



A PROSPECTIVE STUDY ON THE RATIONAL USE OF RESTRICTED ANTIBIOTICS IN THE ICU'S OF A TERTIARY CARE HOSPITAL

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ABSTRACT

Background

Antibiotics are medicines that fight against bacterial infections in people and animals. They kill bacteria or inhibit their growth. Reserve groups of antibiotics are a class of antibiotics. This group includes antibiotics that should be treated as “last resort” options to highly specific patients and settings, where other antibiotics alternative has already failed or state to be inadequate such as multi drug resistant bacteria, which is a life-threatening infection. Twenty-two reserved antibiotics are currently present on the WHO model list of essential medicines. Hence this study will be driven to determine the statistics for rational use of reserved antibiotics.

Objectives

- To analyze the Impact of rational medication.
- To analyze the Clinical outcomes of reserved antibiotics.
- To analyze the type of infections receiving the type and number of reserved antibiotics.

Method

The proposed prospective study was conducted over 110 patients of the ICU department in Aster CMI hospital, Bangalore (duration-6 months).

Results:

The study on 110 patients were analyzed, 85(77%) patients were male &25(23.6%) were female. The majorly prescribed reserved antibiotic was meropenem (carbapenems -74%). From the various class of drugs prescribed in the study population, carbapenems are the most commonly prescribed class of antimicrobials (76%) followed by glycopeptide (11%).From

the data analysed, we have found that monotherapy (70.7%) is predominantly prescribed over combination therapy (30.5%).

Conclusion

This study proved that meropenem improved patient outcome effectively. Lower urinary infections [24%] along with upper respiratory diseases [20.48%] and bacterial diseases [16.71%] are the most prominently found infections.

Key words: Reserved Antibiotics, Drug resistance.

INTRODUCTION

Antibiotics are defined as the substance used to kill or fight against bacterial infections in humans and animals to a great extent. The antibiotics that kill bacteria are called bactericidal and the ones that stop their growth are termed as bacteriostatic. Examples of bacteriostatic are Tetracycline's, Sulfonamides, Trimethoprim, Chloramphenicol, Macrolides and Glycosamides are examples for bactericidal antibiotics are aminoglycosides, Fluoroquinolones, Glycopeptides and Beta lactams.

Antibiotics are used in both prophylaxis and treatment; unfortunately, the inappropriate approach of prescribing had resulted in the growth of drug resistant bacteria.

The main reason for this increase of antibiotic resistance is in appropriate selection of the drugs, doses and duration of the therapy.

Overuse of antibiotics also results in increased risk of adverse effects, highest rate of antibiotic resistance.

The antibiotics are classified into Narrow and broad-spectrum antibiotics. These Broad-spectrum antibiotics are more likely to cause resistance to the drugs. These infections that last longer which increases the cost of treatment, more chances of spreading to family and friends.

Antibiotics are the most frequently and commonly prescribed drugs among all the hospitalized patients. More concerns are reported that the continuous indiscriminating and over use of these drugs.

Since there is a massive use of antibiotics, a significant increase in the prevalence of bacterial resistance has been observed on an international scale; for ensuring the optimum use of antibiotic measures are taken to prescribed the appropriate antibiotics and hence there is a potential impact on reducing the resistance of microorganisms which are widely used.

Reserve groups of antibiotics are one such class of antibiotics along with others; watch and observe group. This group includes the antibiotics which should be treated as the "last resort" options to highly specific patients, where other antibiotics alternative has already failed or state to be inadequate such as multidrug resistant bacteria, which is a life-threatening infection. These medications should be prioritized and protected as a key target of national and international stewardship programs, where they involve in utilization, monitoring, and reporting the antibiotics to their safety use and effectiveness.

Twenty-two reserved antibiotics are present currently, seven of them are listed individually based on WHO model list of medicines. Measuring the consumption of antibiotics in each of the AWARE categories allows us to estimate some inferences about quality of antibiotic used in the country.

