics in a tertiary care hospital's High-Intensity Care Unit (HICU), quantify their use based on the WHO-recommended Anatomical Therapeutic Chemical (ATC) classification and Defined Daily Dose (DDD) per 100 bed-days, and assess prescribing trends, pathogen distribution, and antimicrobial resistance patterns, including hospital-acquired infections (HAIs) such as Surgical Site Infections (SSI) and central line-associated bloodstream infections (CLABSI).

Methods: A prospective observational study was conducted from January to June 2024 among 85 adult HICU patients who received antibiotics. Paediatric, pregnant, and lactating patients were excluded. Data on demographics, diagnosis, antibiotic usage, culture results, and HAIs were collected. Antibiotic utilization was measured using the WHO ATC/DDD system, and statistical analysis assessed associations between hospital stay and infection acquisition.

Results: Among 85 patients (mean age 56.5 ± 17 years; median stay 15 days), eleven reserve antibiotics were prescribed, mainly for sepsis (20.3%), urinary tract infections (19%), and septic shock (16.3%). Meropenem (28%), colistin (17%), and linezolid (14%) were the most frequently used. Tigecycline showed the highest DDD (226.5; 13 DDD/100 bed-days), while colistin had the lowest (13.8; 0.79 DDD/100 bed-days). From 137 isolates, predominant pathogens included *Enterobacter* (23%) and *Klebsiella* spp. (18.9%), with multidrug resistance most prevalent in *Klebsiella* spp. Prolonged hospitalization significantly correlated with microorganism acquisition ($p = 0.0019$).

Conclusion: The findings underscore heavy dependence on reserve antibiotics in HICUs due to severe infections and antimicrobial resistance, emphasizing the need for strengthened stewardship and continuous surveillance to mitigate AMR burden.

INTRODUCTION

Antibiotic consumption serves as a crucial indicator for assessing the effectiveness of antimicrobial stewardship programs (ASP), particularly in ensuring the appropriate use of antibiotics and controlling antimicrobial resistance.

In intensive care units, the implementation of ASP faces significant challenges due to the frequent administration of antibiotics—largely in response to healthcare-associated infections, a high burden of multidrug-resistant organisms, and the routine use of empirical treatments (1).

Correspondence: nishajose365@gmail.com (Nisha Jose)

¹Department of Pharmacy Practice, Karnataka College of Pharmacy, Rajiv Gandhi university of health sciences, Bengaluru, Karnataka, India.

The specific metric that best quantifies antibiotic use remains a challenge (2). However, the Defined Daily Dose (DDD) is the commonly used metric by the World Health Organization (WHO) for this purpose (1). As defined by WHO, the DDD refers to “the assumed average maintenance dose per day for a drug used for its main indication in adults” (2). This standardized metric enables hospitals to assess antibiotic usage intensity and compare it with other institutions. The recommended unit for reporting antibiotic use in hospitals is DDD per 100 bed-days. This is an important tool for assessing and improving the quality of antimicrobial stewardship efforts (3).

Antimicrobials are among the most commonly misused drugs globally. Numerous ecological studies have demonstrated a direct correlation between elevated antimicrobial consumption and increased levels of antimicrobial resistance (AMR) across different countries. The global rise in AMR has significantly contributed to increased patient morbidity and mortality, along with a substantial rise in healthcare expenditures (4). While resistance eventually develops to all antibacterial agents, overuse significantly accelerates this process (5). Gram-negative pathogens, such as *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, and *Acinetobacter* spp., are particularly concerning due to their resistance to most antibiotics. Alarming, multidrug-resistant strains, including ESBL-producing *E. coli* and resistant *Neisseria gonorrhoeae*, are also emerging in community settings (6).

In 2019, the global burden of drug-resistant infections was estimated at 4.95 million deaths (95% uncertainty interval [UI]: 3.62–6.57 million) across 88 pathogen–drug combinations, with 1.27 million deaths (UI: 0.911–1.71 million) directly attributable to antimicrobial resistance (AMR).

