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# Utilization of Antibiotics and Identification of Antibiotic Resistance in Different Microbes

Bollineni Likitha[1], Teepalapudi Balaji[1], Durga Kaivalya P V N[1], Pavan Kalyan Reddy K[1], Palakurthi Yanadaiah*[2], Kudipudi Harinadha Baba[3]

[1]Narayana Pharmacy College, Chinthareddy Palem, SPSR Nellore – 524002, Andhra Pradesh, India
[2]Department of Pharmacy Practice, Narayana Pharmacy College, Chinthareddy Palem, SPSR Nellore – 524002, Andhra Pradesh, India
[3]Department of Pharmaceutical Analysis, Narayana Pharmacy College, Chinthareddy Palem, SPSR Nellore – 524002, Andhra Pradesh, India

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ABSTRACT

The inappropriate use of antibiotics contributes to the development of resistant bacteria and has a significant influence on the treatment failure. The increasing rapid development and spread of ABR (Antibiotic Resistance) has become a big issue through worldwide during the past few decades. The main objective is to identify most prescribing antibiotics in clinical practice. To evaluate the prescribing pattern of antibiotics for different microbial infection. It is a prospective observational study of antibiotic prescribing patterns conducted over 6 months in outpatient and inpatient departments of Narayana General Hospital, Nellore. Collected data was analysed based on demographics like age, gender, monotherapy, dual therapy, triple therapy and quadrupole therapy. In 614 antibiotic prescribed patients, utilization of antibiotic is more in 45+years. The mono, dual, triple & quadruple therapy of antibiotics was observed as 79.8%, 17.2%, 2.6% & 0.3% respectively. The most commonly prescribed antibiotics are Cefuroxime and Metronidazole (5%), Ceftriaxone and Doxycycline (6%), Ciprofloxacin (7%), Cefixime (11%), Ceftriaxone (13%), Cefpodoxime (14%), Amoxicillin (24%). Utilization of antibiotics is more in general medicine, followed by surgery departments. Most of the infections are due to Escherichia coli (54%) and Klebsiella species (34%) and were mostly isolated from urine and blood specimens. Antibiotics which are highly prescribing in clinics were Amoxicillin, Ciprofloxacin, Ceftriaxone and Cefuroxime. Most of the isolated bacterial species in the community had developed resistance to above antibiotics. Re-evaluation and advancement in antibiotic therapy is strongly recommended to overcome antibiotic resistance.

*Corresponding Author

Name: Palakurthi Yanadaiah
Phone: +91 9963109893
Email: yanathulasi@gmail.com

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## INTRODUCTION

Antibiotic is defined as A chemical substance derived from a microorganism or produced by chemical synthesis that kills or inhibits growth of other bacteria *in vitro* and *in vivo* selectively at low concentration. Antibiotics are the drugs used for the treatment of infections caused by bacteria, and they have rescued many lives [1]. Antibiotics are the commonly prescribed and administered drugs in hospitals throughout the world. However, the inappropriate use of antibiotics contributes to the develop-

ment of bacterial resistance, which accelerates the development and spread of resistant microorganisms. Antibiotic resistance (ABR) develops when a bacteria covert in such a way that it decreases or eliminates the effect of the antibiotic and become potentially dangerous one. The inappropriate prescribing and dispensing of antibiotics are increasing the incidence of ABR [2]. ABR has been identified in almost all parts of the world; it is one of the toughest challenges to global public health and the problem is still alarming. The aim of the study is to observe antibiotic prescribing patterns and to understand the antibiotic resistance in different microbial species. The major objectives are to identify most prescribing antibiotics in clinical practice. To evaluate the prescribing pattern of antibiotics for different microbial infection. To study the antibiotic resistance & susceptibility of different microbes in community. To identify best susceptible antibiotic for most common infectious diseases [3].

**Selection of Antibiotics**

The selection of antibiotics depends on

1. Host related factors like age of the patient, Pregnancy and neonatal period, Immunocompetency status of the patient, Severity of the infection, History of previous allergic reactions or intolerance to antibiotic, Hepatic and renal insufficiencies.

2. Pathogen related factors, i.e. The probable causative organism and the expected clinical course of the infection, Identification of the causative micro-organism and its sensitivity to antibiotics, Possibility of drug resistance.

