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Research Article

Pharmacy practice for good health promotion

A Prospective Antimicrobial Prescription Audit in the Inpatient Department of Pulmonology in a Tertiary Care Hospital

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Abstract: Antibiotics are medicines used to prevent and treat bacterial infections. Antibiotic usage is increasing rapidly day by day with or without prescription. Irrational prescription usage, negligence of standard guidelines and antimicrobial resistance are increasing complexity in the therapy and the desired outcome. High-volume prescription of antibiotics in primary health care is a major factor contributing to antibiotic resistance. Educating physicians and patients can lower prescribing errors and the aim of this study was to do a prospective observational prescription audit in inpatient department of pulmonology in a tertiary care hospital and limiting the inappropriate use of antimicrobials. The primary objective of the study is to determine the Antibiotic prescription, find out the inappropriate drug selection, dose selection, dosage form and course of antibiotics to monitor the culture test as well as antibiotic sensitivity and resistance and also to analyze the drug interaction, allergic medication prescribed and omission of the dose. The study was conducted with 234 patients in Erode district, Tamilnadu. The study conducted by strictly observing the antimicrobial prescription in the inpatient pulmonology department in a tertiary care hospital, limiting the inappropriate drug selection, dose selection, dosage form, course of antibiotics and hence decreasing the antibiotic resistance. The prescribing and administering details were collected in a data acquisition form; the collected data were interpreted with Sanford and GOLD Standard Guidelines and analyzed with descriptive statistics. The study found that irrational use of medication was high (53.41%) and a highly significant medication error also reported. The major concomitant disorder was Chronic Obstructive Pulmonary Disorder (21.79%) and most administered drug was Ceftriaxone (20.51%) (Third generation Cephalosporins). Culture test (32.90%) as well as antibiotic sensitivity and resistance test were done in very less cases, empirical therapy dominates over targeted therapy which affects rationality.

KeyWords: Antimicrobial prescription audit, Antibiotic resistance, Pulmonology, Medication error, rational use of antibiotics.

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1. INTRODUCTION

Antibiotics are the substances produced by microorganisms, which selectively suppress the growth or kill other microorganisms at very low concentrations. This definition excludes other natural substances which also inhibit microorganisms but are produced by higher forms (e g. antibodies) or even those produced by microbes but are needed in high concentrations (ethanol, lactic acid, Hydrogen Peroxide).[1]Antibiotics are commonly prescribed medicines in hospitals. The antibiotics are prescribed both as prophylactically or to treat ongoing infection. Antibiotic resistance is now a major issue confronting health care providers and their patients. Changing antibiotic resistance patterns, rising antibiotic costs and the introduction of new antibiotics have made selecting optimal antibiotic regimens more difficult now than even before. Literatures have reported the unnecessary or incorrect use of antimicrobials ranging from 9% to 64%. This practice apart from development of drug resistance results in higher morbidity, mortality, treatment cost and prolonged length of hospital stay with unnecessary exposure of patients to potentially harmful drugs. Due to rapid spread of multi-resistant microorganisms and decreasing accessibility of new antibiotics, resistance to antibiotics has become a major public health issue.[2]

1.1 Problems that arise with the use of Antimicrobial agents (AMAs)[1]

The major problems arises with the use of AMAs are as follows,

1.1.1 Local Irritancy

This is exerted at the site of administration. Gastric irritation, pain and abscess formation at the site of IM Injection, thrombophlebitis of the injected vein are the complication. Practically all AMAs, especially erythromycin, tetracyclines, certain cephalosporins and chloramphenicol are irritants.

1.1.2 Systemic toxicity

Almost all AMAs produce dose related and predictable organ toxicities.

1.1.3 Hypersensitivity reactions

Practically all AMAs are capable of causing hypersensitivity reactions. These are unpredictable and unrelated to dose. The more commonly involved AMAs in hypersensitivity reactions are: penicillins, cephalosporins, sulfonamides, fluoroquinolones.