AMR has also been acknowledged at the international policy level through the Global Action Plan on AMR (6). Healthcare costs associated with resistant infections are significantly higher than those for non-resistant infections due to prolonged illness duration, additional diagnostic procedures, and the need for more costly treatment options (7). Between 2000 and 2015, antibiotic consumption rose sharply from 3.2 to 6.5 billion DDDs in India (an increase of 103%), from 2.3 to 4.2 billion DDDs in China (79%), and from 0.8 to 1.3 billion DDDs in Pakistan (65%) (8).

The AWaRe (Access, Watch, and Reserve) classification system, introduced in 2017 by the WHO Expert Committee, categorizes antibiotics into three groups: Access, Watch, and Reserve (1). The Reserve category comprises antibiotics that are intended for use only in confirmed or suspected cases involving multidrug-resistant pathogens. Reserve group antibiotics should be used only as a “last resort” option (9). Evidence indicates a global increase in human antibiotic consumption over the past two decades, largely driven by rising usage in low- and middle-income countries. Concurrently, there has been a noticeable shift toward the use of broad-spectrum and last-resort antibiotics (7). These critical drugs should be safeguarded and prioritized through national and international antimicrobial stewardship initiatives, which emphasize monitoring and responsible usage to maintain their efficacy (1).

This study primarily aims to quantify the reserve antibiotic consumptions using the WHO-prescribed ATC code classification and DDD/100 bed days and to assess the prescribing trends of reserve antibiotics. The study secondarily aims to identify common pathogens that require restricted antibiotic intervention and to evaluate the distribution of HAI (CLABSI and SSI) and superinfections.

METHODS

A prospective observational study was carried out in the High-Intensity Care Unit (HICU) of a tertiary care hospital in Bengaluru, enrolling 85 participants in total over 6 months. Adults above 18 years of age receiving reserve antibiotics were included, whereas pregnant and lactating women, along with pediatric patients, were excluded. Detailed information was gathered for all eligible participants, covering demographics, primary diagnosis, reason for prescribing restricted antibiotics, antibiotic dosage, frequency and duration of treatment, length of hospitalisation, and the occurrence of hospital-acquired infections (HAIs) or superinfections. All collected data were systematically documented and analyzed using Microsoft Excel. Antibiotics were classified using the Anatomical Therapeutic Chemical (ATC) Classification System, and their utilization was assessed in terms of Defined Daily Dose (DDD) per 100 patient-days, based on the guidelines provided in the WHO ATC/DDD Index 2015.

For each antibiotic, DDD was calculated by dividing the total dose of antibiotic prescribed by the standard DDD for that antibiotic as provided by the ATC/DDD index.

- $DDD = \frac{\text{Number of items (antibiotic) issued} \times \text{Amount of drug per item (mg)}}{\text{WHO recommended DDD of the antibiotic}}$
- DDD per 100 bed days was calculated using the formula:
- $DDD/100 \text{ bed days} = \frac{\text{Total dose in mg during study period}}{DDD \text{ of drug} \times \text{study duration} \times \text{bed strength} \times \text{occupancy index}} \times 100$
- $\text{Occupancy index} = \frac{\text{Total inpatient service days for a period}}{\text{Total inpatient bed count} \times \text{no. of days in the study period}} \times 100$

The study also tracked hospital-acquired infections (HAIs), such as surgical site infections (SSIs) and central line-associated bloodstream infections (CLABSI), and detected superinfections using culture reports obtained during the patient's hospital stay.

Superinfections were characterized by the emergence of a new pathogen, distinct from the original, either after 48 hours of starting antibiotic therapy or within one week of its discontinuation. JASP 0.16.4 was used for statistical analysis. To evaluate the relationship between the length of hospital stay (LOS) and the development of infections during hospitalization, a chi-square test was performed. The chi-square test was used to evaluate the associations between qualitative variables. A p-value of < 0.05 with a 95% confidence interval was considered statistically significant.

