

## TO STUDY THE PRESCRIPTION PATTERN OF ANTIBIOTICS IN RESPIRATORY TRACT INFECTION IN PATIENTS IN TERTIARY HOSPITAL

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### ABSTRACT

Inappropriate use of antibiotics specifically, the broad-spectrum antibiotics in respiratory tract infections results in resistance to antibiotics. Irrational antibiotic use may result in increased cost of treatment, drug-drug interactions and cause severe adverse reactions. The study of prescribing pattern concludes to monitor, evaluate and suggest modifications in the practitioner's prescription habits, to make patient care reasonable and effective. The aim of our study is to assess the prescription pattern of antibiotics in respiratory tract infections in a tertiary care hospital, Mangalore. From the study the average encounters with an antibiotic prescribed were in accordance with WHO recommendations but the average no. of total drugs per prescription was not according to WHO recommendation. A very few drugs were prescribed in generic names. There was a slight difference in the value of drugs from EDL from the recommended values and the injections were given according to WHO recommendations.

**KEYWORDS:** Antibiotics, Prescription Pattern, RTI.

### INTRODUCTION

A respiratory tract infection (RTI) is defined as any infectious disease of the upper and lower respiratory tract. Infectious diseases remain a significant threat to public health, posing risks to individuals regardless of age, sex, ethnic background, socioeconomic status, or lifestyle.

In India, acute respiratory tract infections (ARTI) are responsible for one million deaths. Out of these 10-15% is due to acute lower respiratory tract infections (ALRTIs). There is inadequate information from India on various lower respiratory tract bacterial pathogens and their resistance patterns in hospital settings.

The RTIs includes Upper respiratory tract infection (URTI), it is a nonspecific term used to describe acute infections such as common cold pharyngitis, sinusitis, and tracheobronchitis.

Lower respiratory tract infections (LRTIs) are frequent and include community acquired pneumonia (CAP), exacerbations of chronic bronchitis (ECB), acute bronchitis (AB), and viral lower respiratory tract infections (VRTI)<sup>[1]</sup>

#### Upper Respiratory Tract Infection

*Streptococcus pneumoniae*, the leading bacterial cause of meningitis, pneumonia, otitis media, and sinusitis.

#### Otitis Media

Otitis media is an inflammation of the middle ear. The diagnosis of acute otitis media includes signs and symptoms of infection of the middle ear, such as otalgia, fever, and irritability, as well as the presence of fluid in the middle ear

#### Sinusitis

Sinusitis is an inflammation and/or infection of the Para nasal sinus mucosa. The term *rhino sinusitis* is used by some specialists because Sinusitis typically also involves the nasal mucosa. Viruses are responsible for most cases of acute sinusitis.

#### Pharyngitis

Pharyngitis is an acute infection of the oropharynx or nasopharynx. Viral causes are most common, group A beta-hemolytic *Streptococcus*, or *S. pyogenes*, is the primary bacterial cause and is the focus of this section. Viruses cause the majority of acute pharyngitis cases.<sup>[2,3]</sup>

#### Lower Respiratory Tract Infection Bronchitis

Bronchitis and bronchiolitis are inflammatory conditions of the large and small elements, respectively, of the tracheobronchial tree. The inflammatory process does not extend to the alveoli. Bronchitis frequently is classified as acute or chronic. Respiratory viruses are by

far the most common infectious agents associated with acute bronchitis. *Mycoplasma pneumoniae* appears to be a frequent cause of acute bronchitis. Additionally, *Chlamydia pneumoniae* and *Bordetellapertussis*.

### **Bronchiolitis**

Bronchiolitis is an acute viral infection of the lower respiratory tract that affects approximately 50% of children during the first year of life and 100% by age 3 year. The incidence of bronchiolitis appears to be more common in males than in females.

Respiratory syncytial virus (RSV) is the most common cause of bronchiolitis, accounting for up to 70% of all cases.

### **Pneumonia**

Pneumonia can be classified as “atypical” or “typical” type based on the patient presentation, clinical observations, causative pathogens, and course of the disease. Patients with atypical pneumonia have slightly different course than typical pneumococcal pneumonia. Otherwise, many clinical features of typical and atypical pneumonia are similar. Typical pneumonia is associated with acute fever, chills, pleuritic chest pain, and productive cough whereas atypical CAP is commonly associated with myalgia, fever without chills, headache, and unproductive cough.<sup>[4]</sup>

### **Antimicrobials**

An antimicrobial agent is a natural, synthetic or semi synthetic substance with the ability of inhibiting or destroying the growth of pathogens. Antimicrobial agents may cause meager or no harm. Antimicrobial agents can destroy pathogens by inhibiting cell wall synthesis, DNA replication or protein synthesis, and altering intermediary metabolic activities. The discovery of many new antibiotic drugs and their wide application has prompted the microbes to evolve and develop antibiotic resistance properties.

