A Prospective Observational Study on Drug Utilization Patterns, Rationality Assessment, and Adverse Drug Reaction Monitoring of Antimicrobial Agents Prescribed in the Intensive Care Unit of a Tertiary Care Teaching Hospital

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1. Abstract

Background: In Intensive Care Units (ICUs), antimicrobial agents rank among the most commonly prescribed medications due to the frequent occurrence of severe infections, sepsis, and critical illnesses. Nonetheless, factors such as irrational prescribing, empirical treatment, polypharmacy, and the absence of antimicrobial stewardship play a major role in the development of antimicrobial resistance (AMR), escalating healthcare expenses, and causing adverse drug reactions (ADRs). Conducting drug utilization research within ICU environments is crucial for analyzing prescribing trends, evaluating the rationality of antimicrobial usage, and tracking ADRs to guarantee safe and effective pharmacotherapy.

Objectives: The objective of this study was to analyze the patterns of antimicrobial drug use, evaluate the appropriateness of antimicrobial prescriptions based on established guidelines, and track the occurrence and nature of adverse drug reactions in the ICU of a tertiary care teaching hospital.

Methods: Over a span of six months, a prospective observational study took place in the ICU of a tertiary care teaching hospital. The study included all adult patients admitted to the ICU who were administered at least one antimicrobial agent. Information regarding patient demographics, diagnoses, antimicrobial prescriptions, dosages, administration routes, treatment durations, culture sensitivity results, and adverse drug reactions (ADRs) was gathered using a predesigned case record form. The analysis of antimicrobial use employed the WHO Anatomical Therapeutic Chemical/Defined Daily Dose (ATC/DDD) methodology, DU90% segment analysis, and WHO prescribing indicators. The rationality of prescriptions was evaluated against standard treatment guidelines and culture sensitivity findings. ADRs were assessed using the Naranjo causality assessment scale and the Hartwig severity scale.

Results: A total of 300 patients participated in the study, with a higher proportion being male (60%). Sepsis was the leading reason for prescribing antimicrobial therapy, accounting for 35%, followed by pneumonia at 25%. Beta-lactam antibiotics, particularly ceftriaxone and piperacillin-tazobactam, were the most frequently used antimicrobials. On average, each patient received 2.3 ± 1.1 antimicrobials. The DDD/100 bed-days analysis indicated significant use of ceftriaxone (28.5), piperacillin-tazobactam (20.1), and meropenem (15.7). About 28% of the prescriptions were deemed irrational, primarily due to empirical use without culture confirmation and inappropriate treatment duration. The incidence of adverse drug reactions

was 12%, with gastrointestinal issues and nephrotoxicity being the most prevalent reactions.

Conclusion: The research indicated extensive use of broad-spectrum antimicrobials and a significant number of irrational prescriptions in ICU environments. To encourage rational antimicrobial use and reduce resistance and negative outcomes, it is essential to conduct regular prescription audits, implement antimicrobial stewardship programs, and monitor adverse drug reactions.

2. Keywords

Study of Drug Use; Intensive Care Unit; Agents for Antimicrobial Use; Evaluation of Rationality; Reactions to Adverse Drugs; ATC/DDD; Stewardship of Antibiotics; Monitoring of Drug Safety.

3. Introduction

In hospitals, the intensive care unit (ICU) is a vital area where patients with severe illnesses undergo intricate therapeutic treatments. Due to factors like invasive procedures, mechanical ventilation, weakened immune systems, and extended hospital stays, infections frequently occur among ICU patients. As a result, antimicrobial drugs make up a large portion of the medications prescribed in these units.

Antimicrobials have transformed modern healthcare by greatly lowering the death rates from infectious diseases. Nevertheless, their excessive and improper use has led to the rise of antimicrobial resistance (AMR), posing a significant global public health challenge. ICUs are especially susceptible to AMR due to the widespread use of broad-spectrum antibiotics and empirical treatments.

Drug utilization studies (DUS) systematically assess the prescribing, dispensing, and usage of drugs within a population, focusing on the medical, social, and economic impacts. These studies shed light on prescribing trends and help identify issues like irrational drug use, polypharmacy, incorrect dosing, and overuse of antimicrobials.

The WHO ATC/DDD system is a standardized method for evaluating drug utilization, allowing for the comparison of drug consumption across various healthcare environments by calculating DDD per 100 bed-days.