3. Drug related factors like nature of the drug, Risk of drug toxicity, Pharmacokinetic properties of the drug, Cost of therapy and drug compliance by the patient.

**Prophylactic Use of Antibiotics**

Antibiotics are frequently given prophylactically.

1. Prophylaxis against specific organisms. This in general is easy as the choice of drug is clear cut because the organism was already known (e.g., For Rheumatoid fever a long-acting penicillin G is the drug of choice to prevent infection by group A streptococci which cause recurrences).

2. Prevention of infection in high-risk situations. These include surgeries for head & neck cancer, GI surgeries, caesarean delivery, surgeries for implanting a device (such as a pacemaker or defibrillator) etc. Failure of prophylactic antibiotic therapy is due to resistance of bacteria to antibiotics [4].

**Spectrum of Antibiotics**

Spectrum of antibiotics is determined by testing its activity on a wide range of bacteria *In vitro*. Narrow spectrum antibiotics act against limited/specific group of bacteria. It is used only when causative bacteria is identified (e.g. Penicillin G, Streptomycin, Erythromycin etc.). Broad spectrum antibiotics act against a wide number of bacterial species. It is used when bacterial infection is identified but causative bacteria has not been identified (e.g.: Tetracycline's, Chloramphenicol etc.). The bacteria should be susceptible to the antibiotic to show its effect on bacteria. If the bacteria is resistant to the antibiotic, then the antibiotic cannot show its effect on such bacteria [5].

**Misuse of Antibiotics**

At present, total consumption of antibiotics in relation to the known incidence of infections is very much in excess. Indication of antibiotics are often misused. Once treatment started, the drug must not be changed without valid reasons. Too large or too low dosage should be avoided as it may either produce toxicity or cause bacterial resistance [6]. There are many ways that bacterium can acquire antibiotic resistance i.e., through mutations that occur in the DNA of the cell during replication, through horizontal gene transfer, development of antibiotic efflux pumps and production of antibiotic inactivating enzymes.

**Mechanisms of Bacterial Resistance**

There are different mechanisms through which bacteria develops resistance towards antibiotics.

**Biochemical Mechanisms**

1. Bacteria produce enzymes that destroy the active drug (eg: *Staphylococcus* produce beta-lactamase and becomes resistant to penicillin G). 2. Bacteria change their permeability to the drug (eg: Resistance to polymyxins is associated with change in permeability to the drugs, *Streptococcus* has natural permeability barrier to aminoglycosides, and *Pseudomonas* possess impermeable cell membrane which prevent influx of drug. 3. Micro-organisms develop an altered structural target for the drug. (eg: Erythromycin resistant bacteria have altered receptor on the 50S subunit of the ribosome, Penicillin resistance in the Streptococcus pneumonia and Enterococci was due to altered Penicillin Binding Proteins (PBPs)). 4. Micro-organisms develop an altered metabolic pathway that bypasses the

reaction inhibited by the drug (eg: Some sulfonamide resistant bacteria do not require extracellular PABA (Para Amino Benzoic Acid) as they can utilize preformed folic acid. 5. Microorganisms develop an