Inappropriate use of antimicrobials is wide spread all over the world. Even for trivial infections of viral etiology, an increasing trend is noticed for use of combinations, broad spectrum and newer generation antimicrobials<sup>5</sup>. RTI is one of the major reasons of antimicrobial agent/s (AMA/s) use on a large scale and because changes in AMA resistance pattern are a threat to its effective treatment, there is increasing concern about such unnecessary AMA prescription in the community.

To tackle this problem antibiotic resistance can be done by effective auditing of production of the drugs manufacturers, sales by wholesalers and retailers, and prescription by health care professionals. Standard of treatment of ailments have been found to be improved at all levels of the health care system if a medical audit is done. Lack of rationality and homogeneity in prescribing AMAs and finally, lack of monitoring and control over

use of the same. Therefore, it is dire need of the hour, to promote rational use of AMAs. The use of antibiotics has become a routine practice for the RTIs.<sup>[6]</sup>

Early administration of appropriate antimicrobials has been postulated as a key strategy in the survival of patients with very severe infections. Antibiotics can be lifesaving drugs, but also carry significant potential harms.

The selection and use of appropriate antibiotics will determine the success of treatment and can avoid the occurrence of antibiotics resistance. The threat caused by injudicious use of antibiotics can be optimized by implementing appropriate use of antibiotics. Effectiveness of antibiotics influenced by several factors relating to characteristics and use of antibiotics (i.e., diagnosis, resistance, patient compliance with treatment and treatment failure). So physicians need to take into account of these factors when prescribing on antibiotics and assess whether a specific antibiotic treatment adds sufficient value to justify its cost.<sup>[7]</sup>

### **Treatment Guide**

Most cases of pharyngitis are caused by viruses and do not require treatment with antimicrobials. Benzathine benzyl penicillin 1.2 million IU i.m. in a single dose for adults and children >30 kg (children ≤30 kg: 30000 IU/kg (maximum 1.2 million IU) i.m. in a single dose). Fluoroquinolones, tetracycline's, sulfamethoxazole + trimetho-prim and combinations with aminopenicillins and beta-lactamase inhibitors are not recommended.

Rhinitis of bacterial origin, including diphtheria in infants can occur. The common cold is caused by viruses and does not require treatment with antimicrobials.

Acute otitis media is an infection of the middle ear that occurs mostly in infants and children under 2 years of age. The Bacterial infection is suggested by the presence of acute onset of pain in the ear, fever, and redness and decreased mobility of the tympanic membrane. Patients presenting with these signs require antimicrobials; meningitis can be a complication.

Treatment Amoxicillin 500 mg (children: 15mg/kg; maximum 500 mg) orally every 8 hours for 5 days or amoxicillin 500 mg + clavulanic acid (children: amoxicillin 7.5–15 mg/kg + clavulanic acid; maximum 500 mg) orally every 8 hours for 5 days.

Acute sinusitis usually occurs as a complication of viral infections of the upper respiratory tract, the presence of persistent purulent nasal discharge alone (with or without cough) is not an indication for anti-microbial therapy. However, antimicrobials should be considered if sinus tenderness, facial or periorbital swelling, persistent fevers are also present. Fluoroquinolones and most cephalosporins are not recommended.

Acute bronchitis is usually a viral infection which, unless there is a special disposition, does not require antibiotic therapy. For the initial oral chemotherapy of bacterial infections of the lower respiratory tract (chronic bronchitis, pneumonia) the effective and well tolerated cephalosporins, macrolides and amoxicillin plus beta-lactamase--inhibitor are recommended. In complicated cases with severe underlying disease, longer history or frequent exacerbations, quinolones should be given if Gram-negative infections are suspected or if initial therapy with other substances has failed.

