

# A PROSPECTIVE OBSERVATIONAL STUDY TO ASSESS THE PRESCRIPTION PATTERN OF ANTIBIOTICS IN INTENSIVE CARE UNIT AT TERTIARY CARE HOSPITAL

## ABSTRACT

**Aims:** The aim of the study is to assess antibiotic utilization patterns among critically ill and post-operative ICU patients, with the goals of optimizing prescribing practices, evaluating adherence to guidelines, and minimizing risks associated with antibiotic resistance.

**Study design:** Prospective Observational.

**Place and Duration of Study:** BAPS Pramukh Swami Hospital, Surat between November 2022-March 2023.

**Materials and Methods:** The study included 108 patients directly admitted to the ICU, selected based on specific inclusion criteria. Eligible patients were aged 18 years or older and categorized as critically ill or post-operative patients requiring ICU admission. Additionally, patients needed to have been prescribed at least one antibiotic, whether for prophylactic or therapeutic purposes. Detailed demographic and clinical data were recorded for each patient using a pre-established case report form. The study aimed to analyze adverse events associated with antibiotic usage among these ICU patients, utilizing Microsoft Excel for data analysis.

**Results:** The total number of prescribed antibiotics was 235, the empirically prescribed antibiotics were Cefoperazone + Sulbactam 54 (21%) followed by Ceftriaxone (14%) and Meropenem (12%). The multiple therapy was prescribed in 63 (58%) patients. The most utilized were from WHO Watch Class 163 (69%). The value obtained for the average number of antibiotics per encounter was 2.15 (WHO optimal value: 1.6 – 1.8). The adverse events associated with antibiotics were observed in 16 patients. A culture sensitivity test was performed in 28.7% of patients. The most common pathogen detected was E.coli and K. pneumoniae.

**Conclusion:** The study reflects the requirement of antimicrobial stewardship practice, which should focus on promoting rational antibiotic prescription, which will help in combat with critical resistance issues in the future

*Keywords:* Antimicrobial Stewardship, Prescription Pattern of Antibiotics, Antimicrobial Resistance, ICU, WHO AWaRe

## 1. INTRODUCTION

The advent of antibiotics was a pivotal moment in medical history, transforming the treatment landscape for infectious diseases. However, the widespread and often indiscriminate use of these life-saving medications has led to a concerning phenomenon: antibiotic resistance. As

antibiotic usage escalates, so does the emergence of resistant strains of bacteria, rendering once-effective treatments ineffective and resulting in therapeutic failure and poor patient outcomes. A report published in the Lancet in 2019 highlighted the severity of the situation, estimating that approximately 4.95 million deaths are attributed to bacterial resistance each year [1].

In India, the situation is particularly dire, with antimicrobial resistance (AMR) claiming the lives of an estimated 700,000 individuals annually. Alarming projections suggest that by 2050, this number could soar to a staggering 10 million deaths, surpassing the combined toll of cancer and road traffic accidents [2,17,18,19,20]. Within intensive care units (ICUs), where patients are often critically ill and undergo invasive procedures, antibiotic prescriptions are especially prone to misuse and overuse. Patients in ICU settings frequently receive multiple broad-spectrum antibiotics without the result of a culture sensitivity test, increasing the risk of selecting for drug-resistant pathogens [3]. The primary objective of this study is to assess the utilization patterns of prescribed antibiotics within the Intensive Care Unit (ICU) setting. Secondary objectives include determining the distribution of infections in terms of their etiology and pathophysiology, evaluating adverse drug reactions associated with antibiotic usage, identifying prescription errors related to antibiotics, and advocating for the optimal use of antibiotics. Through a comprehensive analysis, this research aims to provide insights into antibiotic prescribing practices in ICUs, shed light on potential areas for improvement, and ultimately promote more effective and judicious antibiotic use to combat emerging challenges such as antimicrobial resistance.

To address these challenges, patient risk stratification plays a pivotal role. By systematically categorizing patients based on their health status and other relevant factors, healthcare providers can better identify individuals at heightened risk of acquiring multidrug-resistant pathogens. This enables targeted interventions and antibiotic prescribing practices, optimizing the use of limited resources and proactively managing patient populations. Additionally, risk stratification aids in tailoring empirical therapy selection and facilitating timely adjustments, such as escalation or de-escalation of antibiotic regimens, based on patient response and evolving clinical scenarios [4].

Infection Prevention and Control Programs prioritize patient and healthcare professional safety by focusing on reducing healthcare-associated infections and antimicrobial resistance. They also emphasize Antimicrobial Stewardship Programs, advocating for the safe use of antimicrobials to combat resistance through guideline review and local implementation.[5] Aligned with global efforts to combat antimicrobial resistance, the World Health Organization (WHO) introduced the AWaRe classification of antibiotics in September 2021. This classification system categorizes 180 antibiotics into three groups: Access, Watch, and Reserve. The primary objective of the AWaRe classification is to promote the judicious use of antibiotics and enhance monitoring practices. Access antibiotics, which have minimal resistance potential, are recommended as first-line agents for initial therapy. Watch antibiotics, while effective, require vigilance due to concerns such as toxicity or emerging resistance. Reserve antibiotics are reserved for the treatment of multidrug-resistant infections, serving as critical last-resort options to preserve efficacy and combat antimicrobial resistance [6, 7].

In summary, the integration of patient risk stratification alongside the AWaRe classification framework represents a multifaceted approach to enhance antibiotic stewardship efforts. By addressing the complex challenges posed by antimicrobial resistance through targeted interventions, optimized antibiotic use, and strategic resource allocation, healthcare systems can mitigate the devastating impact of drug-resistant infections and safeguard patient outcomes.

