Evaluation of Restricted Antimicrobial Utilization in a Tertiary Care Hospital

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ABSTRACT
The World Health Organization has declared that antimicrobial resistance is one of the top ten public health threats faced by humanity. In addition to death and disability, prolonged illness results in longer hospital stays, more expensive medicines and financial challenges for those impacted. The emergence of antimicrobial resistance was mainly attributed to the inappropriate prescribing and overuse of antimicrobials including self-medication. The main objective of our study was to study the prescribing patterns of restricted antimicrobials among in-patients in a tertiary care hospital. A prospective observational study was conducted among 108 in-patients and the rationality of prescriptions with restricted antimicrobials was analyzed. There were 174 antimicrobials prescribed in 108 patients, out of 174 antimicrobials prescribed 140 drugs were restricted antimicrobials and 34 drugs were non-restricted antimicrobials. Among restricted antimicrobials prescribed 53(49.07%) were Penicillin and Beta-lactamase inhibitors, 40(37.03%) were Carbapenems, 30 (21.42%) were third-generation Cephalosporins, 7(6.48%) were Oxazolidinones,7(6.48%) were glycopeptide antibiotic and 2(1.85%) Vancomycin. Out of 108 patients, 16(14.81%) patients were prescribed antimicrobials for prophylactic use, 63(58.33%) patients were prescribed with antimicrobials based on empirical therapy and 29(26.85%) patients were prescribed antimicrobials based on culture and sensitivity reports. The study concluded that the restricted antimicrobials were mostly prescribed based on empirical therapy (58.33%) in the study population which shows the need to control the use of restricted antimicrobials.

Keywords: Drug Use Evaluation, Restricted Antimicrobials, Utilisation Pattern, Antimicrobial Stewardship Committee, Culture Sensitivity Test

INTRODUCTION
The World Health Organization (WHO) defines Drug Use Evaluation (DUE) as a continual, systematic, criteria-based medicine evaluation program aimed at ensuring appropriate medication use. DUE's primary goal is to facilitate drug utilization and promote rational drug use in the population.[1] Drug Utilization Evaluation (DUE) serves to identify variations in drug usage and support interventions to enhance patient therapeutic outcomes and quality of life. Antimicrobials are potent drugs combating microbial infections by killing microorganisms or inhibiting their replication.

India was the world's largest consumer of antibiotics for human health. Antimicrobial use is influenced by prescribers' and patients' knowledge, expectations, interactions, economic incentives, healthcare system characteristics, and regulatory factors.

Globally, multi-drug resistant nosocomial infections are a leading cause of morbidity and mortality in hospitalized patients, burdening patients and public healthcare systems. Critically ill patients face a 5–7 times higher risk of nosocomial infection compared to ward patients. Intensive care unit (ICU) infections constitute 20%–25% of hospital-acquired infections, driven by invasive devices, immunosuppressive drugs, and irrational antimicrobial therapy in ICUs. ICU patients often receive empiric antimicrobial therapy due to their critical condition, with no time for culture reports[2]. This study includes analyzing antimicrobial consumption patterns in the ICU and the antimicrobial sensitivity of bacteria isolated from critically ill patients.

Antimicrobial resistance is a significant global public health threat, arising from inappropriate prescribing and overuse of antimicrobials, leading to prolonged hospitalization, higher costs, and increased mortality[3]. Mitigating antimicrobial resistance involves reducing antimicrobial use through policies and regulations encouraging appropriate use. Changes in prescribing practices can curb resistant pathogens. Evaluating high-end antibiotics can enhance treatment efficacy, conserve costs, and prevent antimicrobial resistance. New antibiotics, such as Eravacycline, are crucial for combating colistin resistance[4].

Antimicrobial stewardship aims to optimize antimicrobial use by selecting the right drug, dose, duration, and route. Pre-authorization and restricted use of high-end antibiotics are key strategies. Surveillance is essential to track antimicrobial use and resistance, identify targets for improvement, and correlate with resistance surveillance programs[5].