Antibiotic resistance is one of the world wide public health concerns; studies have been reported a good relationship between the antibiotic utilization and the level of resistance. Currently, in India schedule H1 was introduced to control the use of antibiotics. In developing countries various problems with prescription of the drugs have been identified in the health sectors which includes unnecessary poly pharmacy, and excessive use of the drugs with poor efficacy, this irrational use of antibiotics can leads to increase in mortality, morbidity, adverse drug e reactions and resistance of the drug and health care utilization.

The exposure and spread of resistance is becoming aggravated where antibiotics are used without prescription. Antibiotics are the most sold drugs segment in India with sales of over Rs. 1000 crore. In India additional lives can be lost till 2050 due to drug resistance stated by E times, 2019.

Experts predict that without intervention the problem of MDR could be catastrophic by 2050, killing nearly 10Million/year.

Antibiotics are effective when used correctly, also appropriate use can also save patient lives with life threatening antimicrobial infections, and however there is a serious depletion in use of antibiotics which can help in decreasing the spread of antimicrobial-resistant and disease.

To handle this problem, world widely initiatives are demanding to promote this rational use of antibiotics to handle this issue, which requires a proper guidance to physicians, nurses and education to patients.

Infections with drug resistance bacteria have been increased not only mortality and morbidity but also duration of hospitalization and treatment cost. When infections become more resistant to first line antibiotics, more expensive second line therapies must be used, resulting in prolonged duration of illness, stay of hospitalization and economic burden.

In USA, more than 35,000 people die from antibiotic resistance every year and antibiotic resistance is the negative impact on economy. it was estimated, if by 2030 it is left uninvestigated the world will be incurring annual cost of about 1 trillion USS.

In one of study, the participants selected for this study 75% were given meropenem as reserved antibiotic first choice and showed least resistance to it.

For the definitive treatment of infection of presumed or confirmed infection, vancomycin 20% and meropenem 12% were most prescribed agents in neonatal intensive care unit or NICU.

In the developing countries the antibiotics are prescribed about 44% to 97% of hospitalized patients which is unnecessary or unsuitable and it is evaluated that antimicrobial resistance is responsible for more than 2 million infectious disease, increase in the number of infections, has commanded the use of different classes of antibiotics, success of antibiotic treatment is depends on the susceptibility, dose, choice of treatment, duration of treatment.

The problem of over usage of antibiotics is a worldwide phenomenon. In India, the prevalence of use of the antibiotics varies from 29% to 70%.

The antibiotics use has been significantly increased over time, from 42% to 56.2% in 2016. CDC estimated that about 47 million of antibiotic courses are prescribed each year for infections that does not require antibiotics therapy.

Similarly, reserved antibiotics that should be given only in serious ill infections they are now prescribed for every other infection whether ICU or in the general wards.

Meropenem is the most highly prescribed reserved antibiotic in the list of restricted antibiotics, which belongs to class of carbapenems.

The rational use of these restricted antibiotics will help us observe the number of prescriptions containing restricted antibiotics with what infections it is aimed at treating. The pattern prescription will be reflecting the physician understanding of disease and patient's medical history. In developing countries, the antibiotics are highly consumed and the most important and irrational use of antibiotics is common practice.

Hence, with growing number of infections with antibacterial resistant, rational use of drug is highly necessary. Considering this, we investigated prescriptions containing reserved group of antibiotics and their rational use in ICUs of a tertiary care hospital.

Therefore, the present studies are conducted to evaluate the rational use of reserved antibiotics agents, it is an essential component of pharmacy service and clinical practices; it is one of the measures to promote the rational use of restricted antibiotics and analyze the rational use of restricted antibiotics.

Hence, this study will be driven to determine the statistics for rational use of reserved antibiotics. Educate to increase awareness of rational use and resistance to antibiotics.