RESULT

This study included 85 patients who met the inclusion criteria. Of these, 61% were male and 39% were female. The age distribution was as follows: 13 patients were between 18 and 39 years old, 29 patients were aged 40 to 59 years, and 43 patients were between 60 and 99 years old, with the mean value (SD) age being 56.5 (17) years. The length of stay ranged from 4 to 57 days, with a median (IQR) = 15(0). 11 reserve antibiotics as per the WHO recommended WATCH list were used in the hospital. Reserve antibiotic courses were administered mainly for therapy of sepsis (20.26%), septic shock (16.34%), UTI (18.95%), LRTI (15.69%), and infected wound (9.15%). (Table 1)

Prescription pattern of reserve antibiotics in the HICU

As per the hospital infection control protocol, eleven antibiotics were considered as reserve antibiotics meropenem, ertapenem, linezolid, colistin, tigecycline, teicoplanin, polymyxin B, aztreonam, vancomycin, ceftazidime-avibactam, and imipenem-cilastatin.

Table 1. Clinical manifestations and frequencies in patients

Characteristics	Characteristics	N (%)
Age	20-83	56.5 (17%)
Gender	Male	52 (61%)
	Female	33 (39%)
Reason for admission	Sepsis	31 (20.26%)
	Septic shock	16 (34%)
	UTI	29 (18.95%)
	LRTI	24 (15.69%)
	Infected wound	14 (9.15%)
	urosepsis	9 (5.8%)
	*Others	22 (14%)
Length of stay (days) b	4-57	15 (10%)

IQR: interquartile range
a mean (SD) instead of n.
b. Median (IQR) instead of n.
*Others: RTA 7 (4.5%), pyelonephritis 4 (2.6%), endocarditis 2 (1.31%), poisoning 2 (1.31%), cardiogenic shock 2 (1.31%), encephalopathy 4 (2.6%), cellulitis 1 (0.65%).

Upon analyzing the 85 subjects’ medication details collected from the HICU unit, the most frequently used antibiotics were meropenem (28%), colistin (17%), and linezolid (14%). A few reserve antibiotics were used empirically as well. They were meropenem 28.6%, colistin 17.3%, linezolid 14.5%, and tigecycline 9.8%. Table 2 represents the ATC-DDD classification, utilization pattern, ATC codes, frequency, and the calculated DDD/100 bed days. The occupancy index was 0.44 during the study period, with 22 as the total inpatient bed count in the HICU.

However, according to the WHO AWaRe classification, meropenem, ertapenem, vancomycin, and teicoplanin fall under the Watch category. These agents were therefore included in the study as part of the hospital’s reserve antibiotic list defined by institutional protocol.

Table 2: Reserve group antibiotics consumption based on DDD/100bed days

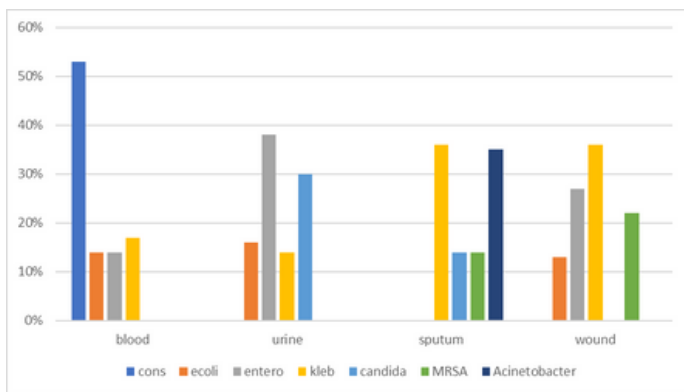
S. NO	DRUG	ATC CODE	ROUTE	DDD (WHO)	DDD	DDD/100 BED DAYS
1	TIGECYCLINE	J01AA12	P	0.1	226.5	13
2	LINEZOLID	J01XX08	P	1.2	224.5	7.9
3	MEROPENEM	J01DH02	P	3	458.1	7.34
4	CEFTAZIDIME+A VIBACTAM	J01DD02	O	4	121.1	6.9
5	AZTREONAM	J01DF01	P	4	108.5	6.2
6	TEICOPLANIN	J01XA02	P	0.4	89	5.11
7	VANCOMYCIN	J01XA01	O	2	59.5	3.4
8	IMEPENAM	J01DH51	P	2	58	3.3
9	POLYMXIN B	J01XB02	P	0.15	27	1.5
10	ERTAPENAM	J01DH03	P	1	21.5	1.2
11	COLISTIN	J01XB01	O	9	13.8	0.79

P- Parenteral route 0-oral route

Distributions of organisms and frequency of resistance

A total of 137 isolates were collected from the 85 patients. The distribution of pathogens in the entire cohort was as follows: 23% *Enterobacter* spp., 18.9% *Klebsiella* spp., 13% *CONS*, 12.4% *Acinetobacter* spp., and 13% *E. coli*. Figure 1 represents the isolated pathogens. *CONS* was isolated mainly from the blood culture; *enterococcus* was predominant in urine samples, and *klebsiella* in sputum secretion and wound sites. We noticed a high percentage of *Acinetobacter baumannii* in sputum alongside *Klebsiella* (as shown in Fig. 1).