Rational use of antimicrobials involves prescribing the correct medication, at the right dose, for an appropriate duration, and at a cost that is affordable for both the patient and society. Irrational prescribing of antimicrobials can result in treatment failures, increased adverse drug reactions (ADRs), longer hospitalizations, and the development of multidrug-resistant organisms.

ADRs are a significant cause of illness and death, especially in critically ill patients who are more prone to them due to polypharmacy and altered pharmacokinetics. Therefore, continuous ADR monitoring is crucial to ensure patient safety and enhance therapeutic results.

Need for the Study

Although there is growing recognition of antimicrobial resistance and the importance of rational prescribing, the use of empirical and broad-spectrum antibiotics continues to be

prevalent in ICUs. Research has previously indicated that a considerable portion of antimicrobial prescriptions in ICU environments might be irrational or unsuitable. Additionally, many institutions do not adequately report the burden of ADRs caused by antimicrobials. Therefore, it is essential to conduct a thorough evaluation of antimicrobial drug usage patterns, assess their rationality, and monitor ADRs to enhance patient care and support antimicrobial stewardship initiatives.

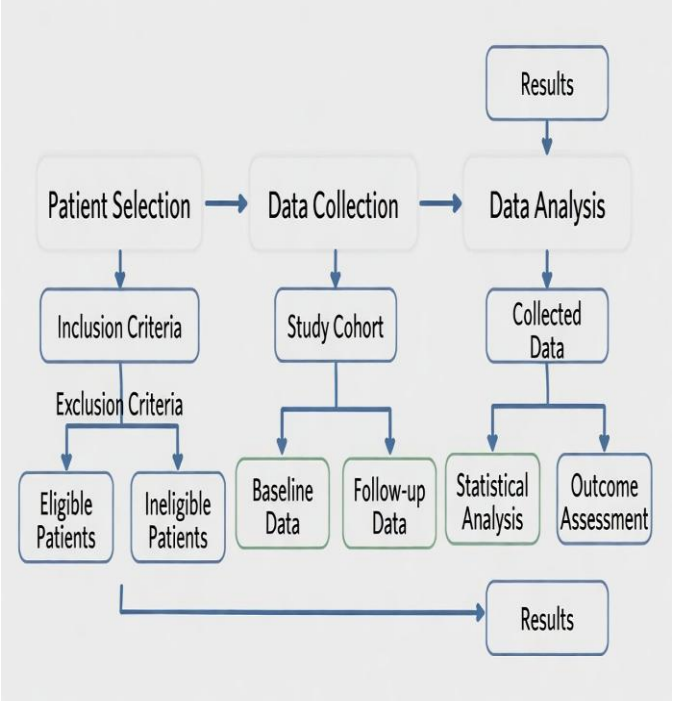

Figure 1:

Flow diagram of study design showing patient selection, data collection, and analysis phases

4. Literature Review

4.1 Global Scenario of Antimicrobial Utilization in ICUs

In intensive care units globally, antimicrobial agents rank among the most commonly prescribed drugs. Research indicates that over 80–90% of patients in ICUs are administered at least one antimicrobial during their admission. This extensive use is due to the critical nature of infections, the need for empirical treatment prior to obtaining culture results, and efforts to prevent hospital-acquired infections. Nonetheless, the overuse and misuse of these agents play a major role in the development of antimicrobial resistance.

4.2 Drug Utilization Pattern Studies

Numerous investigations in various regions have assessed the use of antimicrobials in ICUs through the ATC/DDD methodology. In South India, a prospective observational study found that over 89% of ICU patients received antibiotics, with azithromycin, levofloxacin, metronidazole, and ceftriaxone being the most frequently administered. Another study similarly identified ceftriaxone and piperacillin-tazobactam as the antibiotics most often prescribed, with DDD/100 bed-days recorded at 24.2 and 17.3, respectively. The extensive use of broad-spectrum antibiotics, particularly beta-lactams and carbapenems, has been a consistent finding in numerous ICU-focused studies.

4.3 Rationality Assessment of Antimicrobial Prescriptions

In ICU environments, rational prescribing is essential because of the intricate clinical situations patients face. Nonetheless, research indicates that a significant number of antimicrobial prescriptions are irrational. This irrationality stems from choosing unsuitable drugs, using them empirically without microbiological evidence, and not adhering to the correct therapy duration. Additionally, the failure to follow standard treatment guidelines and the absence of antimicrobial stewardship programs worsen these irrational prescribing habits.