National Treatment Guidelines list "Alert" antimicrobials, including Ciprofloxacin, Ceftazidime, Cefotaxime, Ceftriaxone, Vancomycin, Imipenem, Levofloxacin, Meropenem, Moxifloxacin, Piperacillin-Tazobactam, Linezolid, Voriconazole, Caspofungin, Valganciclovir, Ertapenem, and newer Amphotericin preparations. These antimicrobials are frequently prescribed irrationally, contributing to rising costs, toxicity and resistance. Safer, cheaper alternatives are often available.

Based on this information, a study evaluating the utilization of restricted antimicrobials in a tertiary care hospital is proposed to address irrational antimicrobial use and its consequences.

OBJECTIVES

- To assess the prescribing pattern of restricted antibiotics among the in-patients.
- To analyze the antimicrobial resistance pattern among various organisms.
- To rationalize the use of restricted antibiotics.
- To evaluate the ADR and Drug interactions in the given study population.
- To create awareness about the restricted antibiotics and their specific indications.

METHODOLOGY

A patient data entry form was created for this study, capturing patient demographics (name, age, gender), hospitalization details (reason, duration), smoking history, and culture/sensitivity tests for antibiotics. Monitoring included restricted antimicrobial prescriptions, drug interactions, and administration details. The Prospective observational study was conducted in the General Medicine, Pulmonology, and ICU departments of a 1000-bed private teaching hospital for a duration of 6 months. The study included 200 in-patients was statistically analyzed based on descriptive statistics and was presented graphically and as percentages.

Inclusion Criteria

- Patients prescribed at least one restricted antibiotic.
- Patients above 18 years with consent, or consent from a bystander for critically ill patients.

Exclusion Criteria

- Patients with incomplete information.
- Pregnant and lactating women.
- Outpatients.

In this observational study, inpatient prescriptions with at least one restricted antimicrobials were identified initially. The patient's demographics and clinical data (age, gender, height, weight, IP number, admission/discharge dates, medical history, lab results, diagnosis, drug chart, adverse drug reactions, drug interactions, and interventions) were collected. The restricted antimicrobials use based on 2016 National treatment guidelines for infectious diseases were analyzed and the rationality of prescribed restricted antimicrobials was assessed.

RESULTS AND DISCUSSION

The study entitled "Evaluation of restricted antimicrobials utilization in a tertiary care hospital" was carried out in the Surgery, Pulmonology, General medicine and ICU departments of a 1000-bed multi-specialty tertiary care teaching hospital. A total number of 108 patients who satisfied the inclusion criteria were enrolled in the study after obtaining their consent.

Gender distribution

In a study involving 108 patients, gender distribution revealed that 60(55.5%) were male, while 48(44.4%) were female. (TABLE NO:1) gender-specific data on restricted antimicrobial usage were unavailable. The study found that males were more commonly prescribed restricted antimicrobials than females, consistent with similar studies conducted by Jayalakshmi J, et al., (2019)[5], and Singh A.P, et al., (2016)[6], which also reported a higher proportion of male patients in their study populations.

Table 1: Gender Categorization(n=108)

Sl. NO	GENDER	NUMBER OF PATIENTS	PERCENTAGE
1	MALE	60	55.56%
2	FEMALE	48	44.4%

Age Categorization

The study categorized the population into six age groups (TABLE NO: 2). The highest number of patients, 29 (26.85%), were in the Adulthood (36-50 Years) group, followed by 27 (25.00%) in the Late Adulthood (51-65 Years), and 21 (19.44%) in Young Old (66-74 Years). Patients aged 36-50 Years and 51-65 Years had the highest prescription rates of restricted antimicrobials, possibly due to increased comorbidity alongside infectious diseases in these age groups. This finding aligns with studies by Kumar.S, et al., (2021)[1] and Saxena.S, et al.,(2019)[7], which observed a similar trend in prescribing restricted antimicrobials in the same age groups.

