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 utilize 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 event 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 antibiotics prescription, which will help in combat with critical resistance issue in 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 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. Alarmingly, 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]. 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 result of 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].

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 riskstratified care management, in which practices manage patients based on their assigned risk level to make better use of limited resources, anticipates 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, basically it divide the patient into three types based on pre-determined criteria described below in table, 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:

2.2.1 Primary objective - To evaluate the utilization of prescribed antibiotics in intensive care unit

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

2.3. Study Design : It is single center prospective observational Study Was Conducted in 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 excluded from the study according to inclusion and exclusion criteria mention below. Figure 1 represents the design of our study.

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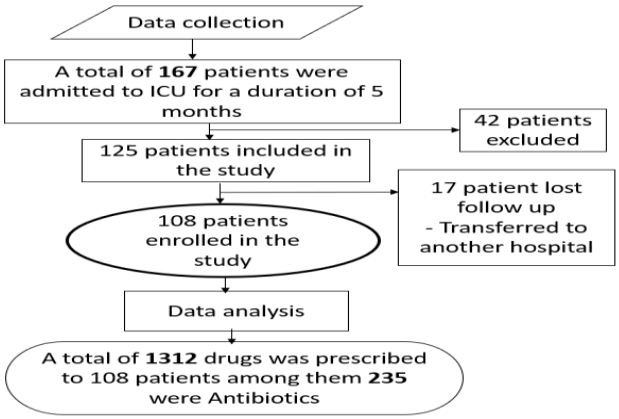
2.4. Study Criteria

2.4.1 Inclusion Criteria : 1. Patient's age ≥ 18 years 2. Patients, who are critically ill patient and post-operative patients admitted to ICU are included 3. patients, who are prescribed with at least one antibiotic either for prophylaxis or therapeutic purpose

2.4.2 Exclusion Criteria : Pediatric population, pregnant and lactating woman 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 event 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.



(**Figure 1** – Study Procedure)

3. RESULTS AND DISCUSSION

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

Table 1 – Demographics Data of Patients (N= Number of patients, % = Percentage of total number of patients

VARIABLES	ANALYSIS
Gender	
Male, N (%)	60 (55.5%)
Female, N (%)	48 (44.4%)
Age distribution (years)	
18-30, N (%)	8 (7.40%)
31-60, N (%)	33 (30.55%)
> 60, N (%)	66 (61.11%)
Reason of admission	
Critical ill, N (%)	80 (74%)
Post-OP, N (%)	28 (25.9%)
Risk stratification	
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%)

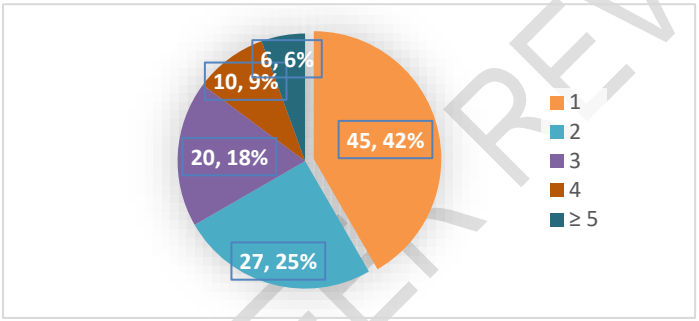
Table 1 represents the patient related demographics. there were total of 108 patients enrolled in this study, among them 55.5 % were male and 44.4% were female.

total 1312 drugs were prescribed among which 235 (17.91%) were antibiotics. number of drugs prescribed per patient were 12.14 ± 4.60 and number of antibiotics prescribed per

Table 2 - Distribution of Site of Infection	
Site of Infection	No of Patients
CNS	3
BLOOD STREAM	4
SKIN AND SOFT TISSUE	8
INTRA ABDOMINAL	17
URINARY TRACT	22
RESPIRATORY	27
PROPHYLAXIS	27
TOTAL	108

patients were 2.15 ± 0.70. the average icu stay of patients was 5.45 ± 5.25 days. out of 108 patients, 25 (23.14%) patients died, among which 14 (56%) deaths were due to infection and 11(44%) of deaths were due to disease severity.