Fig 1: Distribution of the main infection site



Hospital-acquired infections, mainly CLABSI and SSI, were studied during the period, which together accounted for slightly more than one-fourth of the total samples. Among the multidrug-resistant isolates, MDR *Klebsiella* spp. was found to be the highest microorganism. The detailed data of MDR isolates is shown in Table 3. In the study, the average number of microorganisms per patient was 2.4, and the average number of microorganisms acquired was 1.87(1-2). Superinfection is a new isolate pathogen (or pathogens) (other than the initial pathogen) after 48 h of antibiotic treatment or within one week of treatment discontinuation. Table 3 shows microorganism isolates causative for superinfection in the study population

Table 3: Descriptive analysis of infectious micro-organisms and HAI.

M.O	Total	%
ACINETOBACTER SP	17	12.41%
CONS	19	13.87%
ECOLI	13	9.49%
ENTEROCOCCUS SP	32	23.36%
KLEBSIELLA SP	26	18.98%
MRSA	10	7.30%
PSEUDOMONAS AUROGINOSA	5	3.65%
HOSPITAL ACQUIRED		
CLASBI [n (%)]	11	44%
SSI [n (%)]	14	56%
SUPERINFECTION [n (%)]	24	
RESISTANCE PHENOTYPE		
MDR Acinetobacter spp	10	17%
MDR Acinetobacter	7	12%
VRE	5	8.70%
MDR Pseudomonas	3	5.20%
MDR Klebsiella spp	13	22%
MDR klebsiella pneumoniae	3	5.20%
MRSA	10	17%
MDR E. coli	4	7%
MDR Proteus mirabilis	1	1.70%
MDR Providencia rettgeri	1	1.70%

Superinfections occurred in 24 out of 85 cases. Microorganism isolates from superinfections revealed *Candida* and *Enterococcus* in 21%; *Acinetobacter* and *Klebsiella* in 12%; *E. coli* in 3%; VRE and *Burkholderia cepacia* in 6% of cases; and *E. coli*, CONS, VGS, MRSA, and *Providencia rettgeri* in 3%. Major sites of superinfection were in urine.

A chi-square test was performed to evaluate the association between the length of stay (LOS) and the acquisition of microorganisms (M.O.) during hospitalization. A higher proportion of infections were acquired after more than two weeks of hospitalization ($n = 76$) compared to those acquired within the first two weeks ($n = 19$). The chi-square test demonstrated a statistically significant association between the duration of hospital stay and microorganism acquired. ($\chi^2 = 14.87$, $df = 3$, $p < 0.05$). Where χ^2 = Chi-square, n = no. of microorganisms, and df = degrees of freedom.

DISCUSSION

The data of 85 patients admitted to the hospital and diagnosed with infection during the period of January 2024 to June 2024 were analyzed. The demographic result of the study revealed male preponderance. The mean age of patients enrolled in the study was 56.5 years. A wide spectrum of clinical diagnoses for which restricted antibiotics were indicated included various infections like sepsis, septic shock, UTI, LRTI, infected wound, pyelonephritis, and endocarditis. Other conditions included poisoning, RTA, and AFI. Sepsis accounted for 31 cases (20.26%), while septic shock was observed in 25 cases (16.34%). Urinary tract infections (UTIs) were noted in 29 cases (18.95%), and lower respiratory tract infections (LRTIs) in 24 cases (15.69%). Infected wounds were present in 14 cases (9.15%), and urosepsis in 9 cases (5.88%). Road traffic accidents (RTAs) were the cause for 7 cases (4.58%), while pyelonephritis appeared in 4 cases (2.61%).

