



**STUDY ON THE PRESCRIBING PATTERN OF BETA-LACTAM ANTIBIOTICS AND
DRUG RELATED PROBLEMS IN A TERTIARY CARE HOSPITAL**

**Manvi Gulati^{1*}, Arpita Dey², Subin Kumar S.³, Madisa Pale⁴, Nayana P. Kunderi⁵, Dr. E. Satheesh Kumar⁶,
Dr. Narayana Swamy V. B.⁷ and Dr. Smita⁸**

Department of Pharmacy Practice, RR College of Pharmacy, Sapthagiri Institute of Medical Sciences and Research Center, Bangalore – 560090.



*Corresponding Author: Manvi Gulati

Department of Pharmacy Practice, RR College of Pharmacy, Sapthagiri Institute of Medical Sciences and Research Center, Bangalore – 560090.

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ABSTRACT

Background: To conduct a study on the prescribing pattern of beta-lactam antibiotics and drug related problems in a tertiary care hospital. **Methodology:** After obtaining approval from the Institutional Ethics Committee, a cross-sectional study was carried out in 300 patients in a tertiary care hospital in Bangalore. The data was collected from the patient case profile and prescriptions and noted. The statistical analysis of the collected data was performed using SPSS software and Excel. **Result:** In study of 300 patients majority of patients belonged to the age group between 49-60. In the study population 191 were male patients (63.7%) while females were 109 (36.3 %). The number of drugs per prescription was found to be 9 in majority (50). The total number of drugs prescribed for 300 patients was 2654. Out of which 457 were beta lactam antibiotics prescribed to the patients with a percentage of 17.2%. The average antibiotic per prescription was found to be 1.52. The beta- lactam antibiotics were prescribed as monotherapy, two-drug therapy, three- drug therapy and four- drug therapy. The most frequently prescribed beta-lactam antibiotics in the study was ceftriaxone followed by piperacillin, tazobactam and cefixime. **Conclusion:** In the study population of 300 patients reveals that 41.3% of the sample, belonged to the 49-60 age group. Ceftriaxone is the most prescribed antibiotic. These findings emphasize the importance of personalized care and vigilant prescription practices, assessing the prescribing pattern in accordance with the WHO essential list of medicines particularly in the 49-60 age group, and underscore the need for continuous pharmacovigilance for patient safety and treatment efficacy.

KEYWORDS: Beta-lactam antibiotics, prescribing pattern, WHO essential drug list, Drug- related problems.

1. INTRODUCTION

β -Lactams are most widely used class of antibiotics. After the discovery of benzylpenicillin, new penicillin derivatives and related β -lactam classes of cephalosporins, cephamycin, monobactams, and carbapenems have been discovered. β -lactam resistance is primarily because of the enzyme produced by bacteria known as Beta- lactamase enzyme that hydrolyze the β -lactam ring, thereby inactivating the drug.^[1]

Bacterial resistance against beta-lactam antibiotics is increasing at a significant rate and has become a common problem in primary care medicine. One important mechanism of antimicrobial resistance of beta-lactam antibiotics is the production of beta-lactamases, which are enzymes that split the beta-lactam ring. Beta-lactamase activity can occur in gram-positive organisms such as *Staphylococcus aureus* and *Staphylococcus epidermidis* and gram-negative organisms such as *Haemophilus influenzae*, *Neisseria gonorrhoea*,

Moraxella catarrhalis, *Escherichia coli*, and *Proteus*, *Serratia*, *Pseudomonas* and *Klebsiella* species; and anaerobic organisms (*Bacteroides* species).^[2]

The newer beta-lactam antibiotics can also be highly effective in combating infections which are caused by beta-lactamase-producing organisms. When used alone, beta-lactamase inhibitors like clavulanate, sulbactam and tazobactam have weak intrinsic antibacterial activity, but their effectiveness increases when they are combined with a beta-lactam antibiotic (e.g., amoxicillin-clavulanate [Augmentin]).

Orally administered beta-lactam antibiotics are divided into classes based on their antimicrobial spectrum.

Irrational antimicrobial use has been a major challenge in developing countries. Studies has shown that in Ethiopia limited number of studies are done and do not indicate the right use of antibiotic.

The prescription pattern reflects the physician understanding about the disease and the patient history. In India a research states that 1,90,000 deaths happen each year due to infections, among which 30% is due to antibiotic resistance and the cause of which is the inappropriate use of antibiotic.