The patient risk stratification is important to identify patients with the risk of infection by MDR organisms. Risk stratification is a technique for systematically categorizing patients based on

their health status and other factors. It allows for risk-stratified care management, in which practices manage patients based on their assigned risk level to make better use of limited resources, anticipate needs, and more proactively manage the patient population, in terms of prescribing antibiotics, Patient risk stratification helps recognize the patient requiring which coverage of therapy needed in the choice of empirical therapy and also a further assistant in escalation and de-escalation of Antibiotics it divides the patient into three types based on pre-determined criteria: type 1 (low risk, requires short term and prophylactic antibiotics) type 2 (moderate risk, requires relatively long term definitive therapy), type 3 (high risk, requires higher antibiotics that can mitigate the MDR infection), in addition, patient Type 4 can also be added in special circumstances, where suspicion of fungal infection is highly suspect [8]

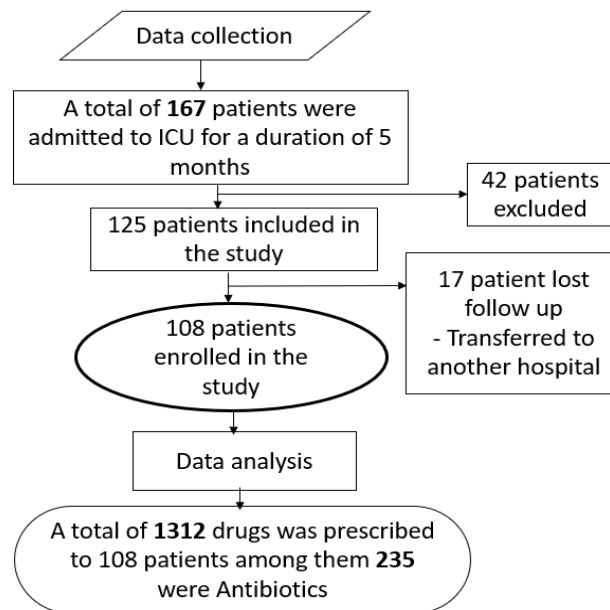
## 2. MATERIAL AND METHODS

### 2.1 Objectives:

**2.1.1 Primary objective** - To evaluate the utilization of prescribed antibiotics in an intensive care unit

**2.1.2 Secondary objectives-** 1. To determine the etiological and pathophysiological distribution of infection 2. To determine adverse drug reactions of antibiotics 3. To determine prescription errors regarding antibiotics 4. To promote the optimal use of antibiotics

**2.2 Study Design:** Single-center prospective observational study conducted in the Intensive Care Unit at Baps Pramukh Swami Hospital, Surat. A total of 167 patients were admitted to ICU for a duration of 5 months, among them 108 patients enrolled in our study, and 59 patients were excluded from the study according to the inclusion and exclusion criteria mentioned below figure 1 represents the design of our study.



(Figure 1 Represents the study design)

## 2.3 Study Criteria

**2.3.1 Inclusion Criteria:** 1. Patient's age  $\geq 18$  years 2. Patients, who are critically ill and post-surgical admitted to ICU are included 3. Patients, who are prescribed with at least one antibiotic either for prophylaxis or therapeutic purpose

**2.3.2 Exclusion Criteria:** Pediatric population, pregnant and lactating women.

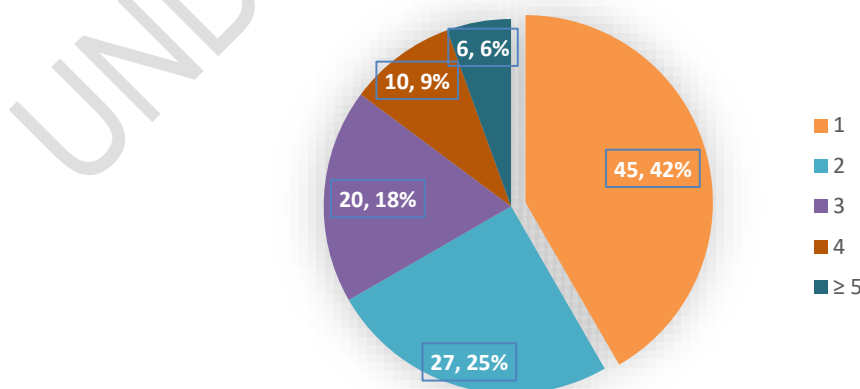
Study-related data like patient's demographic details (age, gender, weight), patient risk stratification at the time of ICU admission, diagnosis, possible site of infection, particular lab parameters, culture test data, prescribed antibiotics details, length of the stay (LOS) in ICU, total hospital stay, mortality score using APACHE – II score and observed adverse events like adverse drug reactions (ADRs), medication error regarding the use of antibiotics were collected in priorly created case report form (CRF) and all the data collection and analysis was conducted by using Microsoft excel.

## 3. RESULTS AND DISCUSSION

Our study involved a comprehensive investigation of 108 patients who were categorized based on several criteria such as demographics, reason for admission, length of stay in the hospital, prescribed antibiotics, types of patients according to patient risk stratification, site of infection, pathogen identified, classification of Prescribed antibiotics per WHO AWaRe guideline, etc. as per our study objectives.

Table 1 represents the patient-related demographics. There was a total of 108 patients enrolled in this study, among them 55.5 % were male and 44.4% were female. A total of 1312 drugs were prescribed among which 235 (17.91%) were antibiotics. The number of drugs prescribed per patient was  $12.14 \pm 4.60$  and the number of antibiotics prescribed per patient was  $2.15 \pm 0.70$ . The average ICU stay of patients was  $5.45 \pm 5.25$  days. out of 108 patients, 25 (23.14%) patients died, among which 14 (56%) deaths were due to infection and 11(44%) deaths were due to disease severity.