NEED FOR THE STUDY

- With the increase in diversity of infectious diseases the resistance to antibiotics have also increased rapidly due to which reserved antibiotics are used therefore, here we will analyze the restricted antibiotics usage and promote their usage.
- Assessing the impact of restricted antibiotic helps to analyze the trend of prescribing of antibiotics and need for any improvement and promoting, ensuring rationality.
- Also, to identify the types of reserved antibiotics given and their rational use with the type of infection.
- Hence, the study on the topic “**A prospective study of rational use of reserved antibiotics in the ICU'S of tertiary care hospital**” is undertaken.

METHODOLOGY

Study site

The proposed study will be conducted at the ICU's departments of pediatrics (PICU), Neurology (NICU), MICU, and Cardiac care unit (CCU) department of the Aster CMI hospital, Hebbal, Bangalore.

Study design: A prospective observational study.

Study duration: The duration of the study was six months.

Sample size: The total number of cases to be collected for this study will be as per calculation i.e.; 110 at Aster CMI Hospital, Hebbal, Bangalore.

Patient type: In-patient.

Study Criteria:

Inclusion criteria:

- Reserved Antibiotics given in patients with serious infections or life-threatening situations admitted in ICU.
- Patients ready to participate of all age groups.

Exclusion criteria:

- Out patient
- Unwillingness to participate in the study
- Left against medical advice (LAMA)
- Discharged against medical advice (DAMA)

Documents:

- Patient data collection form.
- Case records.
- Lexicomp database.
- Ethical committee clearance.
- Patient Informed consent form.
- List of restricted antibiotics

Study procedure

- A Prospective study will be conducted in the Intensive care unit, the case that satisfies the criteria are enrolled for the study. The information such as demographics, medication, clinical data, and antibiotic used in serious situations or last resort medication data is collected and documented in-patient enrolled in the study for analyzing the rational use of reserved antibiotics.
- Reserved antibiotics are not to be given to every patient; hence, patients with antimicrobial resistance are assessed and given these drugs with respect to their dose, dosage form, and frequency along with the type of antibiotic given either monotherapy or combination.
- Number of prescriptions with reserved antibiotics is noted and if inappropriate usage is noted.
- Obtained data is subjected to suitable statistical analysis.

RESULTS

It is a prospective study conducted during time period of six months in a tertiary care hospital. During this study a total number of 110 patient data were collected and analyzed, and patients who were prescribed with restricted/ reserved antibiotics in the ICUs of all departments were taken into this study.

GENDER GROUPING

Of the 110 cases data collected, 85(77%) patients were male and 25(23.6%) patients were female.

Table 1: Total No of Patients as per Gender Distribution

GENDER	FREQUENCY	PERCENTAGE
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Male	85	77 %
Female	25	23.6%

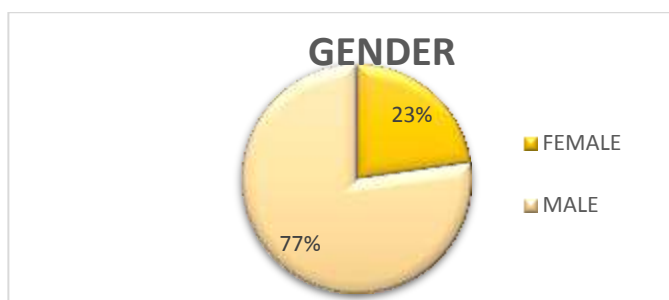


Figure 1: Frequency Distribution of Gender in study Population

AGE DISTRIBUTION:

From the study population, we have observed maximum number of antibiotics were prescribed in age group of 60 And Above 60 (54%) followed by age group of 41-59 (24%).