In many developing countries irrational use of drugs is a common practice therefore the aim of the study is to understand the prescribing pattern of Beta Lactam Antibiotics in Tertiary Care Hospital.^[3]

Classification for Beta-Lactam Antibiotics

The indications for the usage of beta-lactam antibiotics are many and can vary according to the subclass considered.

PENICILLINS

Natural Penicillins: Penicillin G (IV), Penicillin V (PO) are used in the treatment of certain gram-positive and gram-negative infections viz. Penicillin susceptible Streptococcus Pneumonia and meningitis, Streptococcal Pharyngitis, Endocarditis etc.

AMINOPENICILLINS

Amoxicillin (PO), ampicillin (PO/IV) have activity against gram-positive and gram-negative bacteria (e.g., many Enterobacteriaceae) anaerobic organisms. They are commonly used together with beta-lactamase inhibitors.

UREIDOPENICILLINS

Piperacillin (ureidopenicillin) acts against aminopenicillin-resistant gram-negative bacilli (*Pseudomonas aeruginosa*). They are commonly combined with beta-lactamase inhibitors.

CEPHALOSPORINS

First-generation cephalosporins are Cefazolin(IV), Cephalexin (PO), Cefadroxil (PO). They are majorly used for Skin and soft tissue infections, serious infections due to MSSA and also as a perioperative surgical prophylaxis.

Second-generation cephalosporins are Cefuroxime (IV/PO), Cefoxitin (IV), Cefotetan (IV), Cefaclor (PO), Cefprozil (PO). They are used for Upper respiratory tract infections (sinusitis, otitis media), Cefoxitin, cefotetan-gynecologic infections and perioperative surgical prophylaxis.

Third-generation cephalosporins are Cefotaxime (IV), Ceftriaxone (IV), Cefpodoxime (PO), Cefixime (PO), Cefdinir (PO), Cefditoren (PO), Cefdituben (PO). They are used for Community-acquired pneumonia, meningitis, Urinary tract infections, Streptococcal endocarditis, Gonorrhoea and Severe Lyme disease.

Anti-Pseudomonal Cephalosporins

Ceftazidime (IV), Ceftazidime/Avibactam (IV), Cefepime (IV) [Fourth- generation],

ceftolozone/ tazobactam (IV) also been described as "fifth-generation". They are used for Nosocomial infections-pneumonia, Meningitis, Complicated Intra-Abdominal Infections (cIAI) [ceftazolone plus beta-lactamase inhibitor] and Complicated Urinary Tract Infections (cUTI) [ceftazolone plus beta-lactamase inhibitor].

Anti-Methicillin-resistant *Staphylococcus aureus* (MRSA) cephalosporins

Ceftaroline (IV), Ceftobiprole (IV) also been described as "fifth-generation". They are used for Community-acquired pneumonia, Hospital-acquired pneumonia (excluding ventilator-acquired pneumonia) and Skin and soft tissue infection.

CARBAPENEMS

Imipenem/cilastatin (IV), meropenem (IV), doripenem (IV)

- Nosocomial infections-pneumonia, intra-abdominal infections, urinary tract infections
- Meningitis (especially meropenem) ERTAPENEM (IV)
- Community-acquired infections
- Nosocomial infections.

MONOBACTAMS

Aztreonam (IV) is only active against aerobic gram-negative organisms but shows no activity against gram-positive bacteria or anaerobes.

- Nosocomial infections, e.g., pneumonia
- Urinary tract infections.^[2]

2. MATERIALS AND METHODS

2.1 Sources of data and materials

1. Patient case sheet
2. ADR forms
3. Drug- drug interaction forms
4. Patient counseling forms
5. Self-designed patient data collection form

2.2 Method of collection of data

- The data required for the study has been collected by reviewing the prescription list and patient case sheets. The data collected has been noted in a patient data collection form. Patients who are in accordance with inclusion criteria was enrolled into the study. The patients who are admitted to the ward was monitored for 48 hours of their stay, by using patient case sheets, laboratory data and progress chart to analyze which drug is commonly prescribed in various diseases.

2.3 Statistical Analysis

- The data was entered on Microsoft Excel and the Statistical Analysis of collected data was performed using SPSS.
- The results of collected data were analyzed using statistical analysis and frequencies, percentages, mean values were calculated.

3. ETHICAL CONSIDERATION

1. Confidentiality was maintained throughout the study.
2. Written informed consent form was obtained from all the participants.
3. There is no physical harm to the participant, as there is no intervention.