Table 2: Age Categorization(n=108)

Sl. NO	AGE CATEGORY (Years)	NUMBER OF PATIENTS	PERCENTAGE(%)
1	Early Adulthood (19-35 Years)	11	10.18%
2	Adulthood (36-50 Years)	29	26.85%
3	Late Adulthood (51-65 Years)	27	25.00%
4	Young old (66-74 Years)	21	19.44%
5	Old (75-84 Years)	15	13.88%
6	Old (above 85 Years)	5	4.62%

Current Medical Conditions

The current medical conditions were analyzed and categorized. The most prevalent conditions were DM 24 (22.75%) and HTN 21(20.38%), followed by Pneumonia 8(7.75%) and COPD 7(6.45%). Other conditions made up 15 (14.62%) of the diagnoses, including Osteomyelitis, Dyslipidaemia, septic shock, and more. Details are in (Table 3).

Table 3: Current Medical Conditions(n=108)

Sl. NO	DISEASES	PERCENTAGE
1	DM	22.75%
2	SHT	20.38%
3	Pneumonia	7.75%
4	COPD	6.45%
5	Interstitial lung disease	4.37%
6	Asthma	4.09%
7	Fever	4.09%
8	RTI	4.09%
9	CKD	2.87%
10	UTI	2.04%
11	TB	1.50%
12	Hypothyroidism	1.35%
13	Anemia	1.15%
14	Pyelonephritis	1.15%
15	Diabetic Foot Ulcer	0.95%
16	Cellulitis	0.40%
17	Others (Osteomyelitis, Dyslipidemia, septic shock)	14.62%

Categories of Drugs Prescribed to Patients

The study examined drug categories prescribed to the study population. Antibiotics were the most common 108(20.8%), followed by antiulcer and anti-emetic drugs 93(17.4%), analgesics 87(13.47%), and other categories with varying percentages. These results are detailed in (Table 4)

Table 4: Categories of Drugs Prescribed to Patients(n=624)

Sl. NO	CATEGORIES OF DRUGS PRESCRIBED	NUMBER OF PATIENTS
1	Antibiotics	108 (20.8%)
2	Anti-ulcer and anti-emetics	93 (17.4%)
3	Analgesics	87 (13.47%)
4	Antihypertensives	47`(7.3%)
5	Anti-Diabetics	40 (6.23%)
6	Steroids	39 (6.07%)
7	NSAIDS	37 (5.76%)
8	Probiotics	33 (5.14%)
9	Multivitamins	28 (4.36%)
10	Lipid Lowering Agents	24 (3.7%)
11	Anti-Asthmatics	20 (3.11%)
12	Expectorant	18 (2.8%)
13	Anticoagulant	14 (2.18%)
14	Antithyroid Drugs	12 (1.86%)
16	Others	24 (3.7%)

Indications for Antibiotics Use

Antimicrobials were primarily prescribed for skin and soft tissue infections in the study population. The second most common condition was respiratory tract infections, which included pneumonia, LRTI, URTI, COPD, respiratory failure, bronchiectasis, and other respiratory tract infections. UTI, surgical prophylaxis, sepsis, and meningitis were also among the conditions treated with antibiotics. These findings align with Jose.J.E. et al.'s research, where respiratory tract infections were the leading indication for antibiotic prescriptions, similar to our study's RTI rate[8]. Detailed information is in (Table 5).

Table 5: Indications for Antibiotic Use (n=108)

Sl. NO	INDICATIONS	NUMBER OF PATIENTS	PERCENTAGE
1	URTI	1	0.92%
2	Respiratory failure	2	1.85%
3	LRTI	3	2.77%
4	COPD	3	2.77%
5	Bronchiectasis	3	2.77%
6	Other Respiratory tract infections	3	2.77%
7	Pneumonia	8	7.40%
8	Meningitis	11	10.18%