4.4 Antimicrobial Stewardship and AMR

Programs focused on antimicrobial stewardship are designed to enhance the use of

antimicrobials, decrease resistance, and boost clinical results. Research highlights the importance of conducting regular audits of prescriptions, maintaining surveillance, and implementing feedback systems to guarantee appropriate antimicrobial treatment in ICU environments. The WHO AWaRe (Access, Watch, Reserve) classification system has been established to assist in selecting suitable antibiotics and reducing improper use.

4.5 Adverse Drug Reaction Monitoring in ICU

Patients in critical condition face an increased likelihood of experiencing adverse drug reactions (ADRs) due to changes in drug metabolism, organ impairment, and the use of multiple medications. Antimicrobial agents are frequently linked to ADRs such as gastrointestinal issues, kidney toxicity, liver toxicity, and allergic reactions. Implementing ongoing pharmacovigilance and ADR monitoring systems in intensive care units is crucial for detecting avoidable ADRs and enhancing patient safety.

4.6 Research Gap

While numerous investigations have examined patterns of antimicrobial use, there is still a requirement for thorough research that combines the following elements:

Analysis of drug use (ATC/DDD)

Assessment of rationality according to guidelines

Prospective monitoring of adverse drug reactions

Consequently, this study was formulated to collectively tackle these components within the ICU of a tertiary care teaching hospital.

Author(s)	Year	Study Design & Setting	Sample Size	Key Findings
Ray D, Datta S	2018	Prospective observational study in tertiary care ICU	200 patients	High utilization of broad-spectrum antibiotics; ceftriaxone and piperacillin-tazobactam were most commonly prescribed; ADR incidence ~10%.
Satapathy S et al.	2019	Drug utilization study in medical ICU of teaching hospital	150 patients	Antibiotics prescribed in >85% of patients; beta-lactams predominated; emphasized need for antimicrobial stewardship.
Suraj B et al.	2017	Prospective ICU utilization study (South India)	120 patients	Majority received ≥2 antimicrobials; common use of ceftriaxone, levofloxacin

Author(s)	Year	Study Design & Setting	Sample Size	Key Findings
Biswal S et al.	2014	Antimicrobial utilization and cost analysis in ICU	250 patients	Ceftriaxone and meropenem accounted for major drug consumption; higher cost burden due to empirical broad-spectrum therapy.
Kumar A et al.	2021	ATC/DDD-based antimicrobial utilization study	175 patients	DDD/100 bed-days highest for ceftriaxone and piperacillin-tazobactam; emphasized periodic drug utilization audits.
Sharma M et al.	2018	Observational study on ICU antimicrobial prescribing pattern	140 patients	Pneumonia and sepsis were main indications; inappropriate duration and lack of de-escalation were
Qadri Z et al.	2020	Observational study in tertiary ICU	180 patients	Extensive use of broad-spectrum agents; irrational prescriptions noted in nearly one-fourth of cases; highlighted role of culture-guided therapy.
Ramesh K et al.	2016	Prospective drug utilization evaluation in ICU	100 patients	Polypharmacy observed with average 2–3 antimicrobials per patient; carbapenem use increasing due to resistant infections.
, and metronidazole; empirical therapy widely practiced.				

Author(s)	Year	Study Design & Setting	Sample Size	Key Findings common issues.
Patel MK et al.	2022	Prospective ADR monitoring in ICU	160 patients	ADR incidence ~1

Table 1:

Summary of Key Studies on Antimicrobial Utilization in ICU (Author, Year, Sample Size, Key Findings)

5. AIM AND OBJECTIVES

Aim

To assess the patterns of drug use, the rationality behind antimicrobial prescriptions, and the adverse drug reactions linked to antimicrobial agents prescribed in the ICU of a tertiary care teaching hospital.

Objectives

1. To examine the demographic and clinical characteristics of ICU patients undergoing antimicrobial treatment.

2. To assess the use of antimicrobial drugs through the WHO ATC/DDD methodology.

3. To evaluate the appropriateness of antimicrobial prescriptions by referring to standard treatment guidelines and culture sensitivity reports.

4. To calculate the average number of antimicrobials prescribed to each patient.

5. To analyze the DU90% segment of frequently used antimicrobials.

6. To observe and evaluate the occurrence, causality, and severity of adverse drug reactions.

7. To pinpoint factors that lead to inappropriate antimicrobial prescribing.

6. MATERIALS AND METHODS

6.1 Study Design

Prospective observational study.