Figure 2 represents the utilization of single and multiple antibiotics, out of all, 42% of patients were prescribed with single antibiotic and 58% of patients were prescribed multiple antibiotics

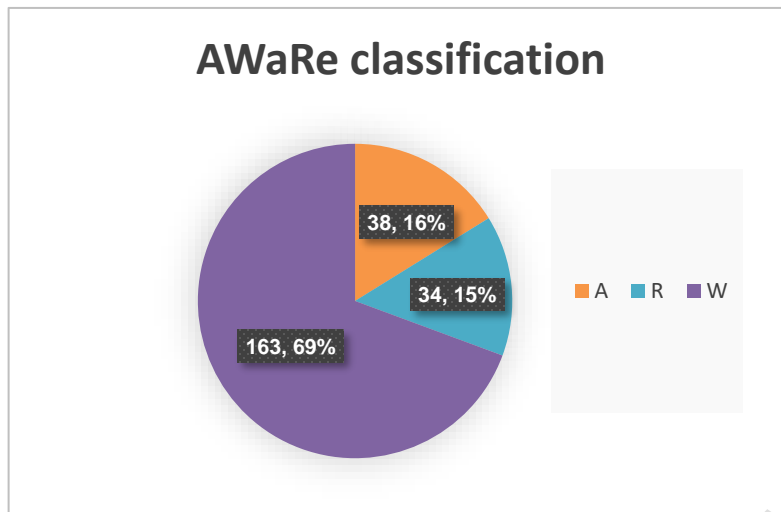


(Figure 2 Number of Antibiotics Prescribed per Patient)

Table 1 Demographic Data of Patients	
VARIABLES	ANALYSIS
<u>Gender</u>	
Male, N (%)	60 (55.5%)
Female, N (%)	48 (44.4%)
<u>Age distribution (years)</u>	
18-30, N (%)	8 (7.40%)
31-60, N (%)	33 (30.55%)
> 60, N (%)	66 (61.11%)
<u>Reason of admission</u>	
Critical ill, N (%)	80 (74%)
Post-Op, N (%)	28 (25.9%)
<u>Risk stratification</u>	
Type-1, N (%)	70 (64.8%)
Type-2, N (%)	33 (30.5%)
Type-3, N (%)	05 (4.6%)
Drugs prescribed	1312 (12.14 ± 4.60 /patient)
Antibiotics prescribed	235 (2.15 ± 0.70 /patient)
1, N (%)	45 (42%)
2, N (%)	27 (25%)
3, N (%)	20 (18%)
4, N (%)	10 (9%)
> 5, N (%)	6 (5%)
APACHE II Score	
0-9, N (%)	33 (30.55%)
10-19, N (%)	54 (50%)
20-29, N (%)	17 (15.74%)
≥30, N (%)	04 (3.70%)
Length of ICU stay (days)	5.45 ± 5.25
1-5, N (%)	72 (66.66%)
6-10, N (%)	25 (23.14%)
11-15, N (%)	05 (4.62%)
>15, N (%)	05 (4.62%)
Outcome	
Better, N (%)	83 (76.85%)
Worsen (Death), N (%)	25 (23.14%)
Reason of death	
Infection-related, N (%)	14 (56%)
Disease-related, N (%)	11 (44%)

(N= number of patients. % = percentage of total number of patients)

From figure 3, out of 235 prescribed antibiotics, 38(16%) antibiotics fall under Access category, 163 (69%) antibiotics fall under watch category and 34(15%) antibiotics fall under reserve category of WHO AWaRe classification.



(Figure 3 Antibiotic utilization according to AWaRe classification)

A- Access, R- Reserve, W- Watch category

Table 2 shows the Pharmacological class-wise utilization pattern of prescribed antibiotics in the ICU. The most prescribed antibiotics fall under the pharmacological class of cephalosporines (37.45%) followed by carbapenems (12.77%), penicillin (9.79%), oxazolidines (7.66%), etc.