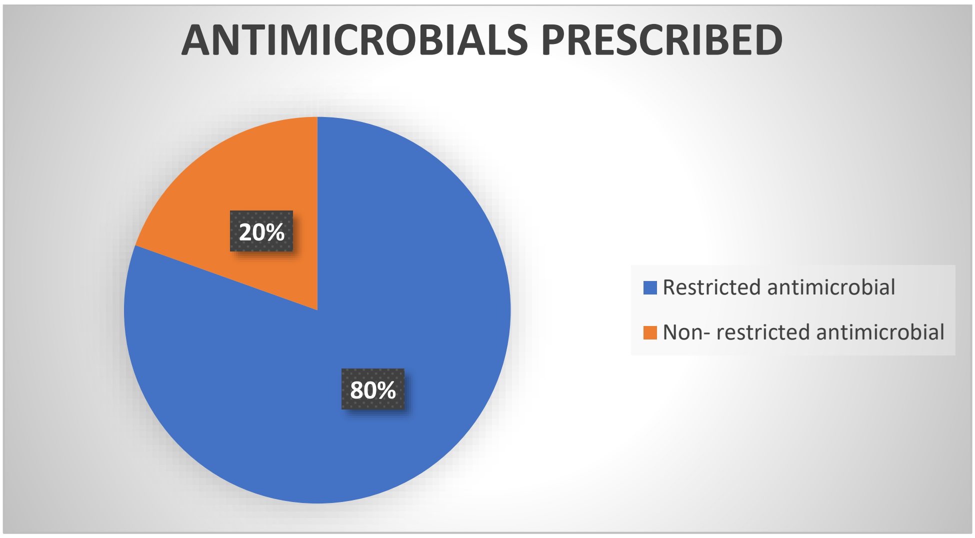
9	UTI	13	12.03%
10	Surgical prophylaxis	16	14.81%
11	Sepsis	17	15.74%
12	Skin and soft tissue	28	25.92%

Categories of Antimicrobials Prescribed

The antimicrobials prescribed for the study population were analyzed and found that out of 174 antimicrobials prescribed, 140 (80.45%) drugs were restricted antimicrobials, and 34 (19.54%) drugs were non-restricted antimicrobials. (Table 6)

Table 6: Categories of Antimicrobials Prescribed(n=174)

Sl. NO	CATEGORIES	NUMBER OF DRUGS	PERCENTAGE
1	Restricted antimicrobials	140	80.45%
2	Non- Restricted antimicrobials	34	19.54%



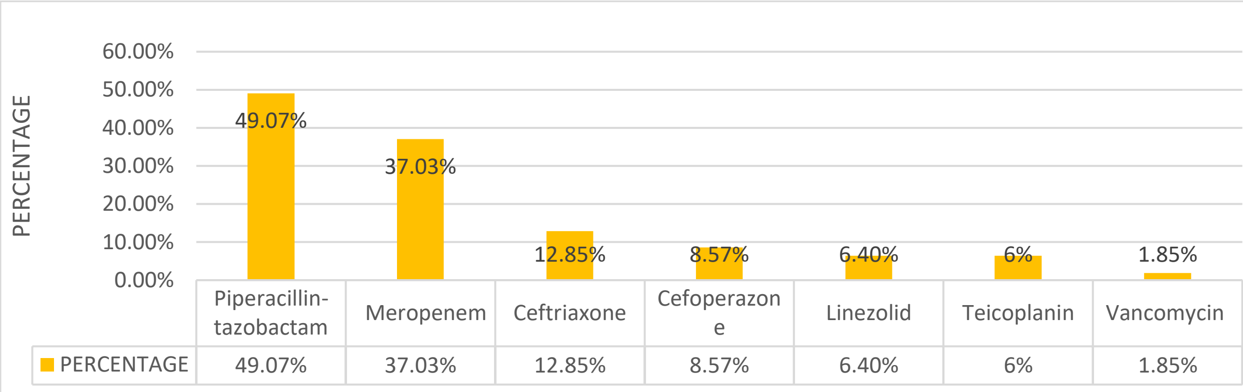
Restricted Antimicrobial Drugs Prescribed