1.1.4 Drug resistance

It refers to unresponsiveness of a microorganism to an AMA, and is akin to the phenomenon of tolerance seen in higher organisms.

1.1.5 Prevention of drug resistance

It is of utmost clinical importance to curb development of drug resistance.

1.2 *Rational drug use*

In contrast to the extensive literature on inappropriate usage of human pharmaceuticals by both public and professionals, there is a little information on how farmers and animal health professionals use antibiotics. Usage affects resistance in two ways. Firstly, the quantity of use, and secondly, quality includes drug choice, content, reconstitution, posology, administration and storage. The quality of veterinary products has received considerably more attention than quality of use. Major concerns include counterfeit, smuggled and improperly kept drugs. Some studies indicates that levels of sub-standard drugs were higher in products bought in the informal sector, others find no difference.[3]

1.3 *Antibiotics in respiratory disorders*

Antibiotics are commonly used in the management of respiratory disorders such as cystic fibrosis (CF), non-CF bronchiectasis, asthma and COPD. In those conditions long-term antibiotics can be delivered as nebulized aerosols or administered orally. In CF, nebulized colomycin or tobramycin improve lung function, reduces the number of exacerbations and improve the quality of life (QoL). Oral antibiotics, such as macrolides, have acquired wide use not only as antimicrobial agents but also due to their anti-inflammatory and pro-kinetic properties. In CF, macrolides such as azithromycin have been shown to improve lung function and reduce the frequency of infective exacerbations. Similarly macrolides have been shown to have some benefits in COPD including reduction in the number of exacerbations. In asthma, macrolides have been reported to improve some subjective parameters, bronchial hyper responsiveness and airway inflammation; however have no benefits on lung function or overall asthma control. Macrolides have also been used with beneficial effects in less common disorders such as diffuse panbronchiolitis or post-transplant bronchiolitis obliterans syndrome.[13] Need of the study Antibiotic resistance is increasing day by day, rational drug use is also been decreasing and a proper care for patients with a good course of antibiotic treatment is relevant. In case of pulmonology department, with the pollution and also with the various seasons the respiratory disorder has been increasing. For most of the infectious disorders in pulmonology department, antibiotics are given as treatment, so in the same department, a rational treatment is needed.

2 MATERIALS AND METHODS

2.1 *Study design*

A prospective observational study was conducted in pulmonology department in the hospital settings who were receiving antimicrobials.

2.2 *Study site*

Present study was conducted in the pulmonology department in a tertiary care hospital.

2.3 *Sample size*

234 patients

2.4 *Study period*

6 months

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2.5 *Study criteria*

2.5.1 *Inclusion criteria*

1. Patients who were receiving AMAs in inpatient department of pulmonology.
2. Patient of either sex
3. Patients of all ages.

2.5.2 *Exclusion criteria*

1. Pediatric and neonatal ICU
2. Opinion/consulting patients in pulmonology department.

2.6 *Data collection*

Data collection was done through self-prepared data collection form.

2.7 *Materials used*

- Sanford Guidelines[13]
- Global initiative for chronic obstructive Lung disease (GOLD) guidelines.[14]
- World health organization (WHO) guidelines.[15]
- Lexicomp database.16

2.8 *Ethical clearance*

All procedures performed in this study involving human participants were in accordance with the ethical standards of the JKK Munirajah College of Pharmacy (EC/PHARM D/2018-3)

3. STATISTICAL ANALYSIS

The data obtained were analyzed by descriptive statistics which is presented as percentage for each result of the study.

4. RESULTS AND DISCUSSION

4.1 *Gender wise distribution*

Majority of the study population were male which is 155 patients (66.2%) and 79 patients (33.7%) were female.