3.1 Ethical clearance

The study was submitted for ethical clearance to the ethical committee of The Sathagiri Institute Of Medical Sciences And Research Center. This study is based on the analysis of approved surveillance data.

4. RESULTS

4.1 Distribution of Age Group

Patients were categorised according to their age groups. Out of 300 patients majority of patients belonged to the age group between 49-60 yrs with frequency of 124(41.3%), followed by age group 39-48 yrs with 63 (21.0%). In age group of 29-38 yrs the frequency was found to be 59 (19.7%). While the least was observed in age group of 18-28 yrs with a frequency of 54 (18.0 %).

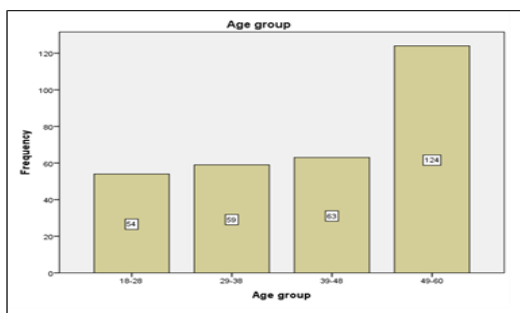


Fig 1: Distribution of Age Group.

4.2 Gender Distribution of Patients

Out of 300 patients 191 were found to be male patients leading in majority with percentage of (63.7%) while females were 109 with a percentage of 36.3 %. Male patients were in higher percentage by 27.4% than females.

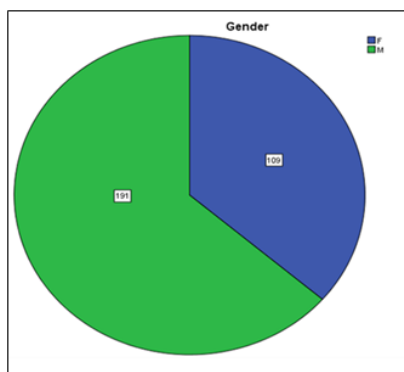


Fig 2: Gender Distribution.

4.3 Comparison of Gender with Age Group

Out of the study population, the major age group of patients were found to be 49- 60 years in which Male (88

patients) was found to be the maximum number, whereas the least is of 29-38 years with female (23) patients.

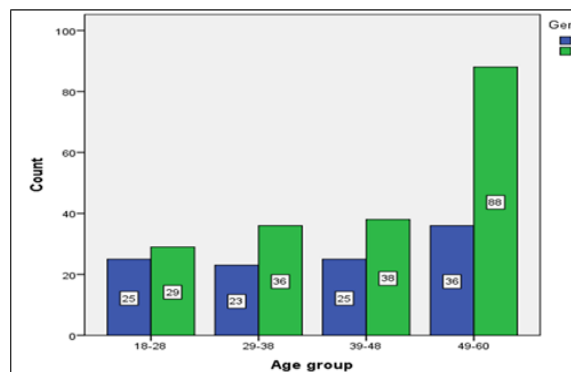


Fig 3: Comparison of age group with gender of the study population.

4.4 Distribution of Addictive Habits

Among the study population, 21.2 % were of smokers which contributed to the highest category, while smoker with alcoholic contributed to 17.0 %. Most of the common social habits were distributed equally by 2.1 % making it to the least in the study.

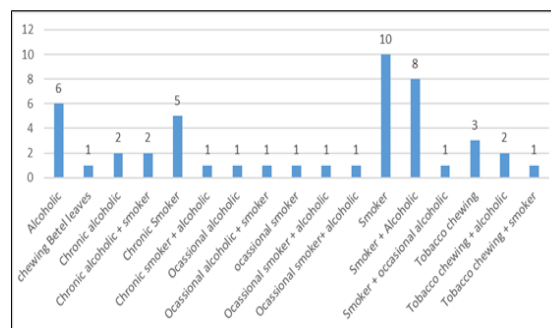


Fig 4: Distribution of Social Or Addictive Habits.

4.5 DISTRIBUTION PATTERN OF COMORBIDITIES

Out of 300 patients, 17% of the patients were having type II Diabetes mellitus as a comorbidity which was the highest among other comorbidities. While 16% patients were having Hypertension.

The study found that the comorbidities are more prevalent in the age group of 49-60 years (39%), where the combination of 2 to 3 diseases and/or disorders were found among the patients who got treated with the antibiotics.