In our study, the analysis of restricted antimicrobial drug usage revealed the following commonly prescribed drugs: Piperacillin-Tazobactam 53(49.07%), Carbapenems 40(37.03%), and third-generation Cephalosporins, including Ceftriaxone and Cefoperazone 18(21.42%). Additionally, Linezolid, Teicoplanin, and Vancomycin were prescribed in smaller percentages. These findings align with a study by Rockenschaub. P, et al. (2020)[9], reported the extent of prescription of major classes of restricted antimicrobial drugs, including Ciprofloxacin, Piperacillin-tazobactam, Meropenem, and Linezolid. Detailed information is available in (Table 7).

Table 7: Restricted Antimicrobials Prescribed(n=108)

Sl. NO	CATEGORIES	NUMBER OF PATIENTS	PERCENTAGE
1	Piperacillin-Tazobactam	53	49.07%

2	Meropenem	40	37.03%
3	Ceftriaxone	18	12.85%
4	Cefoperazone	12	8.57%
5	Linezolid	7	6.40%
5	Teicoplanin	7	6.40%
6	Vancomycin	2	1.85%

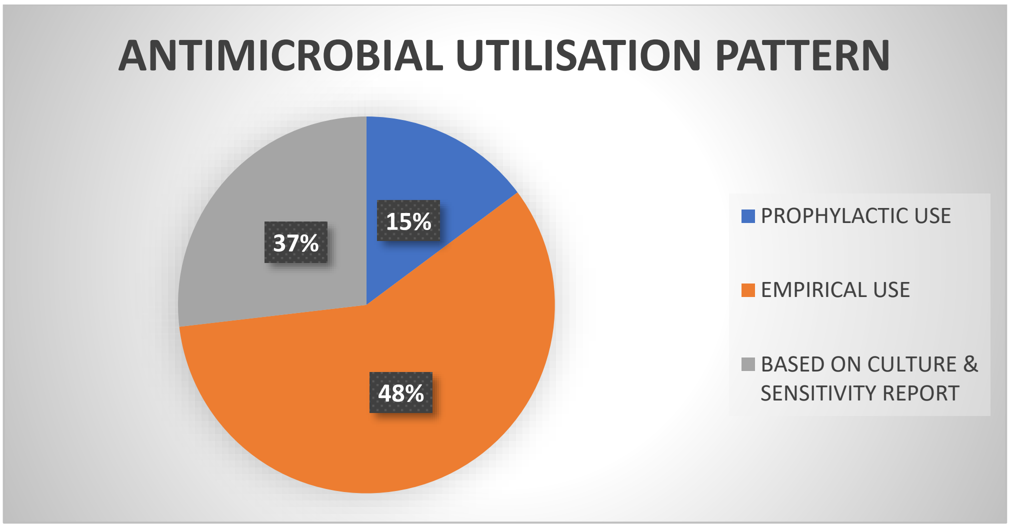


Restricted Antimicrobial Utilisation Pattern

Among 108 prescriptions, 16 (14.81%) were for prophylactic use, 52 (58.33%) were for empirical therapy, and 40(26.85%) were based on sensitivity patterns. The above results are indicative of the irrational use of restricted antimicrobials because restricted antimicrobials are not indicated for empirical therapy without proper guidelines and approval from the antimicrobial committee of the hospital. Our findings contrast with Kumar.S, et al.'s study (2021)[1], which reported lower susceptibility testing (3.71%) and higher empirical use of restricted antimicrobials (96.28%) (Table 8).

Table 8: Restricted Antimicrobial Utilisation Pattern

ANTIMICROBIAL UTILISATION PATTERN	NUMBER OF PRESCRIPTIONS	PERCENTAGE
Prophylactic Use	16	14.81%
Empirical Use	52	48.14%
Based on the Culture and Sensitivity Report	40	37.03%



Prescribing Pattern of Restricted Antimicrobials

Monotherapy was observed predominantly 81(75%) in prescribing restricted antimicrobials, while dual therapy 27(25%) was less common. This aligns with Schmid. A, et al.'s study (2019)[10], which suggests dual therapy may reduce mortality (Table 9).