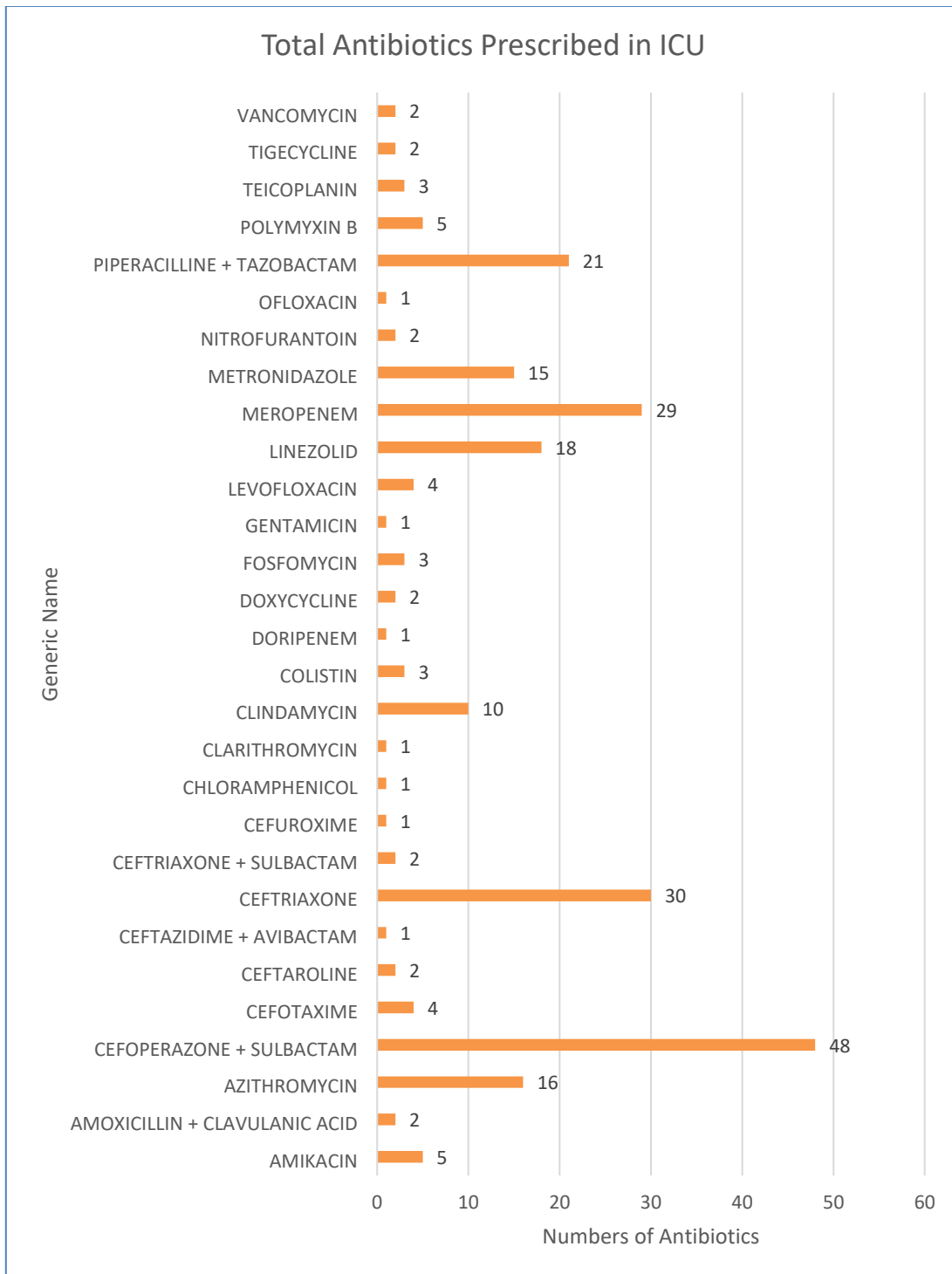
UNDER PEER REVIEW

Table 2 - Pattern of Prescribed Antibiotics According to Pharmacological Class

PHARMACOLOGICAL CLASS	NO. OF ANTIBIOTICS PRESCRIBED
Aminoglycoside	6 (2.55%)
Carbapenems	30 (12.77%)
Cephalosporines	88 (37.45%)
• 2 <sup>nd</sup> Generation	1 (1%)
• 3 <sup>rd</sup> Generation	85 (2%)
• 5 <sup>th</sup> Generation	2 (97%)
Fluoroquinolones	5 (2.13%)
• 1 <sup>st</sup> Generation	1 (20%)
• 2 <sup>nd</sup> Generation	4 (80%)
Glycopeptides	5 (2.13%)
Imidazole	15 (6.38%)
Lincosamides	10 (4.26%)
Macrolides	17 (7.23%)
Oxazolidones	18 (7.66%)
Penicillin	23 (9.79%)
Polymyxins	8 (3.40%)
Miscellaneous	
• Tetracyclines And Chloramphenicol	3 (1.28%)
• Phosphonics	3 (1.28%)
• Glycylcyclines	2 (0.85%)
• Nitrofurans Derivatives	2 (0.85%)
Grand Total	235

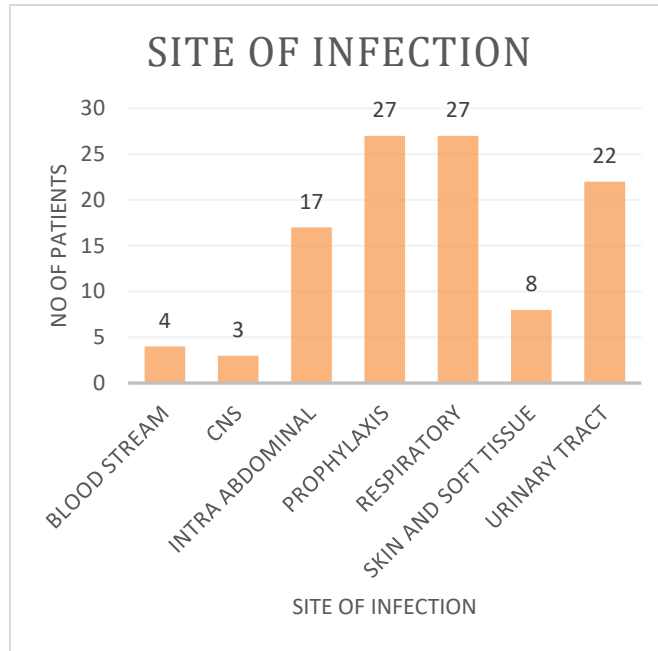
Figure 4 represents the utilization of antibiotics by its generic names, among them most prescribed antibiotic was Cefopreazone + Sulbactam, followed by Ceftriaxone and Meropenem. There is also utilization of last resort antibiotics like Ceftazidime + Avibactam, Colistin, Polymyxin B, Vancomycin and Tigecycline.

UNDER PEER REVIEW



(Figure 4- Total Antibiotics Prescribed in ICU in accordance with Generic Name)

Figure 5 shows the distribution of site of infection among 108 patients, most sites of infection observed were the Respiratory tract (25%), followed by the Urinary tract (20.37%).