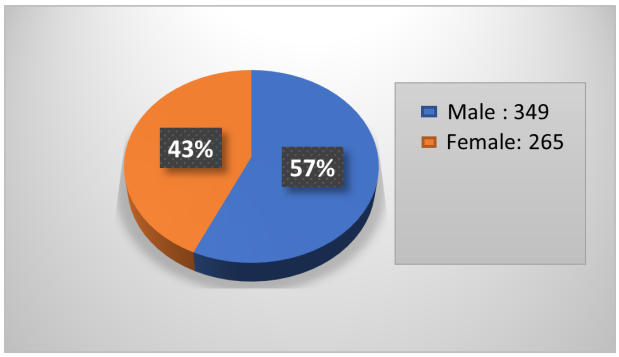


**Figure 1: Antibiotic Utilization According to Gender**

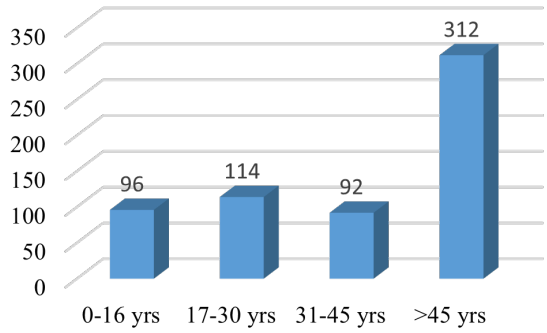


**Figure 2: Usage of Antibiotics in Different Age Groups**

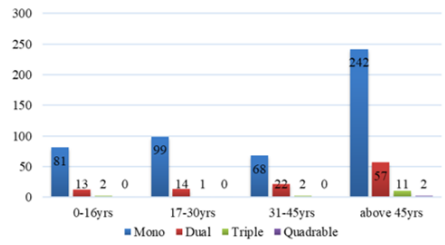


**Figure 3: Prescribing Patterns of Antibiotics in Different Age Groups**

altered enzyme that can still perform its metabolic function but is much less affected by the drug (eg: In trimethoprim-resistant bacteria the dihydrofolic acid reductase is inhibited far less efficiently than in trimethoprim-susceptible bacteria.

### Gene Transfer

1. Transfer of r-genes from one bacterium to another. Conjugation (It is a process where two live bacteria come together and uses conjugation tube to transfer plasmids), Transduction (It is a process where the plasmid DNA enclosed in a bacteriophage is transferred to another bacterium), Transformation (It is uptake of free DNA fragments from surrounding environments and the expression of that genetic information in the recipient cell). 2. Transfer of r-genes between plasmids within the bacterium. By transposons: These are the sequences of DNA that can move around different positions within the genome of single cell. The donor plasmid containing the transposons co-integrate with acceptor plasmid. They can replicate during co-integration. Both plasmids then separate and each contains the r-gene carrying the transposon [7].

### Reasons for Antibiotics Misuse

Some of the reasons for misuse of antibiotics are self-withdrawal of drug immediately after get rid from symptoms. Misuse of antibiotics even for small viral infections like common cold. Availability of antibiotics in stores without prescription [7]. Discontinuation of antibiotic therapy etc.

## MATERIALS & METHODS

### Methodology

### Place of Study

Different departments in Narayana Medical College and Hospital, Chinthareddypalem, Nellore.

### Period of Study

6 months (December 2020 to May 2021).

### Study Population

614-antibiotic prescriptions, 100-culture reports.

### Study Design

Prospective observational study.

### Patient Enrolment

Patients are enrolled in the study based on inclusion and exclusion criteria.

### Inclusion Criteria

Patients who are prescribed with antibiotics.

### Exclusion criteria

Leprosy & Tuberculosis patients are not included in this study.

### Sources of Data

Ward rounds, Medication chart review and Patient interviews etc.

### Observation of Study

After the collection of data by ward rounds, medication chart review and interviews, the 614 patient's data was analyzed and following findings were

**Table 1: Type of Antibiotics Prescribed to the Patients**

| Antibiotic | Frequency | Percentage |
|---|---|---|
| Amoxicillin | 134 | 22% |
| Cefpodoxime | 94 | 14% |
| Ceftriaxone | 85 | 13% |
| Cefixime | 71 | 11% |
| Ciprofloxacin | 49 | 7% |
| Doxycycline | 43 | 6% |
| Cefotaxime | 41 | 6% |
| Metronidazole | 33 | 5% |
| Cefuroxime | 32 | 5% |
| Azithromycin | 21 | 3% |
| Ofloxacin | 21 | 3% |
| Piperacillin | 18 | 3% |
| Cefoperazone | 11 | 2% |
| Total | 653 | 100% |

**Table 2: Frequency of Antibiotics Prescribed in Patients with Different Age Group**

| Age Group | Frequency | Percentage |
|---|---|---|
| 0-16yrs | 96 | 16% |
| 17-30yrs | 114 | 18% |
| 31-45yrs | 92 | 15% |
| Above 45yrs | 312 | 51% |

**Table 3: Type of Bacterial Species Isolated from the Specimen**

| Bacterial Species | Frequency | Percentage |
|---|---|---|
| E. coli | 54 | 48% |
| Klebsiella | 34 | 31% |
| Acinetobacter | 4 | 4% |
| Pseudomonas | 6 | 5% |
| Staphylococcus | 6 | 5% |
| Enterococcus | 6 | 5% |
| Pneumococci | 2 | 2% |