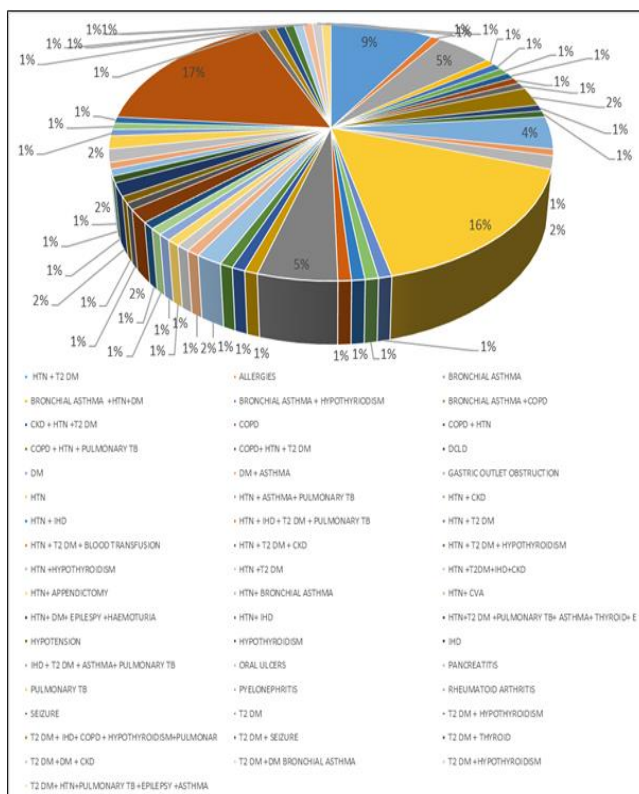


Fig 5: Distribution of comorbidity patterns in the population.

4.6 Number of drugs prescribed per prescription

Out of the study population, the number of drugs per prescription was found to 9 in majority (50). The total number of drugs prescribed for 300 patients was 2654. Out of which 457 were beta lactam antibiotics prescribed to the patients with a percentage of 17.2%. The average antibiotic per prescription was found to be 1.52.

The beta- lactam antibiotics were prescribed as monotherapy, two-drug therapy, three- drug therapy and four- drug therapy. Where monotherapy was most commonly used in the treatment that is 169 while that of two drug therapy was found to be 108 followed by three drug therapy was 20. While the least was four drug therapy which was found to be only 3.

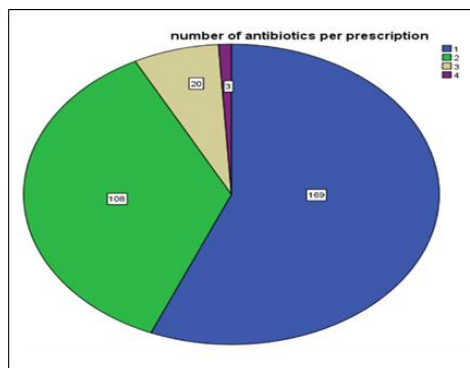


Fig 6.1: Number of antibiotics per prescription.

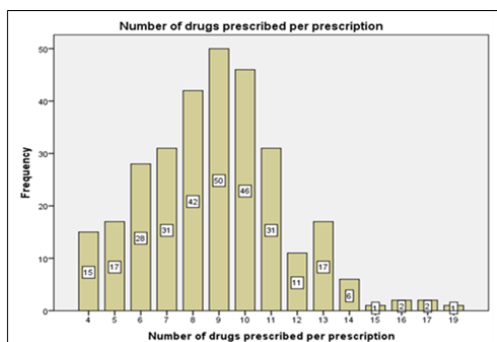


Fig 6: Number of drugs prescribed per prescription.

4.7 Route of administration

The route of administration which was maximum belonged to the Intravenous route of administration was found to be 266. whereas oral route of administration was contributed to 11.

While the combination drug administration, Intravenous with Oral combination was found to be 21 followed by the least preferred combination which was of IV with IV that was found to be only 2.

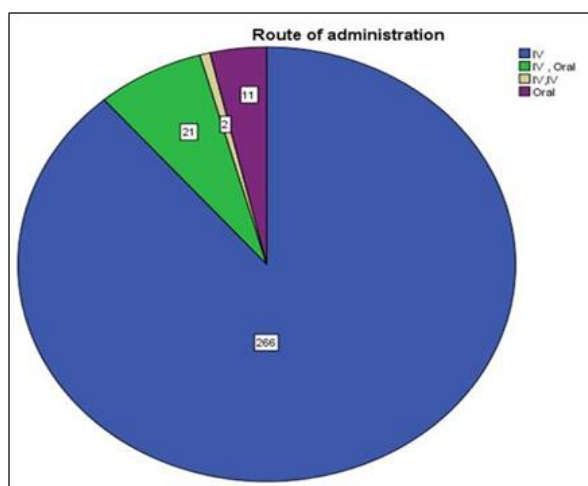


Fig 7: Route of administration.