Table 2 shows the distribution of site of infection in the ICU, out of 108 patients, 25% patients were suspected to have respiratory infection followed by urinary tract infection in 20.37% patients.



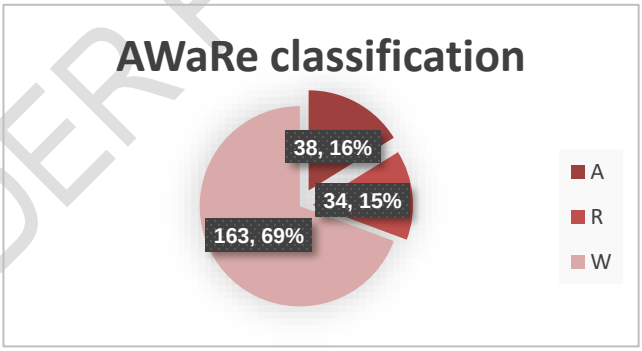


Figure 2 represent the utilization of single and multiple antibiotics, out of all, 42% patients were prescribed with single antibiotic and 58% patients were prescribed with multiple antibiotics

(Figure 2: Number of Antibiotics Prescribed per Patient)

(Figure 3- AWaRe Classification)
(A= Access, W= Watch, R= Reserve)

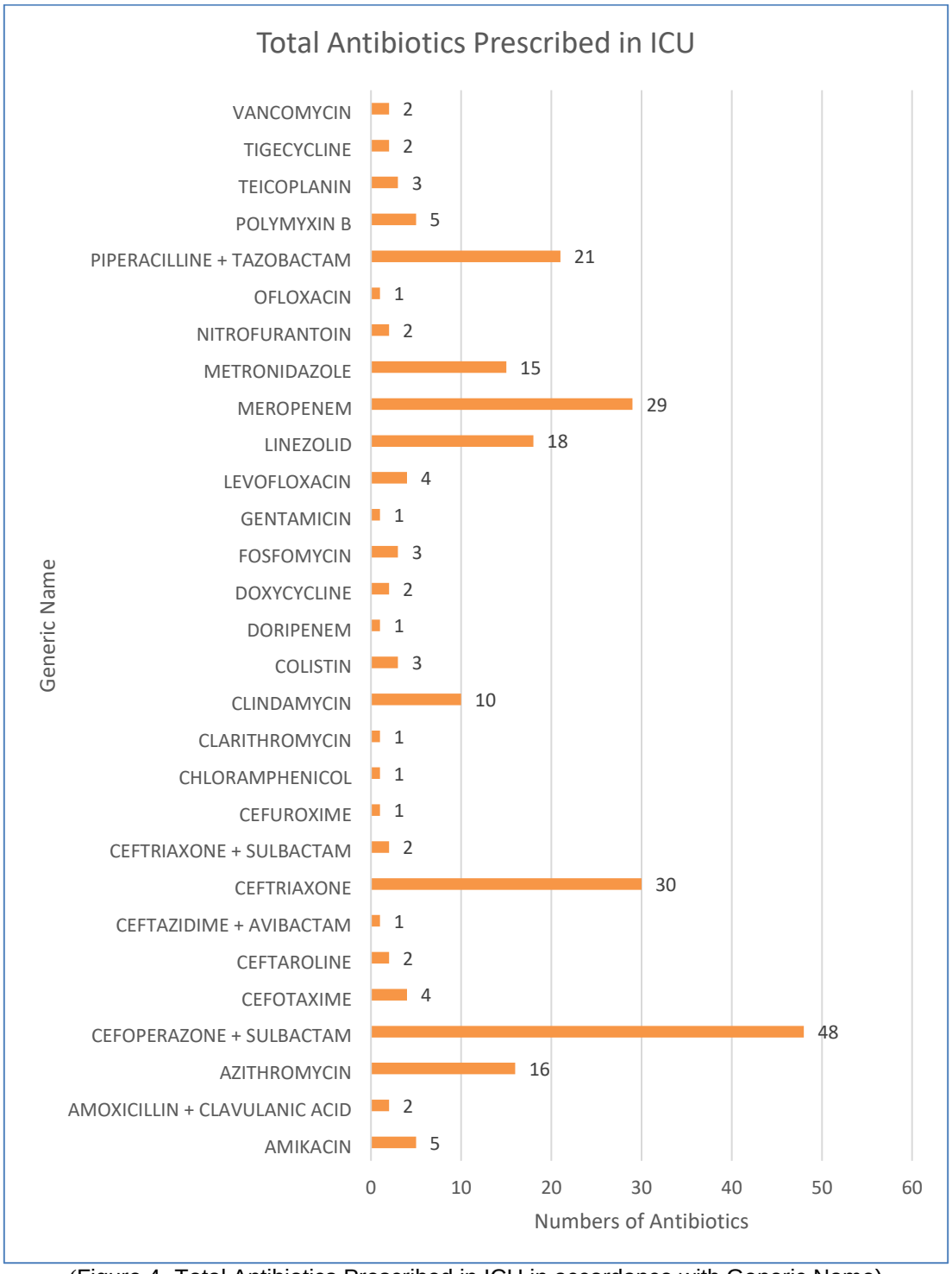
From figure 3, out of 235 prescribed antibiotics, 38(16%) antibiotics fall under Access category, 163 (69%) antibiotics fall under watch category and 34(15%) antibiotics fall under reserve category of WHO AWaRe classification.