(Figure 5- distribution of site of infection)

Out of 108 patients, the culture sensitivity test was performed in 31 patients, and a total of 49 culture samples were obtained from various specimens. Among them, 38.77% of samples were taken before the prescription of antibiotics.

Figure 6 represents the found pathogens in culture sensitivity tests, in which the majorly found pathogen was *E.coli* (16.33%) in which one *E.coli* was ESBL producer. 2<sup>ND</sup> most found pathogen was *Klebsiella pneumoniae* (14.29%) followed by *Pseudomonas aeruginosa* (6.12%) and *Acinetobacter baumannii* (6.12%).

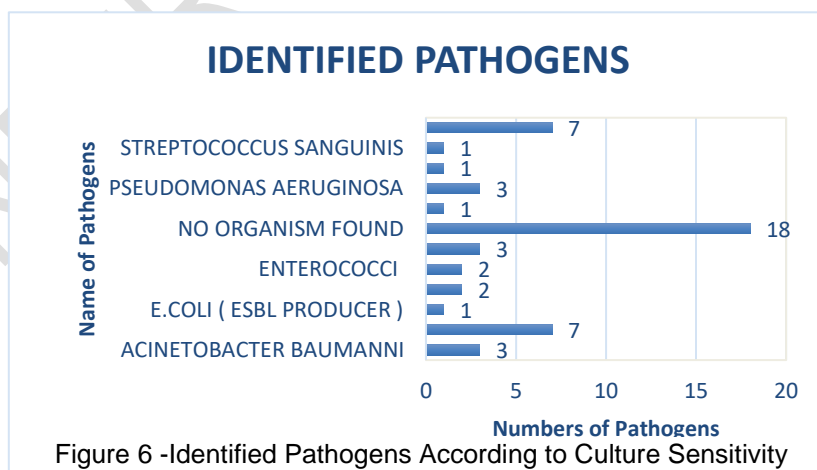


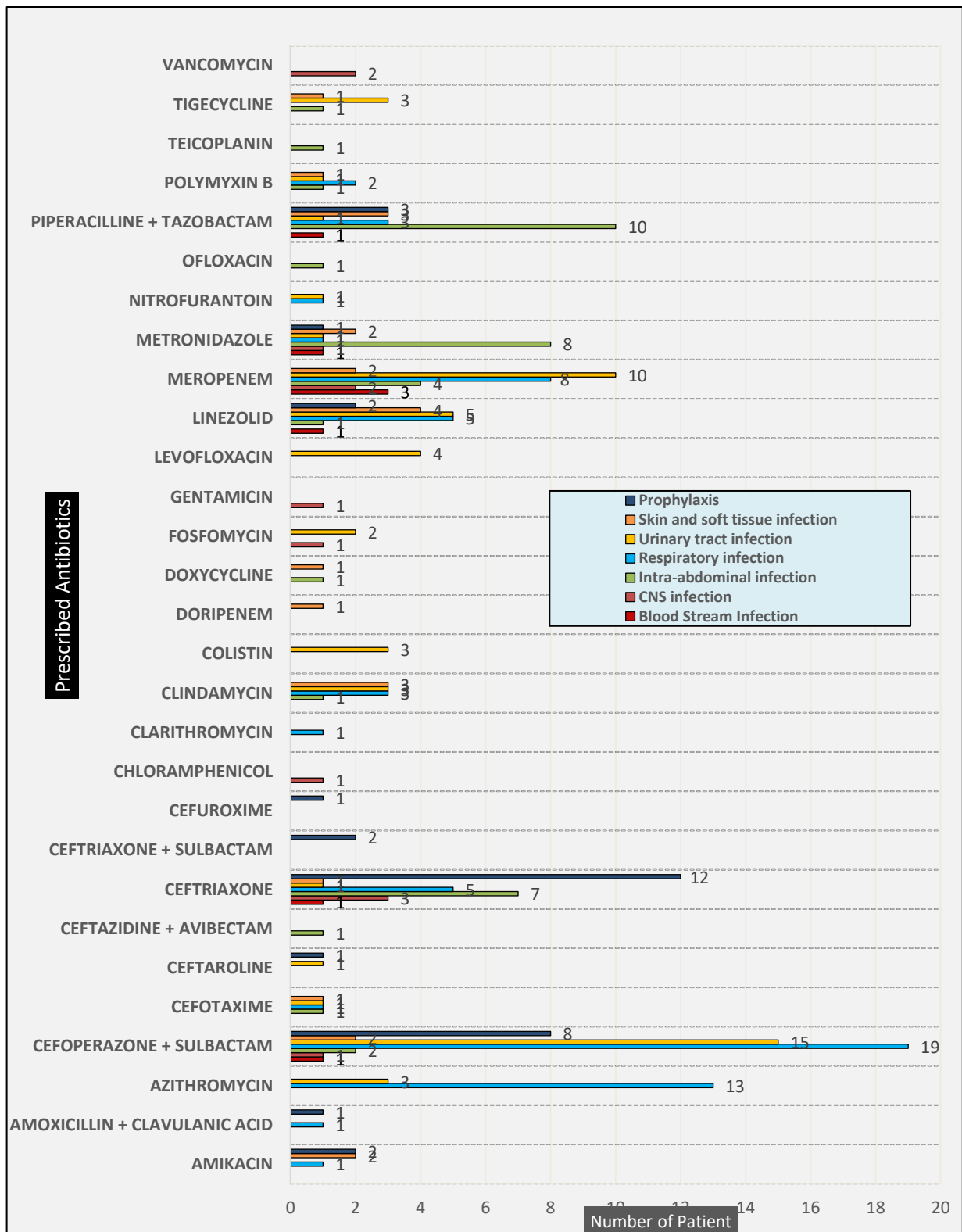
Figure 6 -Identified Pathogens According to Culture Sensitivity Test