4.8 Distribution of drug interactions among beta lactam antibiotics

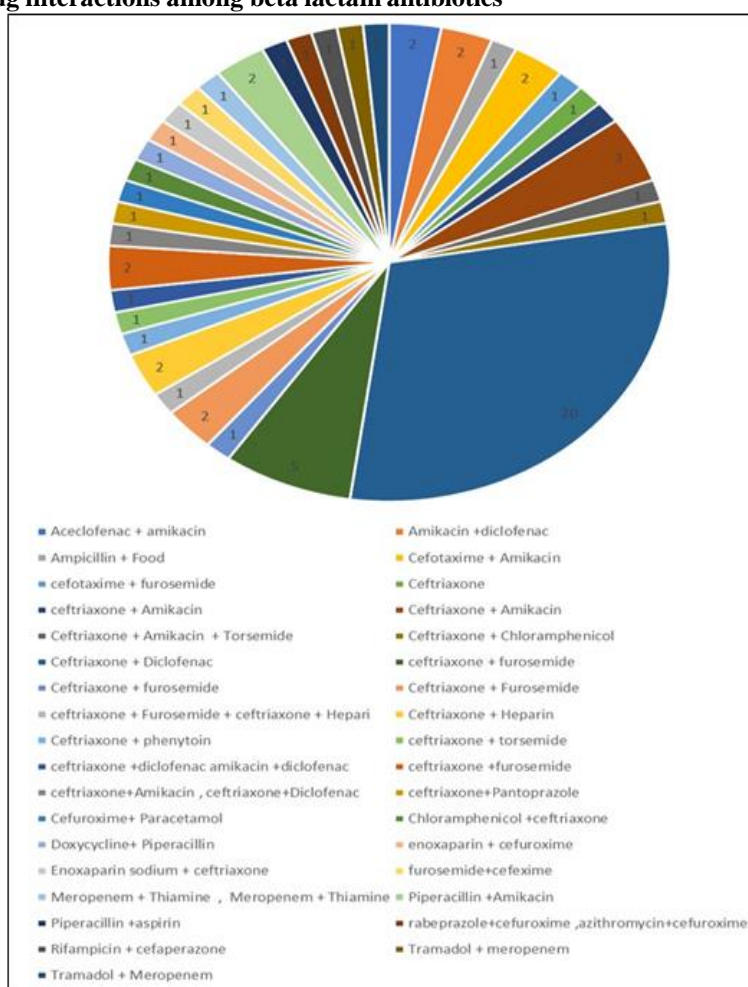


Fig 8: Distribution of drug interactions in beta-lactam antibiotics.

The study population showed that maximum drug interaction was between Ceftriaxone and Diclofenac^[20] which was quite common among other beta lactam antibiotics, followed by ceftriaxone with furosemide which was found to be 10. The other drug interactions was observed with minimum value of 4 which was between Ceftriaxone and Amikacin.

4.9 Commonly prescribed beta lactam antibiotic

Among the study population of 300 patients, Ceftriaxone was mostly prescribed to the patients which was found to be 165 followed by Piperacillin with Tazobactam was used which was found to be 36. Cefexime was found to be 10.