Table 3 show the Pharmacological class wise utilization pattern of prescribed antibiotics in the ICU. The most prescribed antibiotic was fall under the pharmacological class of cephalosporines (37.45%) followed by carbapenems (12.77%), penicillin (9.79%), oxazolidones (7.66%) etc.

Table 3 - Pattern of Prescribed Antibiotics According to Pharmacological Class

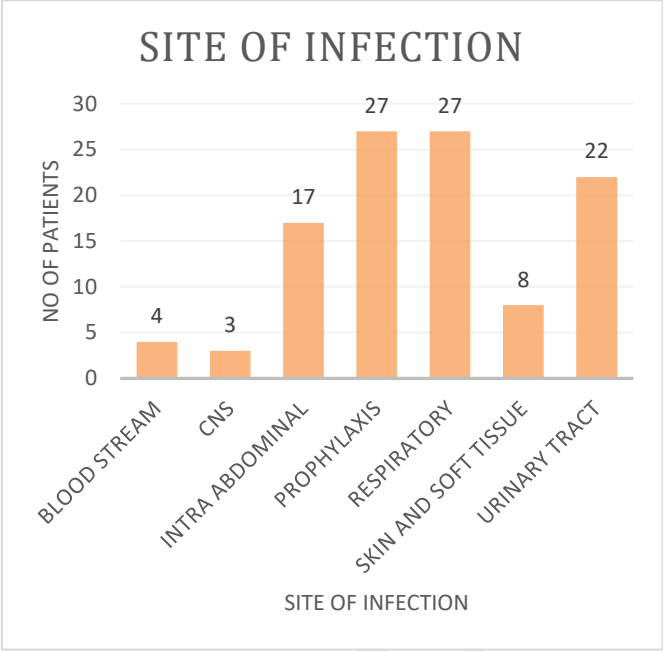
PHARMACOLOGICAL CLASS	NO. OF ANTIBIOTICS PRESCRIBED
AMINOGLYCOSIDE	6 (2.55%)
CARBAPENEMS	30 (12.77%)
CEPHALOSPORINES	88 (37.45%)
• 2nd generation	1 (1%)
• 3rd generation	85 (2%)
• 5th generation	2 (97%)
FLUOROQUINOLONES	5 (2.13%)
• 1st generation	1 (20%)
• 2nd generation	4 (80%)
GLYCOPEPTIDES	5 (2.13%)
IMIDAZOLES	15 (6.38%)
LINCOSAMIDES	10 (4.26%)
MACROLIDES	17 (7.23%)
OXAZOLIDONES	18 (7.66%)
PENICILLIN	23 (9.79%)
POLYMYXINS	8 (3.40%)
MICELLENEOUS	
• TETRACYCLINES AND CHLORAMPHENICOL	3 (1.28%)
• PHOSPHONICS	3 (1.28%)
• GLYCYLCYCLINES	2 (0.85%)
• NITROFURAN DERIVATIVES	2 (0.85%)
Grand Total	235