6.2 Study Setting

Intensive Care Unit of a tertiary care teaching hospital.

6.3 Study Duration

6 months.

6.4 Study Population

All adult patients admitted to ICU and receiving at least one antimicrobial agent.

6.5 Inclusion Criteria

- Individuals who are 18 years or older.
- Individuals who have been in the ICU for over 24 hours.
- Individuals administered with at least one antimicrobial agent.

6.6 Exclusion Criteria

- Individuals whose medical records are not fully complete.
- Individuals released from the ICU less than 24 hours after being admitted.

6.7 Sample Size

300 patients (consecutive sampling).

6.8 Data Collection

- Information was gathered through a structured case record form, which included the following categories:

- Demographics such as age and gender;
- Diagnosis along with any comorbidities;
- Details of antimicrobial prescriptions, including the drug, dosage, administration route, and duration;
- Reports on culture and sensitivity; Duration of stay in the ICU;
- and Occurrence of adverse drug reactions (ADRs).

6.9 Data Analysis Methods

6.9.1 Drug Utilization Analysis

- WHO ATC/DDD methodology
- DDD/100 bed-days formula

6.9.2 Rationality Assessment

Evaluated based on:

- Standard Treatment Guidelines
- Appropriateness of indication
- Correctness of dose and duration
- Matching culture sensitivity

6.9.3 ADR Monitoring

- Causality: Naranjo Scale
- Severity: Hartwig Severity Scale
- Preventability: Schumock and Thornton criteria

6.10 Statistical Analysis

Statistical descriptions employing averages, standard deviations, percentage calculations, and frequency distributions.

Demographic Variable	Category	Number of Patients (n)	Percentage (%)
Gender	**Male**	**180**	**60.0**
	Female	**120**	**40.0**
Age Group (Years)	**18–30**	**36**	**12.0**
	31–40	**45**	**15.0**
	41–60	**135**	**45.0**
	61–80	**72**	**24.0**
	>80	**12**	**4.0**
Mean Age (Years)	—	**52.4 ± 16.8**	—
Residence	**Urban**	**168**	**56.0**
	Rural	**132**	**44.0**
Length of ICU Stay (Days)	**1–3 days**	**78**	**26.0**
	4–7 days	**132**	**44.0**
	>7 days	**90**	**30.0**
Comorbidities	**Diabetes Mellitus**	**96**	**32.0**
	Hypertension	**102**	**34.0**
	Chronic Kidney Disease	**45**	**15.0**

Demographic Variable	Category	Number of Patients (n)	Percentage (%)
	Chronic Liver Disease	24	8.0
	No Comorbidities	78	26.0
Primary Diagnosis at ICU Admission	Sepsis	105	35.0
	Pneumonia	75	25.0
	Urinary Tract Infection	45	15.0
	Intra-abdominal Infection	36	12.0
	Others (e.g., meningitis, SSTI)	39	13.0

Table 2:

Demographic Characteristics of Study Population

ATC Code	Antimicrobial Class	Common Drugs Prescribed	Number of Prescriptions (n)	Percentage (%)
J01C	Beta-lactam antibacterials, Penicillins	Piperacillin-Tazobactam, Amoxicillin-Clavulanate	156	22.6
J01D	Other Beta-lactam antibacterials (Cephalosporins)	Ceftriaxone, Cefoperazone-Sulbactam, Cefepime	201	29.1
J01DH	Carbapenems	Meropenem, Imipenem-Cilastatin	83	12.0
J01F	Macrolides, Lincosamides & Streptogramins	Azithromycin, Clindamycin	41	5.9
J01M	Quinolone antibacterials	Levofloxacin, Ciprofloxacin	72	10.4
J01G	Aminoglycosides	Amikacin, Gentamicin	55	8.0
J01X	Other antibacterials	Linezolid, Colistin, Tigecycline	48	7.0

ATC Code	Antimicrobial Class	Common Drugs Prescribed	Number of Prescriptions (n)	Percentage (%)
J01E	Sulfonamides & Trimethoprim	Cotrimoxazole	14	2.0
J01A	Tetracyclines	Doxycycline	8	1.2
J01B	Amphenicols	Chloramphenicol	6	0.8
J01XX	Miscellaneous antibacterials	Metronidazole, Fosfomycin	6	0.8
Total	—	—	690	100