4.11 Distribution pattern of adverse drug reaction with beta lactam antibiotics

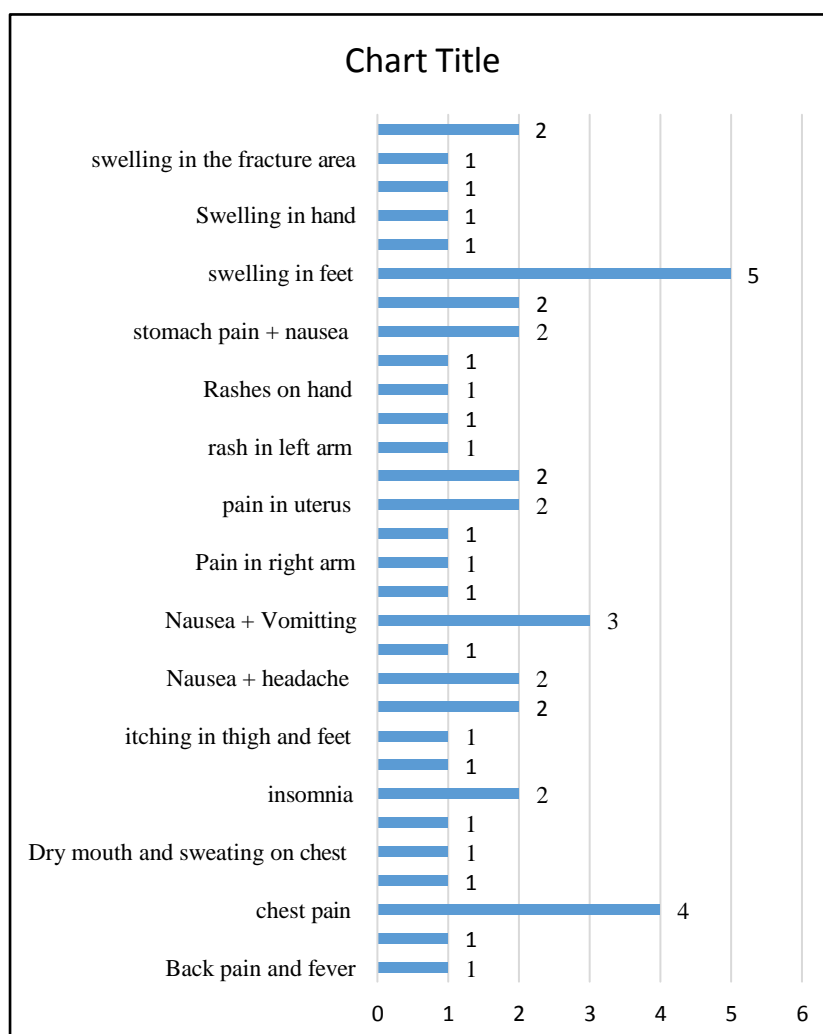


Fig 11: Distribution pattern of ADR in beta-lactam antibiotics.

Among 300 patients, total 47 patients experienced adverse drug reactions with an average of 1.5%. The major adverse drug reaction was observed to be swelling

in feet which was found to be 5 followed by chest pain with frequency of 4. Nausea and vomiting was found to be in 3 patients.

4.12 Distribution pattern of frequency

Frequency

Table 1: Distribution pattern of frequency.

	Frequency	Percent	Valid Percent	Cumulative Percent
OD +BID +BID	1	.3	.3	.3
BID	228	76.0	76.0	76.3
BID + BID	5	1.7	1.7	78.0
BID + BID + O	2	.7	.7	78.7
BID + OD	8	2.7	2.7	81.3
BID + TID	4	1.3	1.3	82.7
OD	15	5.0	5.0	87.7
OD + BID	5	1.7	1.7	89.3
OD +OD	1	.3	.3	89.7
TID	25	8.3	8.3	98.0
TID + BID	3	1.0	1.0	99.0
TID +OD	1	.3	.3	99.3
TID +TID	2	.7	.7	100.0
Total	300	100.0	100.0	

Among 300 patients, the maximum prescribing pattern of beta lactam antibiotics was twice daily in 228 patients. 25 patients were prescribed thrice daily followed by 15

patients who were prescribed once daily in accordance with WHO indicator prescribing policy.