From Figure 7, the most prescribed antibiotic in Respiratory tract infection was Cefoperazone + Sulbactam, followed by Azithromycin and Meropenem. In Intra-abdominal most common

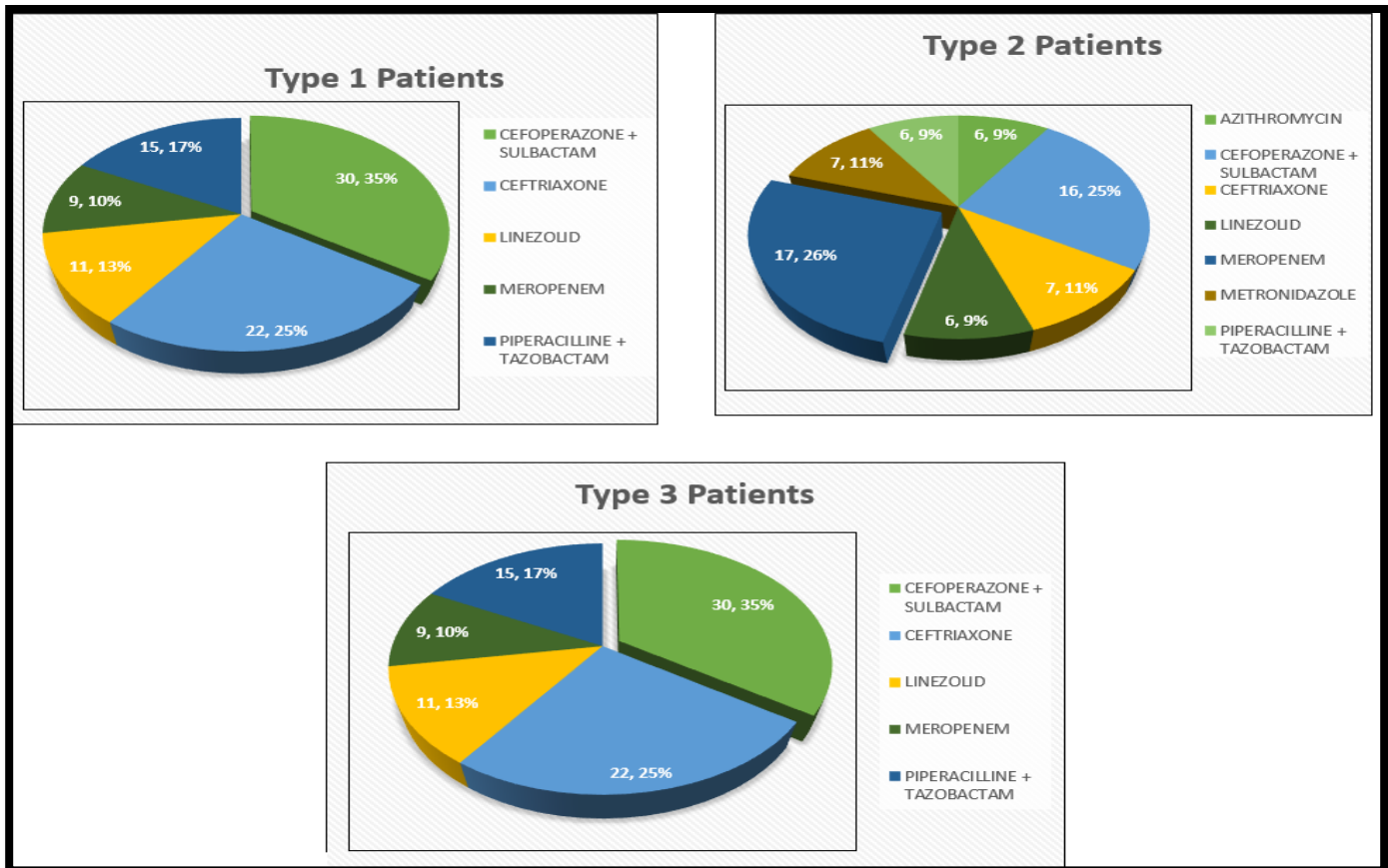
prescribed antibiotic was Piperacillin + Tazobactam followed by Metronidazole and Ceftriaxone. In Urinary tract infections most, the utilized antibiotic was Cefoperazone + Sulbactam, followed by Meropenem and Linezolid. In CNS, the most prescribed antibiotic was Ceftriaxone, followed by vancomycin and Meropenem. In Bloodstream infection, the most prescribed antibiotic was Meropenem followed by other antibiotics such as Linezolid, Piperacillin + Tazobactam, etc. For prophylaxis purposes, Ceftriaxone was utilized followed by Cefoperazone + Sulbactam and Piperacillin + Tazobactam.

Figure 8 represents the correlation between patient risk type and utilization of antibiotics. In Type 1 patients most, prescribed antibiotic was Cefoperazone + sulbactam (35%), followed by ceftriaxone (25%). In type 2 patients most, prescribed antibiotic was Meropenem (26%) followed by Cefoperazone + sulbactam (25%). In type 3 patients most, prescribed antibiotic was Cefoperazone + sulbactam (35%), followed by ceftriaxone (25%) and piperacillin + tazobactam (17%).