Future development in the antibiotic treatment of respiratory infections will follow the current trend of lower dosages, with the clear objective of shortening treatment periods and achieving earlier discharge from hospital.<sup>[8,9]</sup>

### Rational Drug Use

Rational prescribing has been described as the process whereby prescribing decisions are made; appropriate prescribing is what results or should result. And rational prescribing need not be appropriate. The rationality of drug prescriptions has been studied in various developing countries, however most of the studies have limited their evaluation on numeric analysis of certain indicators such as number of drugs per prescription, percentage of antibiotics prescribed etc. Rational prescribing involves "SANE criteria" i.e. safety, affordability, need & efficacy of the drug. Good prescribing involves instruction on appropriate dose, preparation & medication administration.<sup>[10]</sup>

The prescribed medications should be periodically reviewed so that any errors in prescription are detected early & corrective measures be implemented to meet the standards. Prescription based survey may be considered as one of the most cost effective methods to assess & evaluate the prescribing attitude of clinicians & dispensing practices of pharmacists. The rational use of drugs requires that patients receive medications appropriate to their clinical needs, in doses that meet their own individual requirements, for an adequate period of time & at the lowest cost to them & their community.<sup>[11]</sup> The rational use of drugs depends upon three perspectives namely patient, physician & healthcare provider perspective. The drug use indicators recommended by WHO cover all three perspectives. These indicators may be used to study & analyze the pattern of drug use in any hospital-based setting.

### Prescription Pattern Study

Prescription pattern monitoring studies (PPMS) are drug utilization studies with the main focus on prescribing, dispensing and administering of drugs. They promote appropriate use of monitored drugs and reduction of abuse or misuse of monitored drugs. PPMS also guide and support prescribers, dispensers and the general public on appropriate use of drugs, collaborate and

develop working relationship with other key organizations to achieve a rational use of drugs.

The aim of PPMS is to facilitate the rational use of drugs in a population. Irrational use of medicines is a major problem worldwide. WHO estimates that more than half of all medicines are prescribed, dispensed or sold inappropriately, and that half of all patients fail to take them correctly. The overuse, underuse or misuse of medicines results in wastage of scarce resources and widespread health hazards.<sup>[12]</sup>

Inappropriate use of antibiotics, particularly for RTIs, has contributed to the major public health problem of antibiotic resistance in the community. Improper antibiotic use includes too low dose, too short/long duration, wrong choice of antibiotics, improper combination of antibiotics and therapeutic or prophylactic use in unwarranted/unproven clinical situations. An audit of prescribing patterns is an important indicator of the quality and standard of clinical practice. The study of prescribing patterns is a part of medical audit and seeks to monitor, evaluate and if necessary, suggest modifications in prescribing practices to make medical care rational.<sup>[13,14]</sup>

### MATERIALS AND METHOD

The study site was conducted at the general medicine department, pediatrics department, MICU of Father Muller Medical College Hospital, Kankanady, Mangalore, Karnataka. It is a 1200 bedded multispecialty hospital serving the healthcare of massive population. Non-experimental (observational), prospective study. The study was conducted for a period of 6 months from October 2018 to March 2019.

### Ethical Clearance

Ethical clearance was obtained from the Institutional Ethics Committee of Father Muller Medical College Hospital.

Ethical approval number: FMMCIEC/CCM/684/2018

Dated: 22.11.2018.

### Study Criteria

#### Inclusion Criteria

1. Patients of both sexes.
2. All patients of age 1 year to 90 years old.
3. All prescriptions containing antibiotics in in-patients and outpatients with RTI.

#### Exclusion Criteria

1. Pediatrics from neonatal intensive care unit.
2. Antibiotics used for infections other than RTI.
3. Incomplete data.

### Study Parameters

The following parameters were assessed as per the data obtained.

WHO rational use of drugs indicators - prescribing indicators.

- Average number of drugs per prescription.
- Percentage of drugs prescribed by generic name.
- Percentage of AMAs prescribed per patient per prescription.
- Percentage of drugs given by injections.
- Percentage prescribed from National List of Essential Medicines or formulary.

- Co morbidities along with RTIs
- Name and class of the major antibiotic prescribed
- Culture sensitivity test
- Classification of RTIs
- Problems identified

#### Statistical Analysis

Data was entered in Microsoft Excel and analysis was done. Descriptive statistics such as frequencies and percentages were calculated for categorical variables. Mean and standard deviation was computed for continuous variables. Graphical representation was used for visual interpretation of the analyzed data.

#### METHODOLOGY

A non-experimental (observational), prospective study was carried out in a tertiary care teaching hospital. The

Institutional Ethics Committee's was obtained prior to study (FMMCIEC/CCM/684/2018). Visits were made in the general medicine department, pediatrics department, MICU to collect data. Patients demographic details, medical history, diagnosis, treatment regimen of the patients was daily recorded in the patient data collection form. Name of the drug, dose, frequency, class of drugs were also noted. The data was collected and separately kept in computer using Microsoft Excel.