4.13 Distribution of drug duplication

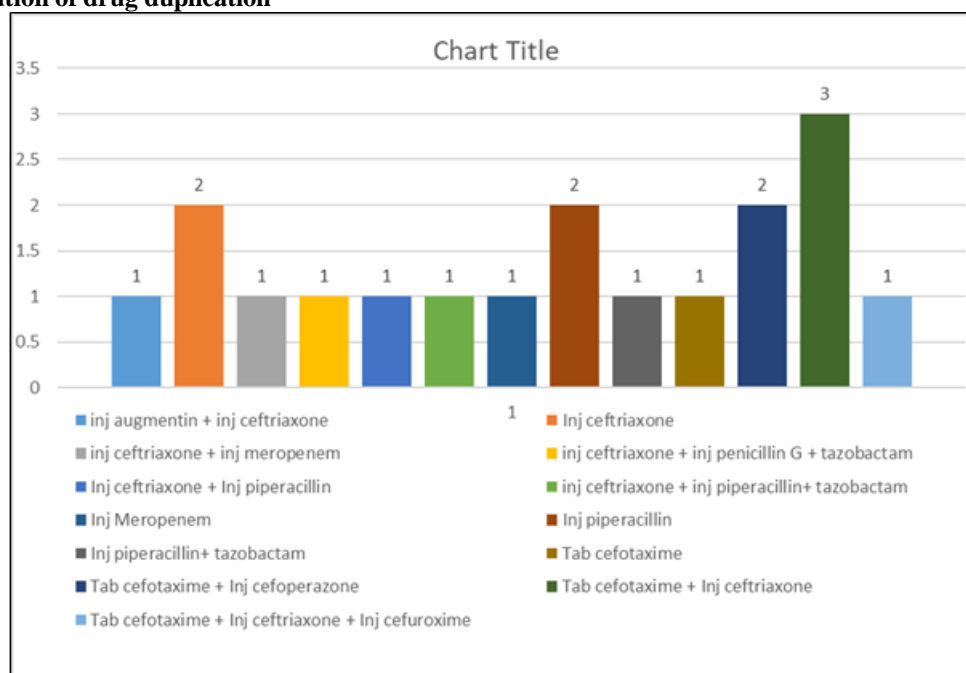


Fig 12: Distribution of drug duplication.

Among 300 patients, Injection Ceftriaxone and injection Piperacillin with Tazobactam had maximum drug duplication in the drug regimen with a frequency of 3 patients. While considering single drug therapy, injection ceftriaxone and injection piperacillin was observed in 2 patients and as combination, tablet cefotaxime with injection cefoperazone was seen in 2 patients.

5. DISCUSSION

In our study, based on the comprehensive analysis of a sample of 300 patients, several key findings emerged, shedding light on the demographic distribution, comorbidities, prescriptions, and related parameters.

The demographic distribution revealed that the majority of patients, constituting 41.3% of the sample, belonged to the 49-60 age group, with 124 individuals. This age group was followed by the 39-48 bracket, which accounted for 21.0% of the patients, totaling 63 individuals. In contrast, the 18-28 age group had the fewest patients, with 54 individuals, making up 18.0% of the sample. (Fig 1) The study found out to be consistent with the study conducted by Hiware SK, et al., where majority of the patients were male (56.38%) with mean age of 35-50 (standard deviation 18) years old.

Gender distribution among the patients showed that 63.7% were male, amounting to 191 individuals, while females comprised 36.3%, with 109 individuals. Male patients were notably higher in percentage, surpassing females by 27.4%. (Fig 2). The study was found to be

consistent with the study conducted by Nikki Soman, et.al: on prescribing pattern of cephalosporins utilization and its compliance towards the hospital antibiotic policy in surgery ward of a tertiary care teaching hospital in india. Out of 250 patients, 69% was male and 31.2% was female population.

The study also explored the correlation between gender and age groups, revealing that the 49-60 age group had the most male patients, with 88 individuals, while the 29-38 age group had the least, with 23 female patients. (Fig 3).

In terms of addictive habits, 21.2% of patients were smokers, with 17.0% of those smokers also consuming alcohol. Various other common social habits were equally distributed among 2.1% of patients, representing the least prevalent category. (Fig 4) The study was found to be consistent with the study conducted by Michael B. Steinberg, et al. Half (49.9%) of encounters that included any infection had an antibiotic prescribed. Adjusted odds of receiving antibiotics among current tobacco users was 1.20 and even higher for encounters of respiratory infections.

Comorbidities were another important aspect of the study, with 17% of patients having type II Diabetes Mellitus, and 16% having Hypertension. The study highlighted that comorbidities were most prevalent in the 49-60 age group, where 39% of patients presented with two to three diseases and/or disorders. (Fig 5) In the

study conducted by Patrick Rockenschaub *et al.*: on Antibiotic Prescribing Before and After the Diagnosis of Comorbidity: A Cohort Study Using Primary Care Electronic Health Records 106 540/1 071 943 (9.9%) eligible patients were diagnosed with comorbidity. Antibiotic prescribing rates increased 1.9- to 2.3-fold in the 4–9 months preceding diagnosis of asthma, heart failure, and COPD before declining to stable levels within 2 months after diagnosis. A less marked trend was seen for diabetes (rate ratio, 1.55; 95% confidence interval, 1.48–1.61). Prescribing rates for patients with vascular conditions increased immediately before diagnosis and remained 30%–39% higher than baseline afterwards. Rates of prescribing to controls increased by 17%–28% in the months just before and after consultation.