**Table 4: Type of Specimen Collected for Culture and Sensitivity Test**

| Specimen | Frequency | Percentage |
|---|---|---|
| Urine | 88 | 78% |
| Blood | 12 | 10% |
| Sputum | 2 | 2% |
| Throat swab | 4 | 4% |
| Stool | 4 | 4% |
| Endotracheal Secretions | 2 | 2% |

**Table 5: Percentage Susceptibility, Intermediate Resistance, Resistance to Different Antibiotics of Bacterial Species Isolated from the Specimen - I**

| Micro Organisms | *E. Coli* | | | *Klebsiella* | | | *Actinobacter* | | |
|---|---|---|---|---|---|---|---|---|---|
| Drugs | S | I | R | S | I | R | S | I | R |
| Amoxicillin | 14 | 0 | 86 | 50 | 0 | 50 | - | - | 0 |
| Ampicillin | 0 | 0 | 100 | 0 | 0 | 100 | 0 | 0 | 100 |
| Cefuroxime | 7 | 7 | 86 | 33 | 0 | 67 | 0 | 0 | 100 |
| Ceftriaxone | 12 | 0 | 88 | 36 | 0 | 64 | 50 | 0 | 50 |
| Ciprofloxacin | 9 | 4 | 87 | 38 | 8 | 54 | 0 | 0 | 100 |
| Meropenem | 56 | 0 | 44 | 77 | 0 | 23 | 100 | 0 | 0 |
| Imipenem | 60 | 0 | 40 | 67 | 8 | 25 | 50 | 50 | 0 |
| Amikacin | 56 | 8 | 36 | 69 | 0 | 31 | 100 | 0 | 0 |
| Cefepime | 16 | 0 | 84 | 62 | 0 | 38 | 50 | 50 | 0 |
| Gentamycin | 42 | 4 | 54 | 73 | 7 | 20 | 100 | 0 | 0 |
| Nalidixic acid | 0 | 10 | 90 | 50 | 0 | 5 | 0 | 0 | 0 |
| Cotrimoxazole | 25 | 0 | 75 | 40 | 0 | 0 | 50 | 50 | 0 |
| Nitrofurantoin | 56 | 37 | 7 | 25 | 50 | 25 | 0 | 0 | 0 |
| Amoxicillin + Clavulanic acid | 6 | 19 | 75 | 37 | 12 | 51 | 0 | 0 | 100 |
| Piperacillin + Tazobactam | 43 | 4 | 53 | 67 | 0 | 33 | 100 | 0 | 0 |
| Cefoperazone + Sulbactum | 33 | 0 | 67 | 50 | 0 | 50 | 100 | 0 | 0 |

Note: S – Sensitive (%), I – Intermediate Resistance (%), R – Resistance (%)

observed. Utilization of antibiotics in different age group. Common infection caused by microbes in community. Most commonly and highly prescribed antibiotics in community. To identify resistant strain of microbe for more number of antibiotics [8].

### Method of Study

The study begins with the selection of patients based on the inclusion and exclusion criteria followed by collection of their prescriptions (614) and culture reports (100-urine, blood, sputum, throat swab, stool, endotracheal secretions). All the required data was collected from the Prescriptions and culture reports. Demographics such as age, gender, Monotherapy, Dual therapy, Triple therapy & Quadruple therapy were analysed against antibiotic usage. Also antibiotic usage in different departments in the hospital was observed. From culture reports the most commonly infected bacteria in humans and antibiotics which shows more resistance to the isolated bacteria were observed [9]. From the collected data we compared the most commonly prescribed antibiotic and the antibiotics which shows resistance to the most commonly infected bacteria to find whether in practice the antibiotics are correctly prescribed or not.

## RESULTS

In this study, 614 antibiotic prescriptions were collected. The collected data was distributed based on antibiotic utilisation according to gender, age group, mono therapy, dual therapy, triple therapy, utilisation in different medical departments. Most commonly prescribed antibiotics in different age groups and in different departments in hospital was identified from the collected information. For the purpose of the study 100 culture reports were collected. From these culture reports the common microbes (i.e., *E.coli, Klebsiella* species) causing community acquired infections were identified. It represents utilization of antibiotics in patients with different genders. Antibiotic usage in male patients was high compared to female patients [Figure 1].

The Age wise prescription of antibiotics were analysed. Among all age groups, patients with > 45 years were highly prescribed with antibiotics. Followed by 17 – 30 years, 0 – 16 years and 31 – 45 years [Figure 2].