#### RESULTS

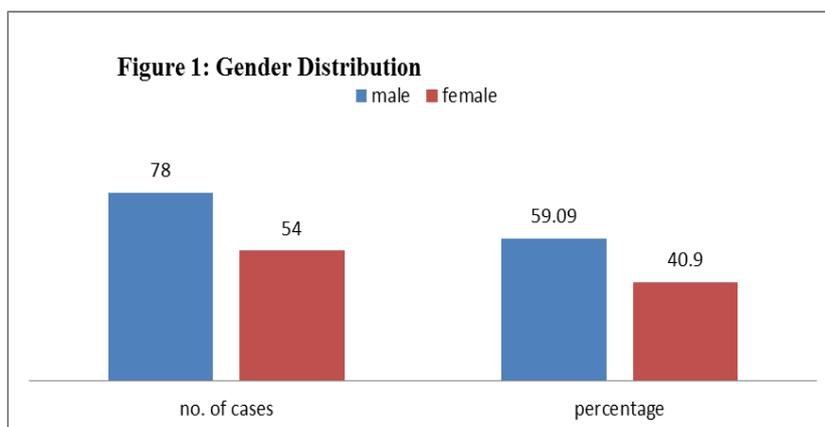
##### Patient Demographics

##### Gender Distribution

In our study out of 132 patients enrolled in the study, 78(59.09%) are males and 54(40.90%) cases were females.

**Table 1: Gender Distribution.**

GENDER	NO. OF CASES	PERCENTAGE
MALE	78	59.09%
FEMALE	54	40.90%



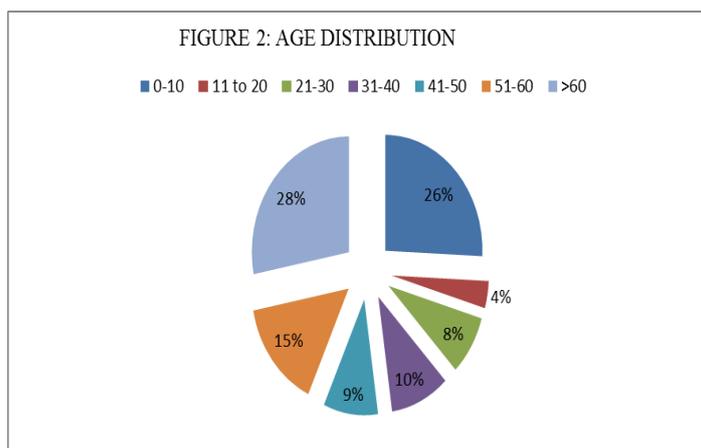
##### Age Distribution

The total population was categorized into seven age groups and patient in each group were recorded. The data from our study represent that patient from age group of

years 0-10 (25.75%)34, years 11-20(3.78%)5, years 21-30(8.33%)11, years 31-40(9.84%)13, years 41-50 (9.09%) 12, years 51-60(15.15%)20, years >60(28.03%) 37.

**Table 2: Age Wise Distribution.**

AGE GROUP	NO. OF CASES	PERCENTAGE
0-10	34	25.75%
11-20	5	3.78%
21-30	11	8.33%
31-40	13	9.84%
41-50	12	9.09%
51-60	20	15.15%
>60	37	28.03%



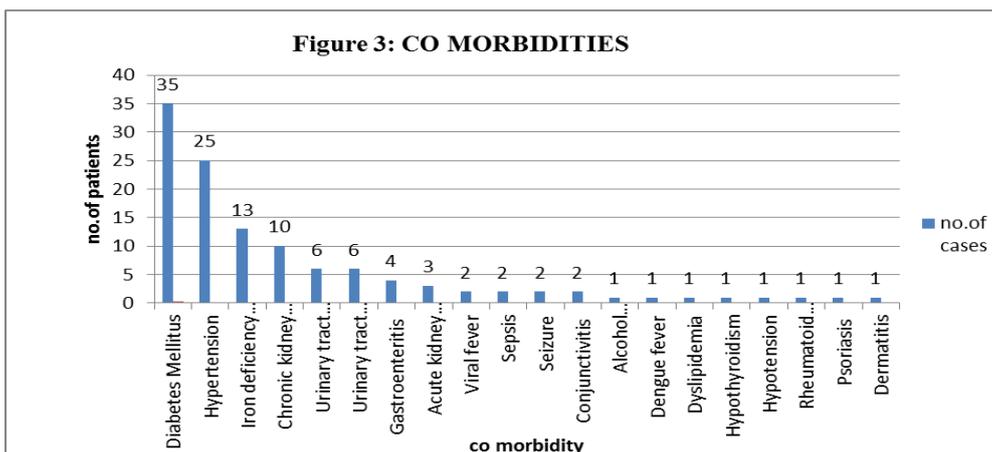
**Co Morbidities**

Majority of patients had Diabetes mellitus 35 (26.52%) as co-morbidity followed by Hypertension 25(18.93) and