Table 9: Prescribing Pattern of Restricted Antimicrobials

VARIABLE	THERAPY GIVEN	NUMBER OF PRESCRIPTIONS	PERCENTAGE
Prescribing pattern of restricted antimicrobials	Monotherapy	81	75%
	Dual therapy	27	25%

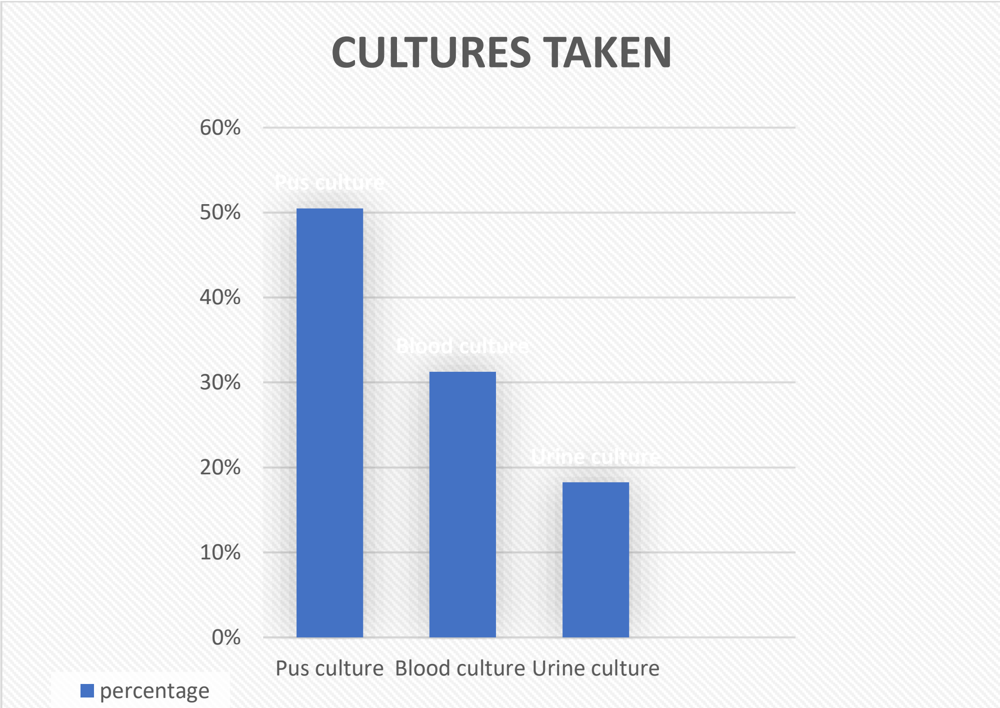
Culture Sensitivity Test

The study found that 29 (26.85%) of patients had culture and sensitivity tests done. From the culture and sensitivity report, it was observed that E.coli exhibited 53.3% resistance to cephalosporins, Staphylococcus aureus showed 35% resistance to fluoroquinolones, Klebsiella pneumoniae displayed 10% resistance to piperacillin-tazobactam, and Proteus mirabilis was resistant to colistin in 4 (2%) cases. These results parallel those in Annamalai. A, et al.'s study (2021)[3], also noted high resistance, particularly in Klebsiella pneumoniae and E.coli (100% resistance to Ceftazidime) (Table 10).