Endocarditis, poisoning, and cardiogenic shock each accounted for 2 cases (1.31%), while encephalopathy was noted in 4 cases (2.61%). Other conditions contributed to 1 case (0.65%). These conditions required restricted antibiotics due to the development of infection during the course of hospitalization.

The most common comorbidities observed were diabetes mellitus (DM) in 38 cases (24.20%) and hypertension (HTN) in 37 cases (23.57%). Chronic kidney disease (CKD) and acute kidney injury (AKI) were each noted in 10 cases (6.37%). Heart disease was present in 19 cases (12.10%), while respiratory disease accounted for 11 cases (7.01%). Hypothyroidism and neurological conditions (neuro) were both observed in 6 cases (3.82%), and liver disease was seen in 3 cases (1.91%). Gastrointestinal (gastro) disorders were present in 7 cases (4.46%), and blood diseases were noted in 10 cases.

Drug Utilization

Drug utilization DDD/100 bed days was applied in the analysis of in-hospital drug use. The ATC/DD system is a tool for presenting drug utilization statistics. DDD of tigecycline was found to be 13, linezolid 7.9, meropenem 7.34, ceftazidime 6.9, aztreonam 6.2, teicoplanin 5.11, vancomycin 3.4, imipenem 3.3, polymyxin B 1.5, ertapenem 1.2, and colistin 0.79. In the study on antimicrobial usage and cost conducted by Fatma Bozkurt in a teaching hospital, the Defined Daily Dose (DDD) was reported to be 2.9 for linezolid and 9.2 for carbapenems. (10) Meropenem was given in 47 cases out of 88, making it the most frequently used reserve antibiotic. It was followed by colistin ($n=37$) and linezolid ($n=31$). (10) Meropenem was used most commonly for empiric treatment prior to the culture sensitivity test, also mostly when patients' clinical condition worsened.

According to a review by Miriam Hurst, meropenem has proven to be effective in treating severe infections, especially those acquired in hospital settings or intensive care units. The most frequently diagnosed conditions in the reviewed studies included pneumonia and other lower respiratory tract infections, along with a significant number of intra-abdominal infections (11).

In the study the use of reserve antibiotics was based on the culture sensitivity. These antibiotics were indicated for resistant strains like MRSA, VRE, and multi-drug-resistant organisms. In a similar study conducted by Emmerson, the major infecting organisms were aerobic Gram-negative bacilli (AGNB), e.g., *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, *Klebsiella aerogenes*, and *Enterobacter* spp., and the Gram-positive cocci, such as methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant *Enterococcus faecium* (VRE), and coagulase-negative *Staphylococcus epidermidis* (CONS) (12).

In our study, *Klebsiella pneumoniae* was predominantly isolated from sputum and wound sites, with fewer cases found in blood and urine samples. Methicillin-resistant *Staphylococcus aureus* (MRSA) was primarily detected in wound sites, highlighting the need for improved postoperative care. Similarly, a parallel study by Carmen et al. reported that *Staphylococcus aureus* was most commonly found in wound secretions, blood, and bronchial aspirates.

The second most frequently isolated organism was *K. pneumoniae*, mainly from bronchial aspirates, urine, and wound sites. Notably, their study also identified a significant proportion of *Candida albicans* in blood cultures. Whereas a higher incidence of *Candida* species was observed in urine samples, followed by sputum in our study (13).

Hospital acquired infection: CLABSI and SSI

Coagulase-negative staphylococci (CONS), *Acinetobacter*, *Burkholderia*, *Klebsiella*, viridans group streptococci (VGS), and *Enterococcus* are the primary organisms responsible for central line-associated bloodstream infections (CLABSI). CONS is the most frequent cause, accounting for 61.54% of cases, while the other microorganisms each contribute 7.69% of infections. In the study population, *Enterococcus* was the leading cause of surgical site infections (SSI), representing 24% of cases. *E. coli* and MRSA were each responsible for 14%. CONS and *Acinetobacter* contributed to 9% of SSIs, while VRE, *Citrobacter*, *Pseudomonas* species, and *Stenotrophomonas maltophilia* each accounted for 5% of infections.