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



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

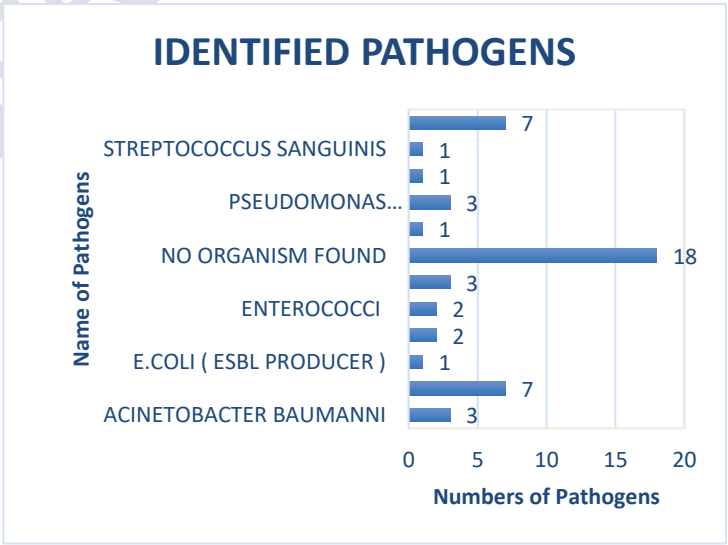
Figure 5 shows the distribution of site of infection among 108 patients, most site of infection observed was Respiratory tract (25%), followed by Urinary tract (20.37%).



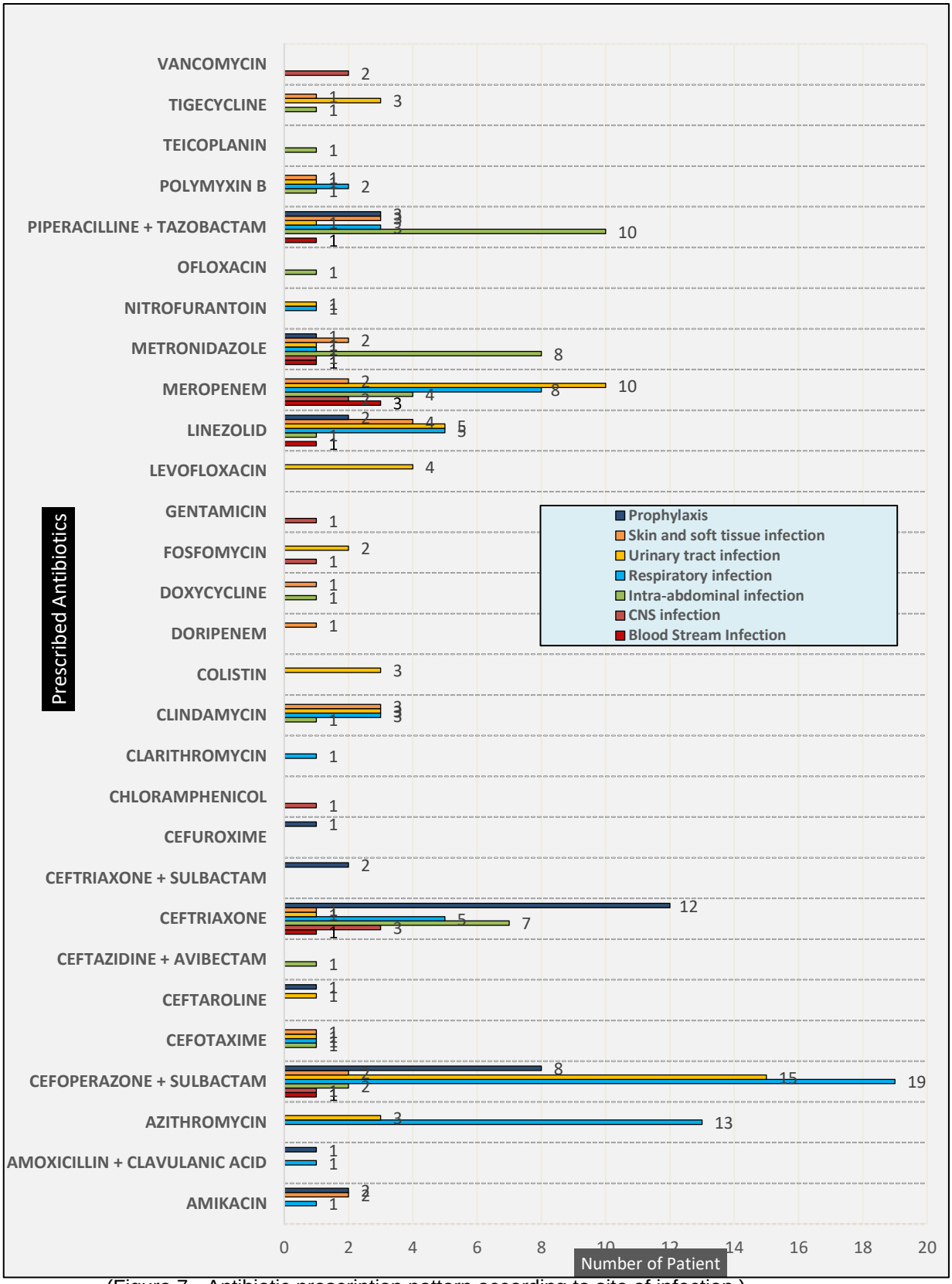
(Figure 5 - distribution of site of infection)