From the collected prescriptions number of antibiotics prescribed during hospital stay in different age groups were identified. In 0-16yrs age group 1, 2 & 3 antibiotics were prescribed to 81, 13 & 2 patients

**Table 6: Percentage Susceptibility, Intermediate Resistance, Resistance to Different Antibiotics of Bacterial Species Isolated from the Specimen - II**

| Micro Organisms | *Pseudomonas* | | | *Staphylococcus* | | | *Enterococcus* | | |
|---|---|---|---|---|---|---|---|---|---|
| Drugs | S | I | R | S | I | R | S | I | R |
| Amoxicillin | 0 | 0 | 0 | 0 | 0 | 100 | 0 | 0 | 0 |
| Ampicillin | 0 | 0 | 100 | 0 | 0 | 100 | 100 | 0 | 0 |
| Cefuroxime | 0 | 0 | 100 | 0 | 0 | 100 | 0 | 0 | 0 |
| Ceftriaxone | 100 | 0 | 0 | 0 | 0 | 100 | 0 | 0 | 0 |
| Ciprofloxacin | 50 | 0 | 50 | 0 | 0 | 100 | 50 | 0 | 5 |
| Meropenem | 100 | 0 | 0 | 0 | 10 | 0 | 0 | 0 | 0 |
| Imipenem | 100 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Amikacin | 100 | 0 | 0 | 0 | 100 | 0 | 0 | 0 | 0 |
| Cefepime | 50 | 0 | 50 | 0 | 0 | 0 | 0 | 0 | 0 |
| Gentamycin | 100 | 0 | 0 | 0 | 50 | 50 | 100 | 0 | 0 |
| Nalidixic acid | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Cotrimoxazole | 0 | 0 | 100 | 100 | 0 | 0 | 100 | 0 | 0 |
| Nitrofurantoin | 0 | 0 | 100 | 0 | 0 | 0 | 100 | 0 | 0 |
| Amoxicillin + Clavulanic acid | 0 | 0 | 100 | 0 | 0 | 100 | 0 | 0 | 0 |
| Piperacillin + Tazobactam | 100 | 0 | 0 | 0 | 0 | 100 | 0 | 0 | 0 |
| Cefoperazone + Sulbactum | 100 | 0 | 0 | 100 | 0 | 0 | 0 | 0 | 0 |

Note: S – Sensitive (%), I – Intermediate Resistance (%), R – Resistance (%)

respectively. In 17-30yrs age group 1, 2 & 3 antibiotics were prescribed to 99, 14 & 1 patients respectively. In 31 - 45 years age group 1, 2 & 3 antibiotics were prescribed to 68, 22 & 2 patients respectively. In > 45 years age group 1, 2, 3 & >3 antibiotics were prescribed to 242, 57, 11 & 2 patients respectively [Figure 3].

**Antibiotics Prescribed to the Patients**

Among all antibiotics, Amoxicillin was the highly prescribed antibiotic with 22% followed by Cefpodoxime with 14%, Ceftriaxone with 13%, Cefixime with 11% [Table 1].

Antibiotics that are commonly used in different age groups were identified. In 0 – 16 years Cefpodoxime was highly prescribed followed by Amoxicillin, Cefixime. In 17 – 30 years Cefotaxime was highly prescribed followed by Cefpodoxime, Amoxicillin. In 31 – 45 years Amoxicillin was highly prescribed followed by Ceftriaxone, Cefixime. In >45 years Amoxicillin was highly prescribed followed by Ceftriaxone, Cefpodoxime [Figure 4].

We observed that patients with above 45yrs (51%) are most highly prescribed with antibiotics followed by age groups of 17-30yrs (18%), 0-16yrs (16%) & 31-45yrs (15%) [Table 2].

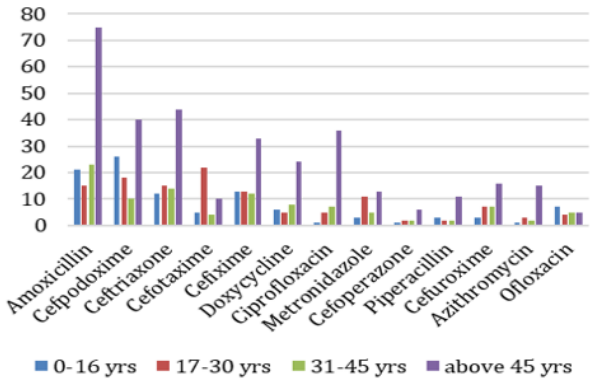


**Figure 4: Different Antibiotics Used in Patients with Different Age Group**

Out of 614 patients, Patients who are admitted in General Medicine (23.37%) are highly prescribed with antibiotics compared to other wards. Followed by General Medicine, General Surgery (14.52%), Pulmonology (14.37%), Paediatrics (13.18%), E.N.T (10.35%), Obstetrics and Gynaecology (9.18%) [Figure 5].