The study found an average of 2.4 microorganisms per patient, with an average of 1.87 microorganisms acquired. Data on healthcare-associated infections (HAI), particularly CLABSI and SSI, revealed a total of 25 HAIs. Superinfections were identified in 24 out of 85 cases, with the majority occurring in the urinary tract. Several multidrug-resistant organisms (MDROs) were detected, including MDR *Acinetobacter* spp., *Acinetobacter baumannii*, and MDR

Pseudomonas aeruginosa, MDR *Klebsiella* spp., MDR *Klebsiella pneumoniae*, MDR *E. coli*, MDR *Proteus mirabilis*, MDR *Providencia rettgeri*, VRE, and MRSA.

Superinfection

The study uncovered that the majority of superinfection was due to fungal infection, mainly *Candida* and *Enterococcus* species (21.88%). *Acinetobacter* and *Klebsiella* were 12%, VRE and *Burkholderia cepacia* were 6% of cases, and *E. coli*, CONS, VGS, MRSA, and *Providencia rettgeri* were 3%.

In a similar study conducted by Hessa Al Muqati, the main isolated microorganisms after 48 h were *Candida* spp., about 43.79% of all superinfections ($n = 67$), followed by *Enterobacteriaceae* spp. 17% ($n = 26$), *Staphylococcus* spp. 11.11% ($n = 17$), *Pseudomonas* spp. 9.80% ($n = 15$), and *Clostridioides difficile* 5.88% ($n = 9$) (14).

CONCLUSION

The analysis of antimicrobial use and microbial isolates in the High-Intensity Care Unit (HICU) revealed high reliance on reserve antibiotics, with meropenem (28%), colistin (17%), and linezolid (14%) being the most prescribed. In terms of utilization as per DDD/100 bed days, the most highly utilized drug was tigecycline, followed by linezolid and meropenem, with a DDD of 226.5 (13 DDD/100 bed days), 224.5 (7.9 DDD/100 bed days), and 458.1 (7.3 DDD/100 bed days), respectively. The least consumed drug was colistin, with a DDD of 13.8 (0.79 DDD/100 bed days). Reserve antibiotics were required for the management of infections caused by *Enterobacter* spp., *Klebsiella* spp., coagulase-negative staphylococci (CONS), *Acinetobacter* spp., *Escherichia coli*, methicillin-resistant *Staphylococcus aureus* (MRSA), and *Pseudomonas aeruginosa*. Out of the 137 isolates identified, 57 were multidrug-resistant (MDR) microorganisms, highlighting a critical concern regarding the rise of antimicrobial resistance (AMR). Extended hospital stays resulted in the acquisition of hospital-acquired infections, which also required reserve antibiotics for management. Our study highlights the considerable reliance on reserve antibiotics, primarily driven by the rise in antimicrobial resistance (AMR). Severe infections and prolonged hospital stays were identified as major factors necessitating their use.

The ATC/DDD system proved to be an effective tool for drug utilization comparison, and the DDD values calculated in this study provide valuable baseline data. This baseline can serve for future comparisons, enabling trend analysis within the same hospital over time or benchmarking against other institutions, and would help in supporting antimicrobial stewardship initiatives.

LIMITATIONS

This study has certain limitations that need to be acknowledged. First, the relatively small sample size restricts the generalizability of the findings. Second, while the Defined Daily Dose (DDD) analysis provides a valuable baseline for measuring the use of reserve antibiotics, it serves primarily as an initial reference point. Further research involving a larger dataset and extended timeframes will be required to validate these findings and enable meaningful comparisons of reserve antibiotic utilisation across different settings. Third, the study primarily focused on a limited number of hospital-acquired infections. As a result, the spectrum of infections captured may not fully reflect the wide range of clinical scenarios in which reserve antibiotics are prescribed. This narrowed scope may have led to underrepresentation of certain pathogens and antibiotic use patterns, highlighting the need for future studies.

ACKNOWLEDGEMENT

Not applicable

Conflicts of Interest

The authors declare that there are no conflicts of interest related to this study. The research was conducted independently, and the findings represent the unbiased results and interpretations of the authors.

Financial Support

This study did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors. It was conducted as part of academic research under institutional support from RDT Hospital, Andhra Pradesh.