Table 2: Total No of Patients as per Age Distribution

AGE	FREQUENCY	PERCENTAGE
<12	10	9%
13-29Y	07	6%
30-40Y	08	7%
41-59Y	26	24%
60 or >60	59	54%

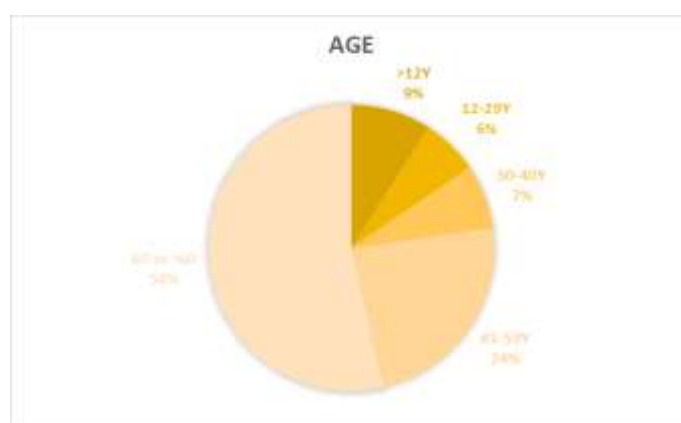


Figure 2: Frequency Distribution of Age in Study Population

TYPE OF PRESCRIBED DRUG THERAPY:

From the data analysed, we have found that monotherapy(70.7%) is predominantly prescribed over combination therapy(30.5%).

Table 3: Total No of Patients prescribed with drug therapy

TYPE	FREQUENCY	PERCENTAGE
Monotherapy	77	70.7%
Combination therapy	33	30.5%

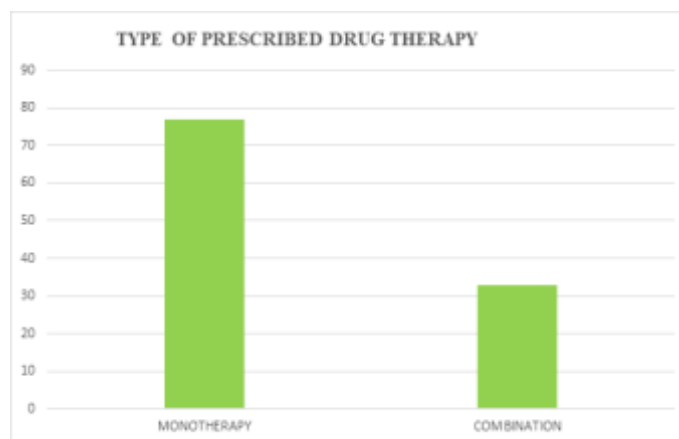


Figure 3: Frequency Distribution of Prescribed Drug Therapy

DISTRIBUTION OF CLASS OF RESERVED ANTIBIOTICS:

From the various class of drugs prescribed in the study population, carbapenems are the most commonly prescribed class of antimicrobials (76%) followed by glycopeptide (11%).

Table 4: Total No of Reserved antibiotics classes prescribed

CLASS OF ANTIBIOTIC	FREQUENCY	PERCENTAGE
Carbapenem	99	76%
Polypeptide	13	10%
Monobactam	4	3%
Glycopeptide	15	11%

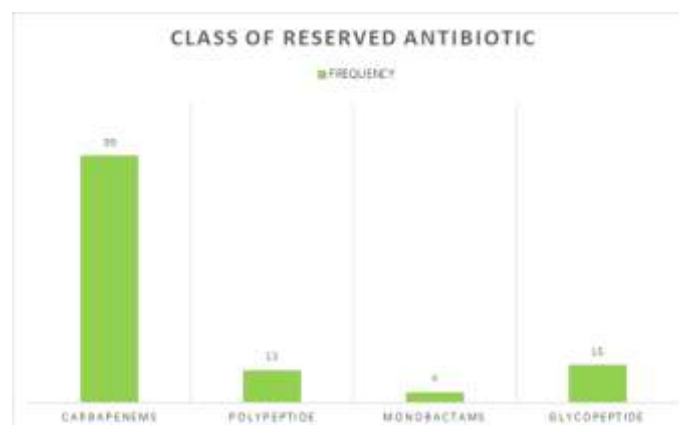


Figure 4: Frequency of Distribution of Prescribed Drug Class

NUMBER OF RESERVED ANTIBIOTICS PRESCRIBED:

The total number of reserved antibiotics prescribed was

Table 5: Total Patients with Number of Reserved antibiotics

NUMBER OF ANTIBIOTICS PRESCRIBED	FREQUENCY	PERCENTAGE
5 OR <5	107	97%
MORE THAN 5	03	3%

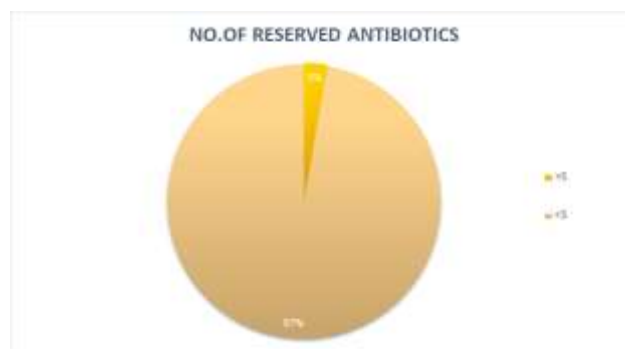


Figure 5: Number of Reserved Antibiotics Given

TYPE OF THERAPY:

The most commonly type of prescribed therapy is target therapy (87.6%) followed by empirical (13%).

Table 6: Total Number of Patients with prescribed therapy

TYPE OF THERAPY	FREQUENCY	PERCENTAGE
EMPIRICAL THERAPY	96	87.6%
TARGET THERAPY	14	13%

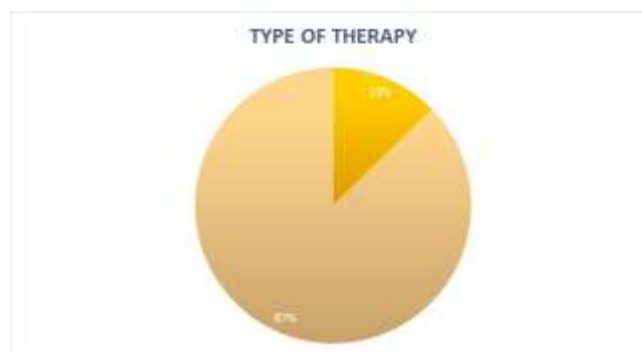


Figure 6: Type of Therapy

DISTRIBUTION OF DRUGS:

Among the 146 reserved antibiotics agents from 110 prescriptions per person, meropenem (43.5%) was the drug of choice for majority of infections

Table 7: Total Number of Patients with different Reserved antibiotics

DISTRIBUTION OF DRUGS	FREQUENCY	PERCENTAGE
Meropenem	101	74%
Colistin	7	5%
Polymyxin B	5	4%
Vancomycin	13	10%
Etrapanem	2	1%
Teicoplanin	8	6%
Azetreonam	6	5%
Imipenem	2	1%
Zavicefta	2	1%