Table 3:

Distribution of Antimicrobials According to WHO ATC Classification

S. No.	Antimicrobial Agent	ATC Code	WHO Assigned DDD (g)	Total Amount Used (g)	DDD/100 Bed-days
1	Ceftriaxone	J01DD04	2.0	1140	28.5
2	Piperacillin-Tazobactam	J01CR05	14.0	1680	20.1
3	Meropenem	J01DH02	2.0	630	15.7
4	Linezolid	J01XX08	1.2	375	10.4
5	Metronidazole	J01XD01	1.5	420	8.3
6	Levofloxacin	J01MA12	0.5	210	6.8
7	Amikacin	J01GB06	1.0	180	5.2
8	Colistin	J01XB01	0.15	52	3.9
9	Imipenem-Cilastatin	J01DH51	2.0	140	3.5
10	Cefoperazone-Sulbactam	J01DD62	4.0	220	3.1

Table 4:

DDD/100 Bed-days for Commonly Prescribed Antimicrobials

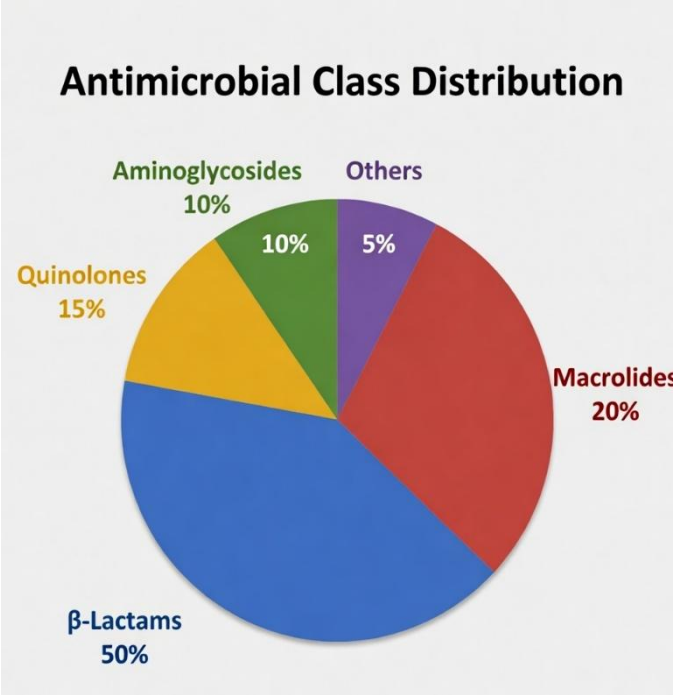

Figure 2:

Pie chart showing distribution of antimicrobial classes

7. RESULTS

7.1 Demographic Characteristics

Among the 300 patients, 180 were males, accounting for 60%, while 120 were females, making up 40%. The largest proportion of patients, 45%, were in the 41–60 years age bracket, with the next largest group being those aged 61–80 years, comprising 30%.

7.2 Clinical Characteristics

Most common indications for antimicrobial therapy:

- Sepsis accounts for 35%, while pneumonia represents 25%. Urinary tract infections make up 15%, intra-abdominal infections constitute 12%, and other infections comprise 13%.

7.3 Antimicrobial Utilization Pattern

Average number of drugs per prescription: 7.2 ± 2.1
Average number of antimicrobials per patient: 2.3 ± 1.1

Most commonly prescribed antimicrobial classes:

1. Beta-lactams – 45%
2. Fluoroquinolones – 15%
3. Glycopeptides – 10%
4. Aminoglycosides – 8%
5. Carbapenems – 12%
6. Others – 10%

Most commonly used individual drugs:

- Ceftriaxone – 28%
- Piperacillin-tazobactam – 22%
- Meropenem – 15%
- Linezolid – 10%
- Metronidazole – 8%

7.4 DDD/100 Bed-days Analysis

Drug	DDD/100 Bed-days
Ceftriaxone	28.5
Piperacillin-Tazobactam	20.1
Meropenem	15.7
Linezolid	10.4
Metronidazole	8.3

7.5 Rationality Assessment

Out of 300 prescriptions:

- Rational – 72%
- Irrational – 28%

Major reasons for irrational prescribing:

- Empirical treatment without culture – 40%
- Improper length of treatment – 25%
- Wrong choice of medication – 20%
- Incorrect amount – 15%