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

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

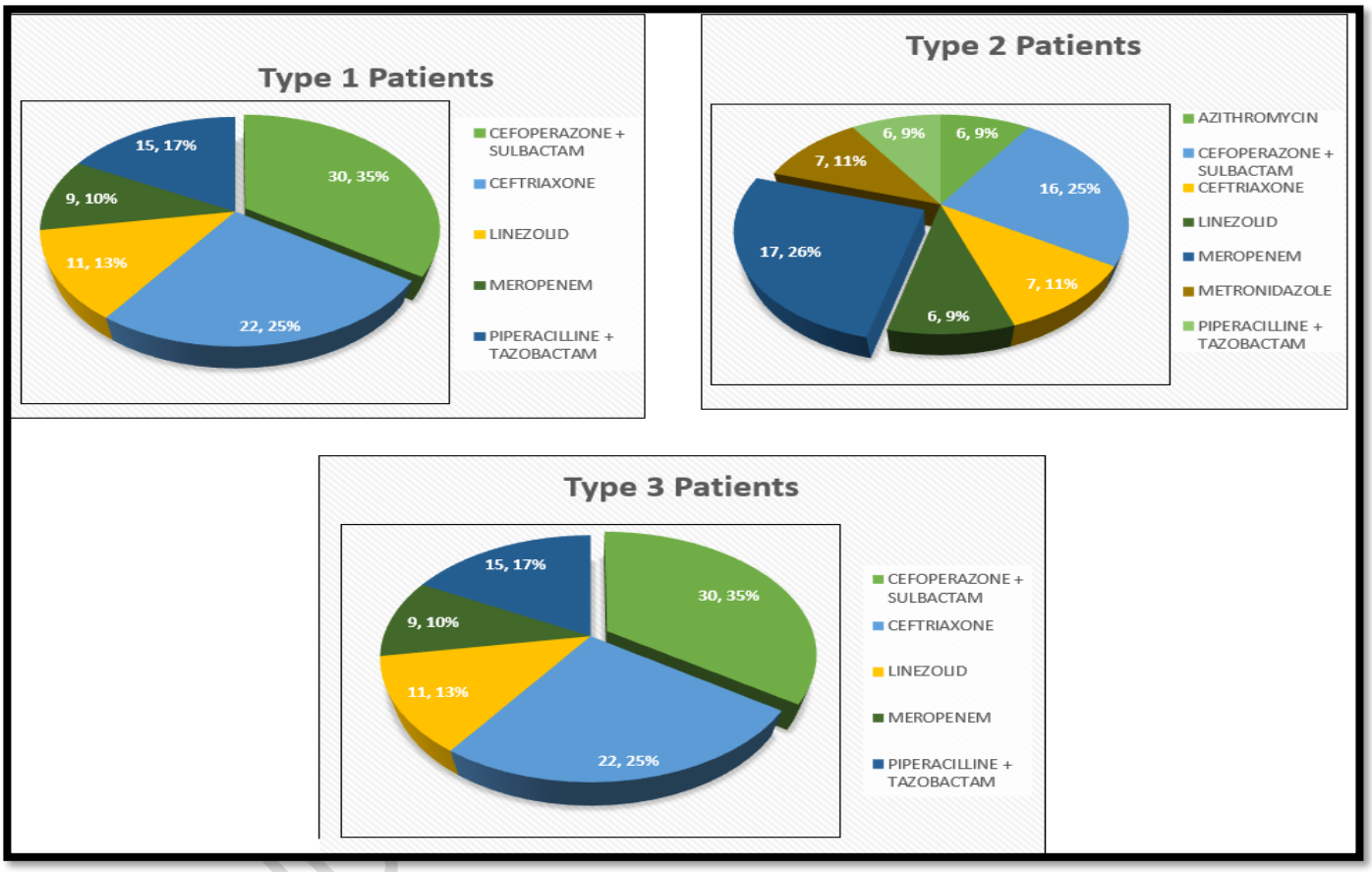


(Figure 6- Identified Pathogens According to Culture Sensitivity Test)



(Figure 7 - Antibiotic prescription pattern according to site of infection)

From figure 7, 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 infection most, utilized antibiotic was Cefoperazone + Sulbactam, followed by Meropenem and Linezolid. In CNS, most prescribed antibiotic was Ceftriaxone, followed by vancomycin and Meropenem. In Blood stream infection, most prescribed antibiotic was Meropenem followed by other antibiotics such as Linezolid, Piperacillin + Tazobactam etc. For prophylaxis purpose Ceftriaxone utilized followed by Cefoperazone + Sulbactam and Piperacillin + Tazobactam.



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

Figure 8 represents the correlation of patient risk type and utilization of antibiotics in them. 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%)

4. DISCUSSION:

Infectious disease are the prime cause of morbidity and mortality among the people living in the developing countries [10]. Prescription pattern evaluation studies have become a special

tool to evaluate the health care system specially in developing countries like India [11]. This study will be helpful in analyzing the prescription pattern of antibiotics used in ICU and also to improve the quality and standards of treatment given to patients. Table 4 represents the total number of prescribed drugs was 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)

In our study, the monotherapy was prescribed in 45(42%) patients and the combination of antibiotics was prescribed in 63(58%) patients. The similar result was observed in the study conducted by *Avinash Khadela et.al, August 2020* which has shown (42%) in, monotherapy and (58%) in patient in combination. The widely prescribed antibiotics was 3rd generation Cephalosporines [Cefoperazone + Sulbactam (21%) and Ceftriaxone (14%)] followed by Meropenem (12%). The