Iron deficiency anemia 13(9.84%). Highest number of co-morbidities seen in one patient was found to be three.

**Table 3: Co Morbidities.**

Co morbidity	No. of patients	Percentage %
Diabetes Mellitus	35	26.51%
Hypertension	25	18.93%
Iron deficiency anemia	13	9.84%
Chronic kidney disease	10	7.57%
Chronic liver disease	7	5.30%
Urinary tract infection	6	4.54%
Ischemic heart disease	6	4.54%
Gastroenteritis	4	3.03%
Acute kidney injury	3	2.27%
Viral fever	2	1.51%
Sepsis	2	1.51%
Seizure	2	1.51%
Conjunctivitis	2	1.51%
Alcohol dependence syndrome	1	0.75%
Dengue fever	1	0.75%
Dyslipidemia	1	0.75%
Hypothyroidism	1	0.75%
Hypotension	1	0.75%
Rheumatoid arthritis	1	0.75%
Psoriasis	1	0.75%
Dermatitis	1	0.75%



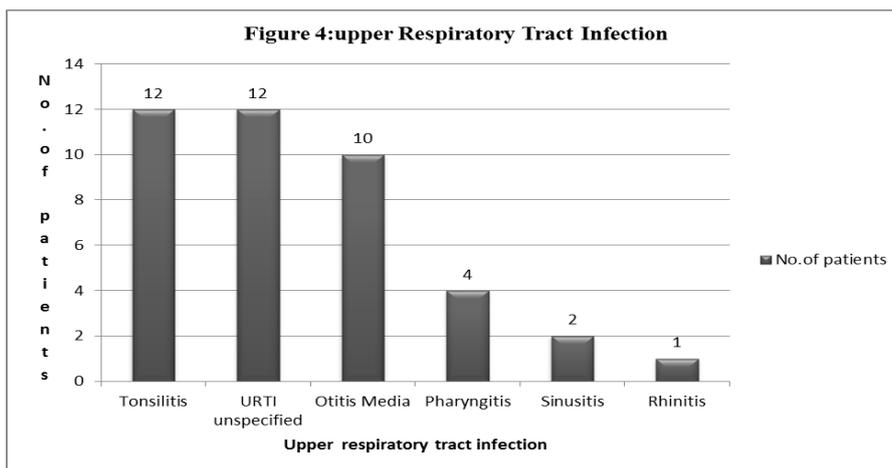
**Classification of RTI**

Among 132 cases, 41(31.06%) cases were diagnosed with URTI in which 12(29.20%) patients had tonsillitis, 12(29.20%) had unspecified URTI, 10(24.3%) had otitis media, 4(9.70%) had pharyngitis, 2(4.8%) had sinusitis

and 1(2.43%) had rhinitis. In study population 91(68.93%) cases were diagnosed with LRTI in which 62(68.10%) were pneumonia, 21(23.07%) were unspecified LRTI, 5(5.40%) were bronchitis, 3(3.20%) were pulmonary tuberculosis.

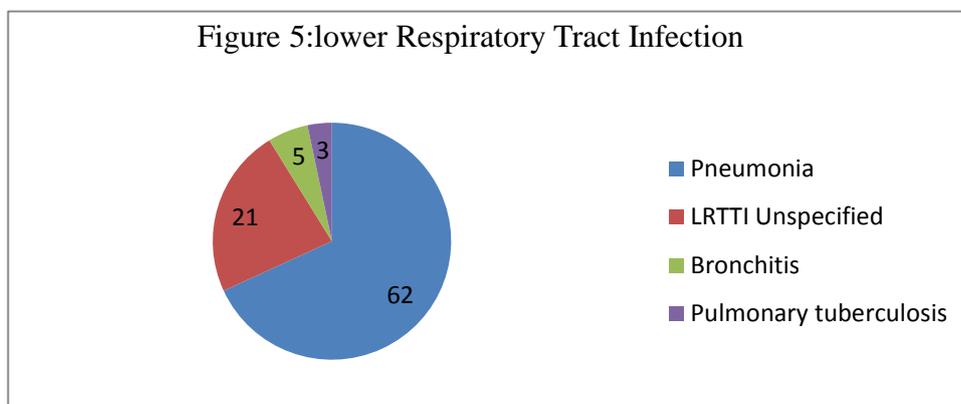
**Table 4: Upper Respiratory Tract Infections.**