It is outlined that, in General medicine Doxycycline is commonly used followed by it is Amoxicillin, Cefixime, Cefpodoxime, Ceftriaxone and Azithromycin. In Pulmonology ward Ceftriax-

**Table 7: Resistance Patterns of Commonly Isolated Organisms (Nt = not tested)**

| | No. of specimens that are resistant/ No. of specimens tested (% resistant) | | | | | |
|---|---|---|---|---|---|---|
| | *E. coli* | *Klebsiella* | *Acinetobacter* | *Pseudomonas* | *Staphylococcus* | *Enterobacter* |
| Amoxicillin | 6/7 (86%) | 2/4 (50%) | Nt | Nt | 1/1 (100%) | Nt |
| Ampicillin | 18/18 (100%) | 8/8 (100%) | 1/1 (100%) | 1/1 (100%) | 2/2 (100%) | 0/2 (0%) |
| Cefuroxime | 14/16 (86%) | 7/11 (67%) | 1/1 (100%) | 1/1 (100%) | 2/2 (100%) | Nt |
| Ceftriaxone | 15/17 (88%) | 7/13 (64%) | 1/2 (50%) | 0/1 (0%) | 1/1 (100%) | Nt |
| Ciprofloxacin | 20/23 (87%) | 9/15 (54%) | 2/2 (100%) | 2/3 (66%) | 3/3 (100%) | 2/3 (66%) |
| Meropenem | 6/21 (29%) | 3/13 (23%) | 0/2 (0%) | 0/3 (0%) | 0/1 (0%) | Nt |
| Imipenem | 8/22 (36%) | 3/13 (23%) | 0/2 (0%) | 0/2 (0%) | Nt | Nt |
| Amikacin | 9/27 (33%) | 3/12 (25%) | 0/1 (0%) | 0/2 (0%) | 0/1 (0%) | Nt |
| Cefepime | 18/22 (82%) | 5/16 (31%) | 0/2 (0%) | 1/3 (34%) | Nt | Nt |
| Gentamycin | 14/25 (56%) | 3/8 (38%) | 0/2 (0%) | 0/3 (0%) | 2/3 (66%) | 0/2 (0%) |
| Cotrimoxazole | 20/26 (77%) | 3/15 (20%) | 2/2 (100%) | 1/2 (50%) | 1/2 (50%) | 0/1 (0%) |
| Amoxiclav | 12/16 (75%) | 6/10 (60%) | 1/1 (100%) | 2/2 (100%) | 2/2 (100%) | Nt |

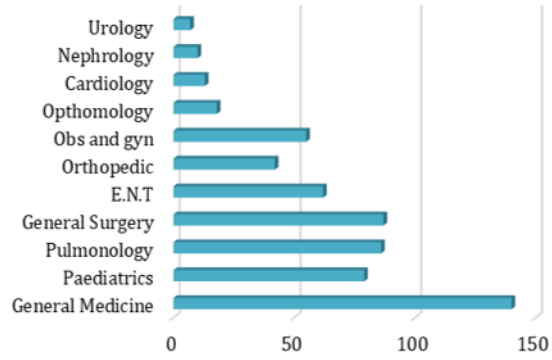


**Figure 5: Frequency of Patients who are Prescribed with Antibiotics Admitted in Different Awards During their Hospital Stay**

one is commonly prescribed followed by Cefpodoxime, Amoxicillin. In General surgery Amoxicillin is commonly prescribed followed by Cefixime, Ciprofloxacin, & Metronidazole. In Paediatrics Cefpodoxime is commonly prescribed followed by Amoxicillin, Ceftriaxone, Cefixime. In E.N.T Cefpodoxime is commonly prescribed followed by Amoxicillin, Ceftriaxone. In Obstetrics and Gynaecology Cefotaxime is commonly prescribed followed by Metronidazole, Ceftriaxone [Figure 6].