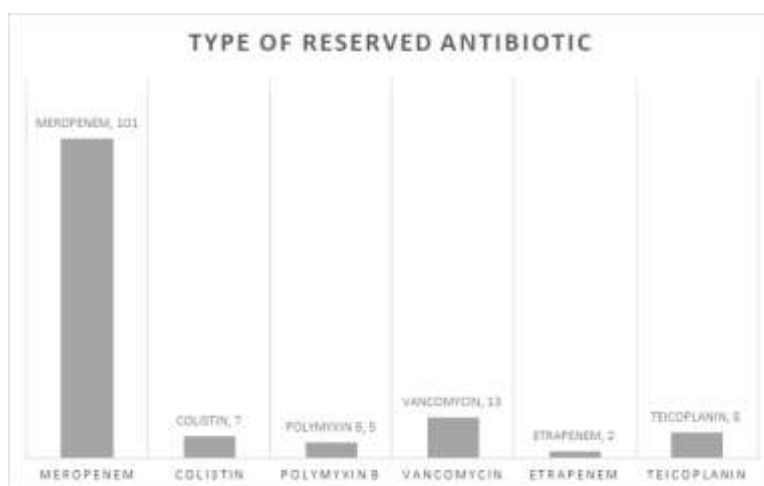


Figure 7: Distribution of Drug

TREATMENT ACCORDING TO DEPARTMENTS:

It is found that, most of the drugs prescribed in each department showed highest prescribed in MICU and least in PICU.

Table 8: Total Number of cases in different ICU's

DEPARTMENT	FREQUENCY	PERCENTAGE
MICU	70	66%
PICU	09	08%
NICU	18	17%
CCU	10	09%

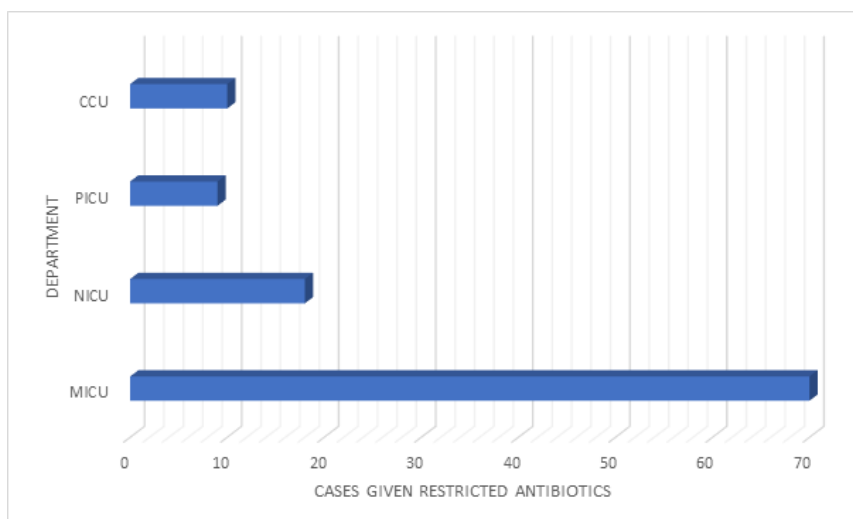


Figure 8: Cases in each Department

COLLECTION OF PRIOR HISTORY OF ANTIBIOTICS:

It is observed that history of antibiotic regarding has been collected in most of the cases (97.99%).

Table 9: Total Number of cases collected with previous antibiotic history

ANTIBIOTIC HISTORY	FREQUENCY	PERCENTAGE
YES	108	97.99%
NO	02	2.97%



Figure 9: Collection of Prior History of Antibiotic

RESULTS &DISCUSSION

Antibiotics are prescribed to patients when they are diagnosed with infections that can be cured merely with antibiotics, in certain cases patients have attained resistance to many of the antibiotics that is nothing but the bacteria have resistant to that particular class of drug. In such cases, patient’s condition can deteriorate gradually and require immediate alternative therapy to control the condition that is when reserved antibiotics are introduced in the therapeutic regimen.

All patients admitted in the ICU should be assessed for their multi drug resistant MDR organism, in cases where condition is consequential or life threatening in that case, empirical therapy is used for immediate action and gradually after lab reports targeted therapy can be

followed up. This helps to improve patient survival rate and reduce the possibility of mortality if no therapy induced. The types of reserved antibiotics used in hospitals are from different classes such as, carbapenems, which has inhibitory action on the cell wall synthesis, upon binding to penicillin-binding proteins (PBPs), monobactams, Glycopeptides etc.