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 3rd generation Cephalosporines [Cefoperazone + sulbactam and ceftriaxone] followed by Fluroquinolones. The culture sensitivity test which is considered as an important aspect for prescribing antibiotics, was performed in 31 (28.79%) out of 108 total patients in our study, which shows improved physician awareness to treat the underlying pathogenic condition compared to similar study conducted by Avinash khadela et.al which shows culture sensitivity test was performed only in 9% of total patients. This suggest that majority of patients were prescribed based on empirical approach to treat underlying pathological condition. In our study, majorly found pathogen in culture sensitivity test was *Escherichia coli* (8, 16.33%) followed by *Klebsiella pneumoniae* (7, 14.29%) followed by *Pseudomonas aeruginosa* (3, 6.12%) and the most observed site of infection in ICU was respiratory (24, 22.22%) followed by Intra – abdominal (17,15.74%).

WHO AWaRe classification of drugs may be a valuable tool to choose antibiotics that are categorized into three group – Access, Watch, Reserve. AWaRe tool is used not only to monitor antibiotic prescribing but also used to guide the policy maker to categorize the essential medical list. In our study we have found that the mostly prescribed antibiotics agents were from Watch class (69%) followed by Access (16%) and Reserve (15%). The results found are slightly altered compared to WHO guideline that recommend a first use of Access group of antibiotics followed by Watch and Reserve, so that we can avoid multidrug resistance in patients. There is need to adopt a proper de-escalation step of antibiotic stewardship programme to prevent irrational use of antibiotic.

5.CONCLUSION

The study highlights concerning 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)

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APPENDIX