Upper Respiratory Tract Infection	No. Of Patients	Percentage
Tonsillitis	12	29%
URTI unspecified	12	29.20%
Otitis Media	10	24.30%
Pharyngitis	4	9.70%
Sinusitis	2	4.80%
Rhinitis	1	2.43%



**Table 5: Lower Respiratory Tract Infection.**

Lower Respiratory Tract Infection	No. Of Patients	Percentage
Pneumonia	62	68.10%
Lrtti Unspecified	21	23.07%
Bronchitis	5	5.40%
Pulmonary Tuberculosis	3	3.20%



**Major Antibiotics Prescribed**

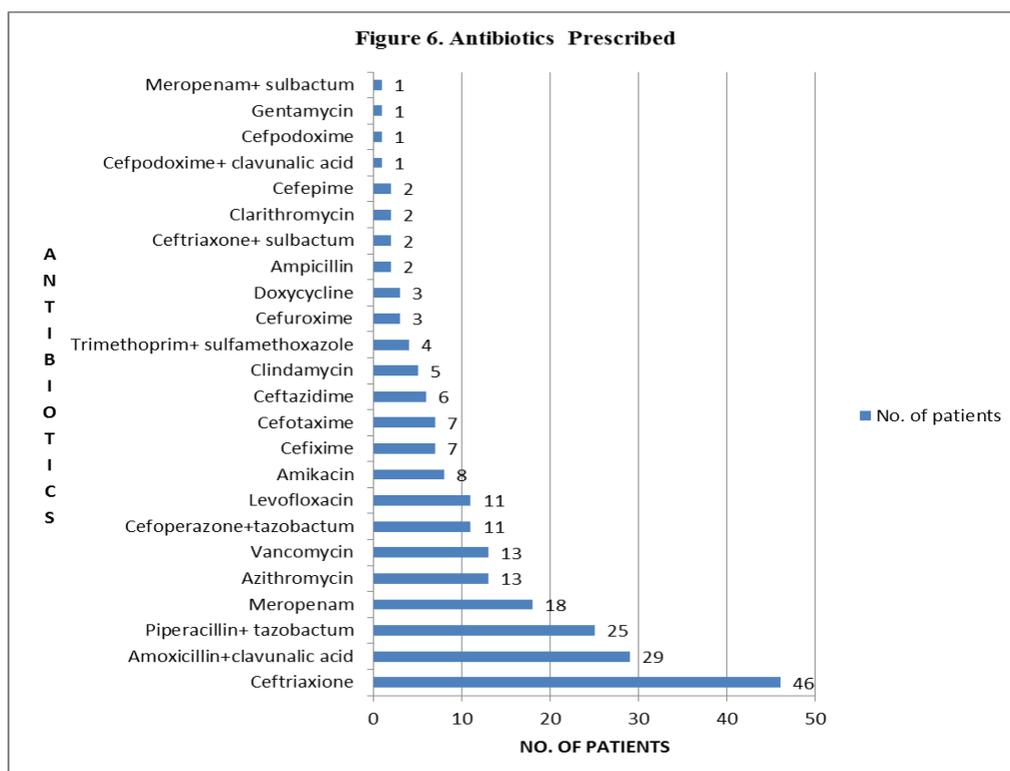
Mostly prescribed antibiotic in our study were Ceftriaxone 46(34.84%), followed by Amoxicillin+ Clavulanic acid 29(21.96%), Piperacillin+ Tazobactam 25(18.39%), Meropenem 18(13.63%), Vancomycin 13 (9.84%), Azithromycin 13(9.84%), Cefoperazone+

Tazobactam 11(8.3%), Levofloxacin 11(8.3%), Amikacin 8(6.06%), cefotaxime 7(5.30%), cefixime 7(5.30%), ceftazidime 6(4.54%), clindamycin 5(3.78%), Trimethoprim+ sulfamethoxazole 4(3.03%), cefuroxime 3(2.27%), doxycycline 3(2.27%), Ceftiaxone +Sulbactam 2(1.51%), clarithromycin 2(1.51%),

ampicillin 2(1.51%), cefepime 2(1.51%), Gentamycin 1(0.75%), Meropenem+ sulbactam 1(0.75%), cefpodoxime 1(0.75%), cefpodoxime+ clavulanic acid 1(0.75%).