Data Availability

The data supporting the findings of this study are available from the corresponding author upon reasonable request. The data will be made available to qualified researchers for non-commercial purposes only, subject to ethical and privacy considerations. Due to privacy restrictions, participant data cannot be publicly shared, but can be accessed by contacting the corresponding author.

Protection of humans and animals.

The authors declare that no experiments involving humans or animals were conducted for this research.

Confidentiality, informed consent, and ethical approval

The authors have followed their institution's confidentiality protocols, obtained informed consent from patients, and received approval from the Ethics Committee. The SAGER guidelines were followed according to the nature of the study.

Declaration on the use of artificial intelligence.

The authors declare that no generative artificial intelligence was used in the writing of this manuscript

REFERENCES

1. Nunes PH, Moreira JP, Thompson AD, Machado TL, Cerbino-
2. Neto J, Bozza FA. Antibiotic consumption and deviation of prescribed daily dose from the defined daily dose in critical care patients: a point-prevalence study. *Frontiers in Pharmacology*. 2022 Jun 16;13:913568.
3. Polk RE, Fox C, Mahoney A, Letcavage J, MacDougall C. Measurement of adult antibacterial drug use in 130 US hospitals: comparison of defined daily dose and days of therapy. *Clinical infectious diseases*. 2007 Mar 1;44(5):664–70.
4. WHO Collaborating Centre for Drug Statistics Methodology. Guidelines for ATC classification and DDD assignment. Oslo (Norway): Norwegian Institute of Public Health; 2025.
5. Balkhy HH, El-Saed A, El-Metwally A, Arabi YM, Aljohany SM, Al Zaibag M, Baharoon S, Alothman AF. Antimicrobial consumption in five adult intensive care units: a 33-month surveillance study. *Antimicrobial Resistance & Infection Control*. 2018 Dec; 7:1–9.
6. Karabay O, Bastug A, Ozturk R, Sencan I, Aksoy M, Simsek H, Gozel MG, Erdogan H, Karlidag GE, Aypak A, Gonen I. Antibiotic consumption, resistance data, and prevention strategies. *Mediterr J Infect Microb Antimicrob*. 2018;7(35):1–39.
7. Ventola CL. The antibiotic resistance crisis: part 1: causes and threats. *Pharmacy and therapeutics*. 2015 Apr;40(4):277.
8. Klein EY, Van Boeckel TP, Martinez EM, Pant S, Gandra S, Levin SA, et al. Global increase and geographic convergence in antibiotic consumption between 2000 and 2015. *Proc Natl Acad Sci*. 2018;115(15): E3463–70.
9. World Health Organization. WHO report on surveillance of antibiotic consumption: 2016 2018 early implementation World Health Organization. WHO Model List of Essential Medicines – 23rd list, 2023. Geneva: World Health Organization; 2023. WHO Reference Number: WHO/MHP/HPS/EML/2023.02. Available from: <https://www.who.int/publications/i/item/WHO-MHP-HPS-EML-2023.02>
10. Ibozkurt F, Kaya S, Tekin R, Gulsun S, Deveci O, Dayan S, Hoşoglu S. Analysis of antimicrobial consumption and cost in a teaching hospital. *Journal of infection and public health*. 2014 Mar 1;7(2):161–9.
11. Hurst M, Lamb HM. Meropenem: a review of its use in patients in intensive care. *Drugs*. 2000 Mar;59(3):653–80.
12. Emmerson M. Antibiotic usage and prescribing policies in the intensive care unit. *Intensive care medicine*. 2000 Feb 1;26: S26.
13. Axente C, Licker M, Moldovan R, Hogeia E, Muntean D, Horhat F, Bedreag O, Sandesc D, Papurica M, Dugaesescu D, Voicu M. Antimicrobial consumption, costs and resistance patterns: a two-year prospective study in a Romanian intensive care unit. *BMC infectious diseases*. 2017 May 22;17(1):358.
14. Al Muqati H, Al Turaiki A, Al Dhahri F, Al Enazi H, Althemery A. Superinfection rate among the patients treated with carbapenem versus piperacillin/tazobactam: Retrospective observational study. *Journal of Infection and Public Health*. 2021 Mar 1;14(3):306–10.