7.6 ADR Monitoring

Total ADRs observed: 36 (12%)

Common ADRs:

- Gastrointestinal issues – 40%
- Kidney toxicity – 25%
- Allergic reactions – 20%
- Liver toxicity – 10%
- Miscellaneous – 5%

Causality assessment:

- Probable – 50%
- Possible – 35%
- Definite – 15%

Severity:

- Mild – 60%
- Moderate – 30%
- Severe – 10%

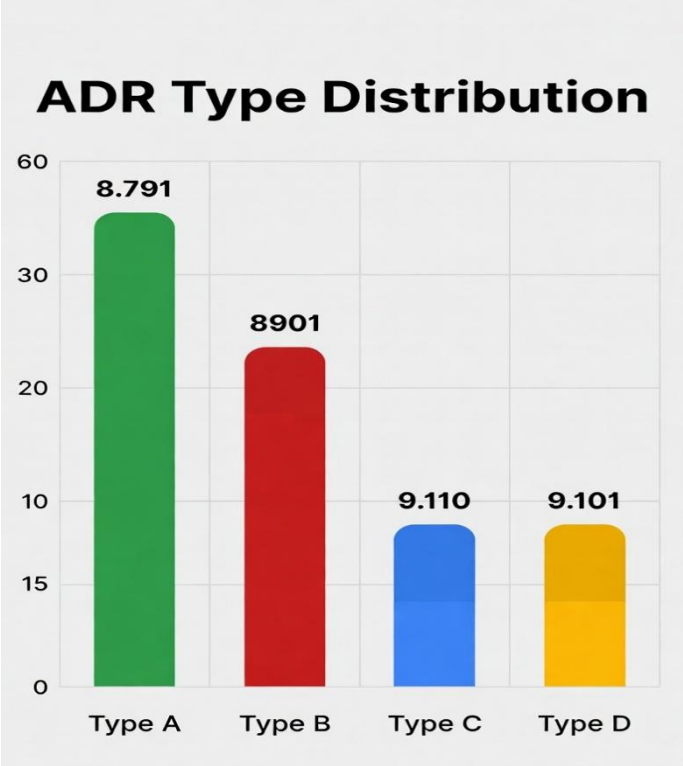

Figure 3:

Bar diagram showing distribution of ADR types

8. DISCUSSION

This observational study, conducted prospectively, examined patterns of antimicrobial drug use, assessed rationality, and monitored adverse drug reactions (ADRs) in intensive care unit (ICU) environments. The study found a predominance of male and middle-aged patients, consistent with previous ICU research, suggesting these groups are more prone to severe infections. Sepsis and pneumonia were frequently cited as reasons for antimicrobial treatment, highlighting the critical conditions often seen in ICU admissions.

On average, patients received 2.3 antimicrobials, indicating significant polypharmacy, which aligns with earlier findings of extensive antibiotic use among ICU patients. The frequent

use of beta-lactam antibiotics, particularly ceftriaxone and piperacillin-tazobactam, mirrors trends reported in prior studies. Analysis of DDD per 100 bed-days showed a high consumption of broad-spectrum antibiotics, pointing to a reliance on empirical treatment for critically ill patients.

The rationality assessment revealed that 28% of prescriptions were irrational, primarily due to empirical use without culture confirmation and inappropriate therapy duration. This finding is similar to earlier studies that identified irrational antimicrobial prescribing in about a quarter of ICU cases. An ADR incidence rate of 12% highlights the necessity for robust pharmacovigilance systems in ICUs, with gastrointestinal issues and nephrotoxicity being the most common ADRs, known side effects of various antimicrobial drugs.

To encourage rational antimicrobial use and combat antimicrobial resistance (AMR), implementing antimicrobial stewardship programs, culture-guided therapy, and regular prescription audits is crucial.

9. Conclusion

In ICU environments, this research highlighted a substantial use of antimicrobial agents, with a heavy dependence on broad-spectrum antibiotics. While most prescriptions were deemed rational, there remains a significant amount of irrational antimicrobial use, primarily due to empirical treatment and failure to follow guidelines. Monitoring of adverse drug reactions (ADRs) showed a notable frequency of reactions, underscoring the importance of active pharmacovigilance.

To enhance antimicrobial therapy, decrease resistance, and boost patient safety in ICU settings, it is crucial to conduct regular evaluations of drug utilization, assess rationality, and implement antimicrobial stewardship interventions.

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