**Table 6: Antibiotics Prescribed.**

Antibiotics	No.Of Patients	Percentage
Piperacillin+ Tazobactam	25	18.39%
Meropenem	18	13.63%
Vancomycin	13	9.84%
Clindamycin	5	3.78%
Cefuroxime	3	2.27%
Ceftriaxone	46	34.84%
Azithromycin	13	9.84%
Cefotaxime	7	5.30%
Clarithromycin	2	1.51%
Cefoperazone +Tazobactam	11	8.33%
Amoxicillin+clavulanic acid	29	21.96%
Cefixime	7	5.30%
Ceftriaxone+ sulbactam	2	1.51%
Trimethoprim+Sulfamethoxazole	4	3.03%
Ampicillin	2	1.51%
Amikacin	8	6.06%
Ceftazidime	6	4.54%
Levofloxacin	11	8.33%
Cefipime	2	1.51%
Gentamycin	1	0.75
Meropenem+ sulbactam	1	0.75%
Cefpodoxime	1	0.75%
Doxycycline	3	2.27%
Cefpodoxime + Clavulanic acid	1	0.75%



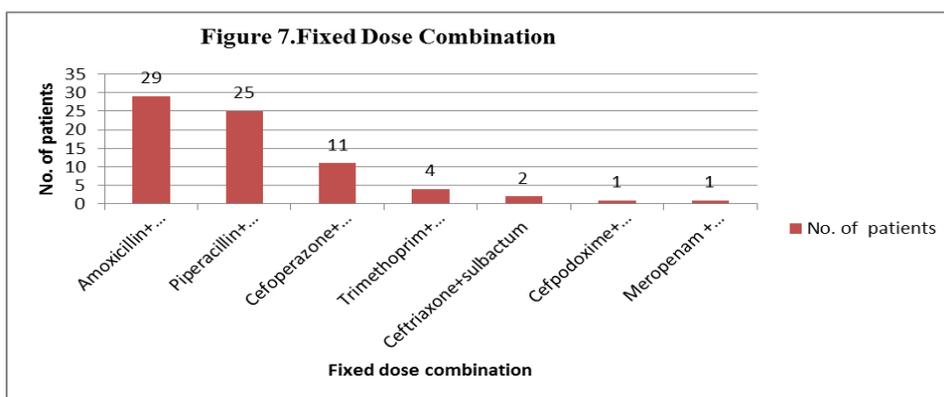
### Fixed Dose Combination

Out of 132 prescriptions, 73(55.30%) prescriptions was prescribed in fixed dose combination. In that 75 prescriptions, Amoxicillin+ clavunalic acid was prescribed in 29 (21.96%), Piperacillin with tazobactam

in 25 patients(18.39%), Cefperazone with tazobactam in 11(8.33%), Trimethoprim+ sulfamethoxazole in 4(3.03%), Ceftriaxone + sulbactam in 2 (1.51%), Cefpodoxime with clavunalic acid and meropenam with sulbactam in 1 patients (0.75%).

**Table 7: Fixed Dose Combination.**

Fixed dose combination	No. of patients	Percentage
Amoxicillin+ clavunalic acid	29	21.96%
Piperacillin+ tazobactam	25	18.39%
Cefperazone+ tazobactam	11	8.33%
Trimethoprim+ sulfamethoxazole	4	3.03%
Ceftriaxone+ sulbactam	2	1.51%
Cefpodoxim+ clavunalic acid	1	0.75%
Meropenam + sulbactam	1	0.75%



### Who Core Drug Prescribing Indicators

Out of 132 prescriptions, total no. of drugs prescribed was 981 with an average of 7 drugs per prescription. Most of the drugs were prescribed by their brand name and the percentage of drugs prescribed by generic name

were 11.7. Out of 981 drugs, an average of 23.8 antibiotics were prescribed and 60.1 drugs were prescribed from essential drug list. An average of patients who receive injections were 35.9.