UNDER PEER REVIEW



(Figure 7 Antibiotic Prescription Pattern According to Site of Infection)



(Figure 8 Most common Prescribed Antibiotics in Accordance with Patient Risk Stratification)

#### 4. DISCUSSION:

Infectious diseases are the prime cause of morbidity and mortality among people living in developing countries<sup>[10]</sup>. Prescription pattern evaluation studies have become a special tool to evaluate the healthcare system, especially in developing countries like India[11]. This study will help analyze the prescription pattern of antibiotics used in ICU and also to improve the quality and standards of treatment given to patients. **Table 1** represents the total number of prescribed drugs 1312, among which 235 (17.91%) were antibiotics, The present study reveals that the percentage of encounters with antibiotics prescribed is 17.91%, which is less, when compared to a WHO optimal reference value (20 – 26.8%), and it indicates that the use of antibiotics is not that much high [12]. The average number of antibiotics per prescription was 2.15, which is slightly higher compared to WHO standard value (WHO optimal value 1.6-1.8), A similar study performed by William A et.al from northern India, A total of 1246 drugs and 418 antibiotics were prescribed in the 200 patients studied, that is, an average of 6.23 drugs/prescription and 2.09 antibiotics/prescription [13]

In our study, the monotherapy was prescribed in 45(42%) patients, and a combination of antibiotics was prescribed in 63(58%) patients. A similar result was observed in the study conducted by *Avinash Khadela et.al, in August 2020* which showed (42%) in, monotherapy

and (58%) in patients in combination. The widely prescribed antibiotics was 3<sup>rd</sup> generation Cephalosporines [Cefoperazone + Sulbactam (21%) and Ceftriaxone (14%)] followed by Meropenem (12%).

A similar finding was observed in the study conducted by *Avinash Khadela et.al, August 2020* and *Shrikala B et. al.* which has shown the maximum utilization of 3<sup>rd</sup> generation Cephalosporines [Cefoperazone + sulbactam and ceftriaxone] followed by Fluroquinolones. A similar study performed by *Sahid et.al* the most frequently used Antibacterial drugs in MICU and SICU was Ceftriaxone (48.3%) and Metronidazole (97.2%) respectively[14].

The culture sensitivity test which is considered as an important aspect for prescribing antibiotics was performed on 31 (28.79%) out of 108 total patients in our study, which shows improved physician awareness to treat the underlying pathogenic condition compared to a similar study conducted by *Avinash khadela et.al* which shows culture sensitivity test was performed only in 9% of total patients[6]. This suggests that the majority of patients were prescribed based on an empirical approach to treat underlying pathological conditions.

In our study, majorly found the pathogen in the culture sensitivity test was *Escherichia coli* (8, 16.33%) followed by *Klebsiella pneumoniae* (7, 14.29%) followed by *Pseudomonas aeruginosa* (3, 6.12%), and most observed site of infection in ICU were respiratory (24, 22.22%) followed by Intra – abdominal (17, 15.74%).

WHO AWaRe classification of drugs may be a valuable tool for choosing antibiotics that are categorized into three groups – Access, Watch, and Reserve. The AWaRe tool is used not only to monitor antibiotic prescribing but also used to guide the policymaker in categorizing the essential medical list. In our study, we have found that the most prescribed antibiotics agents were from Watch class (69%) followed by Access (16%) and Reserve (15%). In a study performed by *Pragnadyuti et.al* the prevalence of antibiotic use was found 92.78%. Average number of antibiotics per patient was 2.85. Frequency of use of AWaRe antibiotics was 21.43%, 67.23%, and 11.34%, respectively as Access, Watch, and Reserve.

Meropenem (15.12%), piperacillin-tazobactam (15.12%), and ceftriaxone (14.70%) were the three most frequently prescribed watch group antibiotics [15]

The results found are slightly altered compared to WHO guidelines that recommend a first use of the Access group of antibiotics followed by Watch and Reserve so that we can avoid multidrug resistance in patients. There is a need to adopt a proper de-escalation step of the antibiotic stewardship programme to prevent the irrational use of antibiotics.

## 5. CONCLUSION

The study highlights trends in antibiotic prescribing practices and underscores the urgent need for rational antibiotic use. Increased empirical use of stronger antibiotics and inappropriate prescription of last-resort medications reflect an emerging problem of resistance. Implementing antimicrobial stewardship programs, including multidisciplinary committees, can help monitor and optimize antibiotic use, promote safety, and facilitate proper de-escalation of antibiotics based on individual patient needs. Moreover, awareness programs for healthcare professionals and communities are essential in addressing the global challenge of antimicrobial resistance effectively.

## **ETHICAL APPROVAL**

The study was ethically approved by Institutional ethics committee of Maliba Pharmacy College, Bardoli. (Ref. number: MPC/IHEC/08/2021)

### **Disclaimer (Artificial intelligence)**

Option 1:

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc) and text-to-image generators have been used during writing or editing of manuscripts.

Option 2:

Author(s) hereby declare that generative AI technologies such as Large Language Models, etc have been used during writing or editing of manuscripts. This explanation will include the name, version, model, and source of the generative AI technology and as well as all input prompts provided to the generative AI technology

Details of the AI usage are given below:

- 1.
- 2.
- 3.