Table 10: Cultures taken for Susceptibility Testing

CULTURES TAKEN	NUMBER	PERCENTAGE
Pus culture	11	50.5 %
Blood culture	10	31.25%

Urine culture	8	18.25%

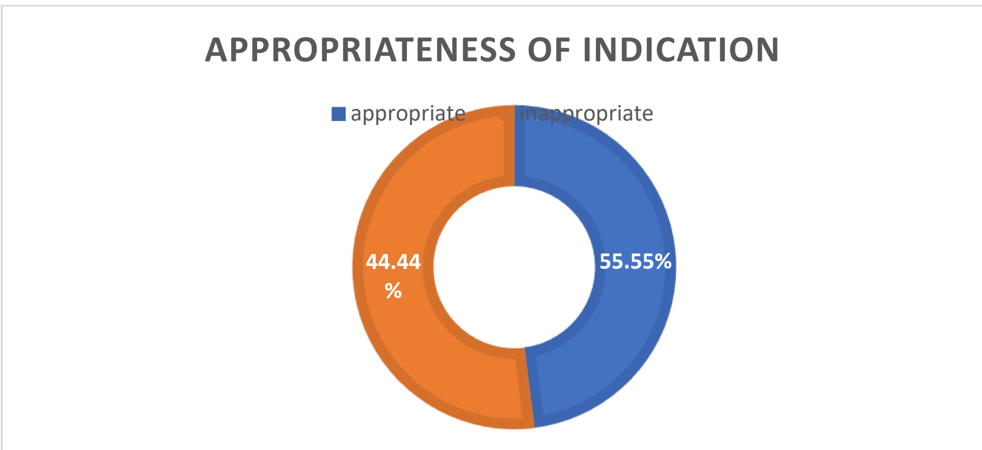


Appropriateness of Indication for Restricted Antimicrobial Therapy

In the study, 48 (44.44%) of prescriptions were appropriate based on national guidelines for restricted antimicrobial use, while 60 (55.55%) prescriptions were inappropriate leading to irrational prescribing. A study by Jose. J.E, et al. (2022)[8] found similar patterns, with 55.9% showing inappropriate restricted antimicrobial prescriptions. (Table 11).

Table 11: Appropriateness of Indication for Restricted Antimicrobial Therapy(n=108)

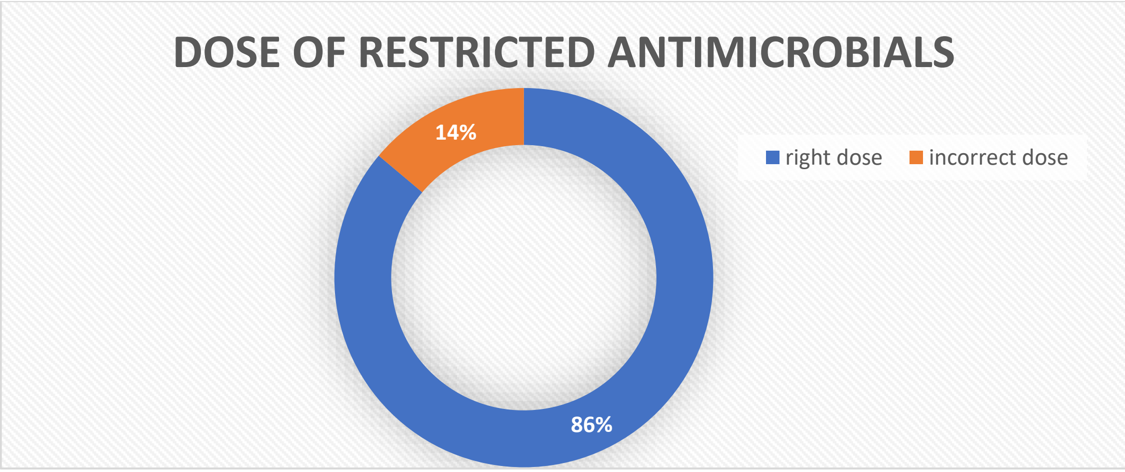
Appropriateness of Indication	Number of Prescriptions	Percentage
Appropriate	48	44.44%
Inappropriate	60	55.55%



In the study, 93(86.11%) of cases received the correct dose of restricted antimicrobials, with 15(13.88%) receiving an inappropriate dose. Similar findings were reported by Patricia, et al. (2015)[11], where 49.82% of prescriptions had incorrect dosing (Table 12).