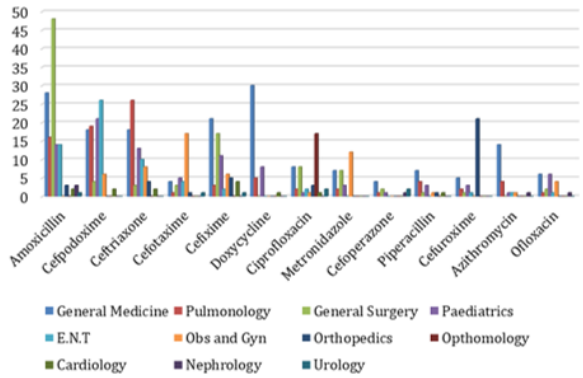


**Figure 6: Prescribing Patterns of Antibiotics in Different Departments**

Hundred and twelve 112 Culture and sensitivity reports were collected. The organisms isolated from them are E. coli (n = 54), Klebsiella pneumonia (n = 34), Acinetobacter species (n = 4), Pseudomonas species (n = 6), Staphylococcus species (n = 6), Ente-

rococcus species (n = 6), Pneumococci species (n = 2) and the specimen collected from patients to perform culture and sensitivity tests are Urine (n = 88), Blood (n = 12), Sputum (n = 2), Throat swab (n = 4), Stool (n = 4), Endotracheal secretion (n = 2) (Table 3 and Table 4).

The most frequent organism isolated was *E. coli* (n = 54). These isolates were resistant to Ampicillin in 100% of cases, to Nalidixic acid in 90% of cases, to Cefuroxime in 88% of cases, to Ceftriaxone in 88% of cases, to Ciprofloxacin in 87% of cases, Amoxicillin in 86% of cases, to Cefepime in 82% of cases. *E. coli* is followed by *Klebsiella* species which shows resistance to Ampicillin in 100% of cases, to Cefuroxime in 67% of cases, to Ceftriaxone in 64% of cases, to Ciprofloxacin in 54% of the cases. Acinetobacter shows resistance to Ampicillin, Cefuroxime, Ciprofloxacin, Amoxicillin + Clavulanic acid in 100% of cases and to Ceftriaxone in 50% of cases [Table 5, Table 6 and Table 7].

## DISCUSSION

Information obtained from the collected prescriptions and culture reports outlines that the most commonly prescribed antibiotics are Amoxicillin (24%), Cefpodoxime (14%), Ceftriaxone (13%), Cefixime (11%), Ciprofloxacin (7%), Doxycycline and Ceftriaxone (6%), Metronidazole and Cefuroxime (5%). The most commonly isolated bacteria from this study are *E. coli* (54%) and *Klebsiella* species (34%). E. coli shows resistance to Ampicillin (100%), Cefuroxime (88%), Ceftriaxone (88%), Ciprofloxacin (87%), Amoxicillin (86%), Cefepime (82%), Cotrimoxazole (77%), Amoxiclav (75%) and Gentamycin (56%). It is susceptible to Imipenem (60%), Meropenem (56%), Amikacin (56%) and Nitrofurantoin (56%). *Klebsiella* species shows resistance to Ampicillin (100%), Cefuroxime (67%), Ceftriaxone (64%), Amoxiclav (60%), Ciprofloxacin (54%), Amoxicillin (50%), Nalidixic acid (50%), Cefoperazone + Sulbactam (50%). It is susceptible to Meropenem (77%), Gentamycin (73%), Amikacin (69%), Imipenem (67%), Piperacillin + Tazobactam (67%), Cefepime (62%).

## CONCLUSION

It is seen that Aminoglycosides and Carbapenems class of $\beta$ – Lactam antibiotics have high susceptibility compared to other antibiotics. Antibiotics highly used in clinical practice are Amoxicillin, Ciprofloxacin, Ceftriaxone, and Cefuroxime. Many microbes developed resistance to the above antibiotics. So, antibiotic selection in treatment should be recommended according to the susceptibility of microbes after culture report.

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### Conflict of Interest

The authors declare that no conflict of interest associated with this work.

### Contribution of Authors

Authors declare that, the work done by the names mentioned in the article and all the liabilities and claims related to the content of the article will be borne by the authors.

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