### **REFERENCES**

1. Murray C, Ikuta K, Swetschinski L, et al. Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis. *The Lancet*. 2022;399(10325):629-655.
2. Taneja N, Sharma M. Antimicrobial resistance in the environment: The Indian scenario. *The Indian journal of medical research*. 2019 Feb;149(2):119.
3. Hameed S, Kumar Yadav S, Kumar M, Mishra H, et al. Prescription pattern, safety and prevalence of resistance of antimicrobial drugs in MICU of IGIMS, Patna: An observational and prospective study. *IP International Journal of Comprehensive and Advanced Pharmacology*. 2019;4(3):110-115.
4. Swamy A, Sood R, Kapil A, Vikram NK, et al. Antibiotic stewardship initiative in a Medicine unit of a tertiary care teaching hospital in India: a pilot study. *The Indian Journal of Medical Research*. 2019 Aug;150(2):175.
5. National Centre for Disease Control, Directorate General of Health Services. *National Treatment Guidelines for Antimicrobial Use in Infectious Diseases*. New Delhi: Ministry of Health & Family Welfare, Government of India;

2016.[accessed on October 11, 2016]. Available from:  
[http://pbhealth.gov.in/AMR\\_guideline7001495889.pdf](http://pbhealth.gov.in/AMR_guideline7001495889.pdf)

6. Khadela A, Vyas B, Rawal N, Patel H, Khadela S, et al. Assessing the Prescription Pattern of Antimicrobial Agents in Intensive Care Unit at Tertiary Care Hospital. *SN Comprehensive Clinical Medicine*. 2020;2(10):1825-1830.
7. Sharland M, Pulcini C, Harbarth S, et al. Classifying antibiotics in the WHO Essential Medicines List for optimal use—be AWaRe. *Lancet Infect Dis*. 2018;18:18-20.
8. Shrestha R, Prajapati S Assessment of prescription pattern and prescription error in outpatient Department at Tertiary Care District Hospital, Central Nepal *J Pharm Policy Pract* 2019 12 16
9. Giuliano C, Patel CR, Kale-Pradhan PB. A Guide to Bacterial Culture Identification And Results Interpretation. *P T*. 2019 Apr;44(4):192-200. PMID: 30930604; PMCID: PMC6428495.
10. Kumar R. N. Selva P. Analysis of Prescription Pattern of Antibiotics Among Patients with Respiratory Tract Infections at A Tertiary Care Hospital. *Biomed Pharmacol J* 2019;12(3).
11. Kumar RN, Selva P. Analysis of prescription pattern of antibiotics among patients with respiratory tract infections at a tertiary care hospital. *Biomedical and Pharmacology Journal*. 2019 Sep 25;12(3):1595-602.
12. Shrestha R, Prajapati S Assessment of prescription pattern and prescription error in outpatient Department at Tertiary Care District Hospital, Central Nepal *J Pharm Policy Pract* 2019 12 1.
13. Williams A, Mathai A, Phillips A. Antibiotic prescription patterns at admission into a tertiary level intensive care unit in Northern India. *J Pharm Bioall Sci*. 2011;3(4):531.
14. Assistant Professor, Department of Pharmacology, Dr V.M. Govt. Medical College, Solapur, Saache S. Antibacterial Prescription Pattern in Medical and Surgical Intensive Care Units of a Tertiary Care Hospital. *jmscr*. 2017 Mar 29;05(03):19472–7.
15. Mandal P, Kayal A, Saha D, Debbarma P, Mazumder A. Assessment of the use of antibiotics based on the WHO access, watch, and reserve index in a multidisciplinary intensive care unit of a medical college in Eastern India. *Natl J Physiol Pharm Pharmacol*. 2024;(0):1.

**17 ALLOUCH, ALIA, HALA SABBAH, SAMARA HASSAN, SANAA SABBAH, NABIL DROUBI, AND IBTISSAM SABBAH. 2015. “ANTIBIOTIC USE, COST, AND CONSUMPTION IN TERTIARY HOSPITALS IN LEBANON: A COMPARATIVE STUDY BEFORE AND AFTER AN IMPLEMENTATION OF ANTIBIOTIC-RESTRICTION PROGRAM (ARP)”. JOURNAL OF ADVANCES IN MEDICINE AND MEDICAL RESEARCH 12 (3):1-15. [HTTPS://DOI.ORG/10.9734/BJMMR/2016/22025](https://doi.org/10.9734/BJMMR/2016/22025).**

**18 PAL , RAHUL, PRACHI PANDEY, DEVANAND JHA, PROTTAY DUTTA, SUBHASHREE SAHOO, RISHABH GUPTA, MOHAMMAD RIZWAN, MADHURI**

SAHDEV KESKAR, VIKASH KUMAR, AND HIMMAT SINGH CHAWRA. 2023. "THE UTILIZATION OF FULL FACTORIAL DESIGN (FFD) FOR OPTIMIZATION OF LINCOMYCIN HYDROCHLORIDE (LNH) LOADED NANOGEL INVOLVING; DESIGN OF EXPERIMENTS (DOE) AN ADVANCED APPROACH". ADVANCES IN RESEARCH 24 (6):272-81. [HTTPS://DOI.ORG/10.9734/AIR/2023/V24I61009](https://doi.org/10.9734/AIR/2023/V24I61009).

19 PATTERSON JE. ANTIBIOTIC UTILIZATION: IS THERE AN EFFECT ON ANTIMICROBIAL RESISTANCE?. CHEST. 2001 FEB 1;119(2):426S-30S.

20 VLAHOVIC-PALCEVSKI V, MOROVIC M, PALCEVSKI G. ANTIBIOTIC UTILIZATION AT THE UNIVERSITY HOSPITAL AFTER INTRODUCING AN ANTIBIOTIC POLICY. EUROPEAN JOURNAL OF CLINICAL PHARMACOLOGY. 2000 APR;56:97-101.

#### APPENDIX

TITLE	PAGE NUMBER
Abstract	1
Introduction	2
Material And Methods	3
Result	4
Discussion	11
Conclusion	12
Refrences	14