Table 12:Dose of Restricted Antimicrobials Prescribed (n=108)

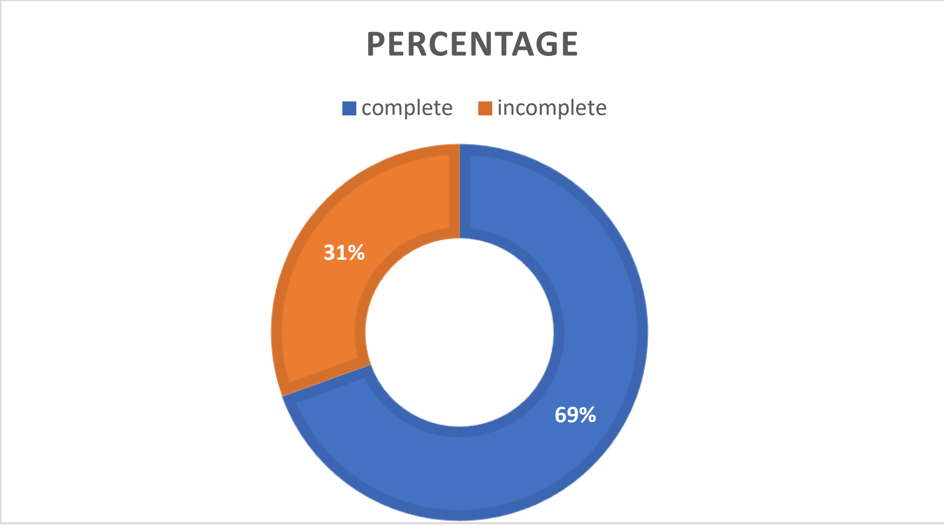
Dose of Restricted Antimicrobials	Number of Prescriptions	Percentage
Right dose	93	86.11%
Incorrect dose	15	13.88%



In 108 cases, 75 (69.44%)completed the therapy, while 33 (30.56%) did not. The study found that 30.5% of cases had inappropriate therapy duration, with piperacillin-tazobactam at 17.4% and ciprofloxacin at 8.4% being mostly predominant (Table 13).

Table 13: Duration of Restricted Antimicrobial Therapy

Duration of Antimicrobial Therapy	Number of Prescriptions	Percentage
Complete	75	69.44%
Incomplete	33	30.5%



Rational Use of Restricted Antimicrobials:

We assessed antibiotic rationality using references obtained from Micromedex and the Indian council of Medical Research guidelines for antimicrobial use in infectious diseases in 2022. It was observed that Penicillin with beta-lactamase inhibitors was most common, followed by fluoroquinolones and third-generation cephalosporins. Only 16 (8.8%) had susceptibility testing, while 70 (64.8%) lacked it, reflecting empirical and irrational antimicrobial use. This often resulted from delayed culture reports or unfeasible sampling, leading to drug misuse. Our findings confirm frequent empirical broad-spectrum therapy, aligning with a study by Willemsen et al. (2017)[12] showing increased inappropriate use of restricted antimicrobials.

CONCLUSION

The study concludes that the restricted antibiotics were mostly prescribed as empirical therapy in the study population. Overuse of restricted antibiotics is the main factor for antibiotic resistance. The large number of empirical prescriptions of restricted antibiotics shows the need to have control over restricted antibiotic use.

The establishment of drug formularies in hospitals and the involvement of the clinical pharmacist in order to ensure rational antibiotic therapy may improve the quality of patient care and reduce the cost of therapy. Developing hospital antibiogram-based policies, strict implementation, coordinated decisions in the use of high-end antibiotics for the treatment of patients along with hospital infection, and control practices are essential components to be developed in every hospital to prevent misuse of these drugs. Clinical audits followed by feedback and intervention can improve the rationalized prescription of such last-resort antibiotics.

CONFLICT OF INTEREST

There are no conflicts of interest concerning the research, authorship, and publication of this article.

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