**Table 8: Who Prescribing Indicators.**

WHO PARAMETERS	MEAN
Average no. of drugs per encounter	7
% of drugs prescribed by generic name	12.7
% of antibiotics per prescription	23.8
% of encounter with an injection prescribed	35.9
% of drugs prescribed from essential drug list	60.1

### Problems Identified

There were some problems identified in the prescription which include mistake in spelling of drug (11.36%),

inappropriate use of letter in prescription (capital/small) (5.3%), drug duplication (3.7%) out of 132 prescriptions.

**Table 9: Problems Identified.**

Problems Identified	No. Of Patients	Percentage
Mistake in spelling	15	11.3%
Inappropriate use of letter	7	5.3%
Drug duplication	5	3.7%

### Culture Sensitivity Test

In this study 68(51.5%) patients were undergone culture sensitivity test. The culture was significant in 44(33.3%) patients and 24(18.2%) werenon-significant. The most

common organism isolates in LRTI and URTI were *Staphylococcus aureus* and *Kleibsiella pneumoniae* respectively.

**Table 10: Culture Sensitivity Report.**

Culture Report	No. Of Patients	Percentage
Significant Report	44	33.3%
Non-Significant Report	24	18.2%

## DISCUSSION

The widespread use of AMAs leads to the emergence of antibiotic resistant pathogens. The study of prescribing pattern of antibiotics is an effective way for reduction in the cost of therapy, minimizing practice of poly-pharmacy and improving rational use of antibiotics.<sup>[52]</sup> The present study includes a total of 132 patients, as per the inclusion and exclusion criteria and there were 78 (59.09%) are males and 54 (40.90%) cases were females. As per the study population the greatest number of patients was in the age group of above 60 years with the mean (SD) age of 38.40(±24.10). The most commonly prescribed antibiotics according to their classes were Cephalosporins 34.84% followed by combination of Amoxicillin + clavulanic acid 21.96%, Penicillin + Beta lactamase inhibitors 18.39%.

Culture sensitivity study was done in 68 (51.5%) patients out of which 33.3% was significant and 18.2% non-significant culture and most common organism isolate in URTI and LRTI was *Staphylococcus aureus* and *Klebsiella pneumoniae* respectively. In present study patients were categorized based on the type of RTI such as LRTI and URTI. Among 132 patients 68.93% of them were diagnosed with LRTI which was further categorized as bronchitis 5.4%, pulmonary tuberculosis 3.2%, pneumonia 68.1%, unspecified 23.07%.

In present study among 132 patients the cases were diagnosed with URTIs out of which 78.04% of cases were specified URTIs while the remaining 12 (29.2%) were unspecified URTIs. Tonsillitis 29%, otitis media and Pharyngitis were the leading types of specific URTIs. In our study, 60.01% drugs were prescribed from Essential medicine list (EML). Drug prescription from EML is beneficial in terms of cost-effectiveness and safety of drugs.<sup>[59]</sup> Out of total drugs prescribed, 12.7% drugs were prescribed by generic name.

Our study identified the presence of some problems with the prescription. In the review of prescriptions, the results showed there were some cases of problems occurred in the prescriptions which include drug duplication, spelling of the drug and inappropriate use of letter in the prescription (capital/small). Out of 132 prescriptions, 3.7% prescriptions were found to have drug duplications. The most common drug duplication was with Levofloxacin. Other problems identified include mistake in spelling of drug 11.3%, inappropriate use of letter in the prescription (capital/small) (5.3%). In a study conducted by Akbari, *et al.* showed that 14.86% prescriptions were have drug duplication which is greater than the present study, 8.76% of prescriptions having

mistake in spelling of drug, less than that of our study and 14.23% are having inappropriate use of letter in prescription, which is greater than the present study.

## CONCLUSION

The present study demonstrates the prescription pattern of antibiotics in respiratory tract infection. The assessment of antibiotic use concludes that the average encounters with an antibiotic prescribed was in accordance with the WHO recommendations and also the average no. of total drugs per prescription was greater than the WHO recommendation. A very few drugs were prescribed in generic names, doesn't meet the WHO recommendations. The physician should encourage the prescribing by generic name. There was a slight difference in the value of drugs from EDL from the recommended values, so there is a need to improve the standard prescription. The injections were given according to WHO recommendations. There is a mandatory need for microbiological investigation before treatment of infections. Even though the problems that are identified in the prescription were less, the physician need to be more careful while prescribing for the therapeutic success.

The prescribing pattern studies and the involvement of clinical pharmacist in prescription analysis can help the physicians to provide feedback on the current clinical practices. This can further contribute in reducing the occurrence of emergence of drug resistance and encourage rational prescribing of antibiotics.

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