Regarding drug prescriptions, the average number of drugs per prescription was found to be 9, totaling 2,654 drugs for the 300 patients. Beta-lactam antibiotics accounted for 17.2% of the prescriptions. Monotherapy with beta-lactam antibiotics was most common (169), followed by two-drug therapy (108) and three-drug therapy (20). Four-drug therapy was the least common, prescribed to only 3 patients. (Fig 6) The study conducted by Nikhila Adla, *et al.*: on a study of prescribing pattern of antibiotics and its resistance in tertiary care hospital it was found that two antibiotics (26.6%) were prescribed predominantly followed by three antibiotics (52%), four antibiotics (44%), 5 antibiotics (29%), seven antibiotics in 11 cases, six and eight antibiotics in 2 patients, ten and twelve in single patient.

The most frequently used route of administration was intravenous (IV) in 266 instances, while oral administration was used in only 11 cases. Intravenous with oral combination was seen in 21 patients, whereas IV with IV combination was the least preferred, prescribed to just 2 patients. (Fig 8) comparing the study conducted by Nikhila Adla, *et al.*: on a study of prescribing pattern of antibiotics and its resistance in tertiary care hospital their study most of the antibiotics were administered through intravenous route(IV).

Among beta-lactam antibiotics, Ceftriaxone was the most commonly prescribed (165), followed by Piperacillin with Tazobactam (36), and Cefexime (10). (Fig 9). The study found to be consistent with the study conducted by Bhavishya Keerthi anna valder, *et al.*, the most frequently used AMA'S were third generation cephalosporins and it was most frequently combined with metronidazoles.

Changes in antibiotic therapy were observed in 71.7% of patients, with the highest rate in the 49-60 age group, where 88 patients showed no change, while 36 patients experienced a change. (Fig 12) The study found out to be consistent with the study conducted by Shirin A Mazumder *et al.* cephalosporins are suitable for switching as early switch therapy after the administration of 1-2 doses of oral antibiotic where studies of intravenous

Cefuroxime followed by oral Cefuroxime suggest that this regimen is both effective and well tolerated as rapid switch therapy and has the potential to reduce overall healthcare cost and to improve patient's satisfaction.

Adverse drug reactions affected 47 patients, with swelling in feet (5) and chest pain (4) being the most common reactions. (Fig 13) The study found out to be consistent with the study conducted by Hanan ahamed bakri, *et al* Antibiotics -Related Adverse Drug Reaction in a Tertiary Hospital in Saudi Arabia; The major type of ADR was rash (52.95%), followed by anaphylaxis reactions (10.59%) of the patients. Based on the Naranjo scale, the ADR was possible in 80% and probable in 18.82% of the cases. The presence of medical conditions displayed a significant association with the development of rashes ($p=0.03$). In addition, the female gender ($p=0.009$) and the presence of medical conditions ($p=0.03$) showed significant association with the development of anaphylaxis.

Another study examined the frequency of drug prescriptions, with twice-daily dosing being the most prevalent (76.0%), followed by thrice-daily (8.3%) and once-daily (5.0%) dosing. (Table 1) the study found to be a consistent with the study conducted by Elvis Dzelamonyuy chem, *et al.* The most frequently prescribed antibiotics were amoxicillin (29.29%) followed by cotrimoxazole (19.08%) and metronidazole (15.59%).

Finally, regarding drug duplication, Injection Ceftriaxone and Injection Piperacillin with Tazobactam exhibited the maximum duplication (3 patients), while a single drug therapy combination, Tablet Cefotaxime with Injection Cefoperazone, was seen in 2 patients. (Fig 14). The study found to be consistent with the study conducted by KLL Sneha, *et al.* There were therapeutic duplications found among five diseases which included drugs such as inj. Magnex forte, Tab. Linezolid, Tab fluconazole, inj meropenem, inj monocef, Tab clarithromycin, inj eterapenem, Tab augmentin.

6. CONCLUSION

The analysis of 300 patients reveals that the 49-60 age group is the largest, with a male majority. Comorbidities like Type II Diabetes and Hypertension are prevalent in this age group. Ceftriaxone is the most prescribed antibiotic, typically taken twice daily, while the drug interactions predominantly with Diclofenac are notable. Nevertheless, 1.5% of patients experienced adverse drug reactions, and concerns exist about drug duplication, mainly with Ceftriaxone followed by Piperacillin with Tazobactam. These findings emphasize the importance of personalized care and vigilant prescription practices, assessing the prescribing pattern in accordance with the WHO essential list of medicines particularly in the 49-60 age group, and underscore the need for continuous pharmacovigilance for patient safety and treatment efficacy.

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