The high prevalence of hospital acquired infections in critically ill ICU patients are associated along with more antibiotics been prescribed.

In this study project, about 110 patients were selected from various different departments of ICU – intensive care unit including pediatric, neuro, cardiac care unit or medical intensive care unit which were mainly observed. The agents that were given to patients were observed and recorded, and concluded that meropenem from the class carbapenem was the major choice of treatment.

The study showed that a total of number of males in the study were 85(77%) and females were 25(23%) out of 110 patients. The patients of different age group were selected under the age groups of <12 years which accounted for 10 out of 110(9%), 13-29 years were 07 (6%), 30-40 years were 08 out of 110(7%), 41-59 years were 26 patients (24%) and aged of 60 or >60 years (54%). The patients aged between 60 or >60 was prescribed with maximum number of reserved antibiotics accounting for 54% of total number of patients. The type of therapy prescribed were categorized into types, monotherapy and combination, the study showed Monotherapy 70% mostly commonly prescribed than the combination 30%.

From the study we found out that from different class of reserved antibiotics, carbapenems (76%) were highly used followed by Glycopeptides (11%) and polypeptide (10%), monobactam (3%) in run.

Out of the following drugs, administered meropenem (74%) was seen to be highly used in every department of ICU as the same results of study conducted by Shantanu and Shakti B Mishra. Meropenem was also prescribed in combination with many other drugs such as teicoplanin or vancomycin.

In the prospective observational study conducted in a tertiary care clinics or hospitals for 110 patients showed that prescriptions prescribed by the health care professional (95%) were more than non-prescribed prescriptions. The mean duration of the prescriptions was 9.76 days which was similar in results with that of study conducted by Mr. Rath.

The number of reserved antibiotics/prescriptions was observed and data was analyzed for <2 (95%) per prescriptions was less than that of >2(5%) antibiotics per prescription. When it comes to correct dose, majority contained correct dose (98%). The other considerations in this study such as side effects of drug after initiation of therapy showed no side effects (98.4%) and prior antibiotic history taken were all accounted for and data resulted in 98% of total were appropriate. The frequency of administration of antibiotic agents was advised to take in morning and night (70%) to a large extent, the rest were evening (3%) and afternoon (29%).

The study also includes a questionnaire, which helps in extracting information regarding patient counseling, assessment of allergy status, development of side effects. Reserved antibiotics given in ICU should have an immediate effect in order to act faster and reduce the probability of mortality or any other co-morbidities.

The route of administration and dosage form used in ICU is prescribed as intravascular (IV) (100%) in the total number of patients.

Upon further analysis, it was seen that the reserved antibiotics were appropriate as they were given for resistant form of infection or in life threatening infections where other antibiotics were not effective. While conducting the study there was one combination therapy was seen which is formulated as a combination of two drugs ceftazidime and avibactam, however it was rarely prescribed (1%).

It is detected that empirical therapy (87%) was the most chosen type of therapy over target therapy (13%) in prescribing reserved antibiotics to fight against infectious diseases similar to that of study conducted by Shiv Kumar. The different kind of infections observed in data collected were lower urinary infections [24%] along with upper respiratory diseases [20.48%] and bacterial diseases [16.71%] are the most prominently found infections, majority of were prescribed for UTI (25%) followed by RTI (13%), Abdominal infection(14%), bacterial infection (8.71%), viral infection(1.01%) along with liver, cardiac and neuro infections.

Out of 110 patients, 70 cases were from MICU which were majorly prescribed with reserved antibiotic (66%) followed by NICU (17%) then CCU (9%) & PICU (8%). In conclusion made it clear that reserved antibiotics were given to more patients admitted in medical intensive care unit.

Authors Contributions

All the authors contributed equally in design of the work, acquisition and interpretation of data, and manuscript preparation, all authors have read and approved the manuscript.

Conflict of Interest

There is no conflict of interest from all the authors.

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Data Availability Statement:

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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