Table 1 Gender wise distribution (N=234)

Gender	No.Of Patients	Percentage (%)
Male	155	66.20
Female	79	33.70

4.2 *Age wise distribution*

Among the total study population majority of the patients (72.22%) fell under the category of age group 15-64 years followed by greater and equal to(≥) 65years (20.51%) and the least were from 0-14 years (7.26%).

Table 2: *Age wise Distribution (N=234)*

Age Group In Years	Number Of Patients	Percentage (%)
0-14	17	7.26
15-64	169	72.22
≥65	48	20.51

4.3 *Social habits*

Among the total study population majority of the patients were smokers (25.21), followed by 14.95% were alcohol consumers and 2.56% of patients had a habit of chewing tobacco. 57.26% of the population had no social habits.

Table3: Social habit pattern (N=234)

Social Habits	Number Of Patients	Percentage (%)
Smoking	59	25.21
Alcohol	35	14.95
Tobacco	6	2.56
No Abuse	134	57.26

4.4 *Various clinical conditions*

Data related to various clinical conditions were monitored. Majority of the population (21.79%) were admitted because of COPD, followed by pneumonia (16.66%), bronchitis (13.67%), tuberculosis (12.39%), asthma (8.54%), emphysema (8.11%), sinusitis (3.84%), tonsillitis (2.99%), ulcerative gingivitis (1.70%), cystic fibrosis (2.13%), epiglottitis, whooping cough, bronchiectasis and diphtheria (1.28%) and bronchiolitis, parapharyngeal space infection, otitis media, tooth odontogenic infection, granulomatous inflammation, pharyngitis each contains one patient i.e. 0.42%.

Table 4: ***Various clinical conditions (N=234)***

Various Clinical Conditions	No.Of Patients	Percentage (%)
Chronic Obstructive Pulmonary Disease	51	21.79
Pneumonia	39	16.66
Bronchitis	32	13.67
Pulmonary Tuberculosis	29	12.39
Asthma	20	8.5
Emphysema	19	8.11
Sinusitis	9	3.84
Tonsillitis	7	2.99
Cystic Fibrosis	5	2.13
Ulcerative Gingivitis	4	1.70
Epiglottitis	3	1.28
Whooping Cough	3	1.28
Bronchiectasis	3	1.28
Diphtheria	3	1.28
Others	7	2.99

4.5 Diagnosis methods

Only 32.90% of the population underwent culture test prior to diagnosis and a significant proportion of the population (67.09%) did not undergo culture test prior to diagnosis.

Table 5: ***Culture wise distribution (N=234)***

Culture Test	No.Of Patients	Percentage (%)
Done	77	32.90
Not Done	157	67.09

A study conducted by Abdulrahman Al -Yamani et al with 178 patients in Oman reported that 25% of his study population received antimicrobials before getting culture report.[4]

4.6 Distribution of organisms

Among the total study population 41 patients underwent sputum culture test and the results are shown in Table-6. The highest amounts of samples (29.62%) were reported with the presence of only gram positive organism. Next was both gram positive and negative organisms (16.66%), then gram negative (22.22%) and the least samples (7.40%) were reported with the presence of mycobacterium tuberculosis. 9 patients underwent pleural fluid test, the highest amount of the samples (5.55%) were reported with gram positive organism, and both gram positive and gram negative organisms. Next was gram negative (3.70%), and the least samples (1.85%) were reported with the presence of Mycobacterium Tuberculosis.3 patients underwent Blood staining test, 2 samples (3.70%) were reported with both Gram positive and Gram negative organisms. 1 patient was reported with Gram positive (1.85%). Only 1 patient underwent Broncho alveolar lavage, the sample is reported with the presence of gram negative organisms.

Table 6: ***Distribution of organisms (N=54)***

Presence Of Organism	Sputum Culture		Pleural Fluid		Blood Staining		Bronchoalveolar Lavage	
	No.of patients (*n*=41)	(%)	No.of patients (*n*=9)	(%)	No.of patients (*n*=3)	(%)	No.of patients (*n*=1)	(%)
Gram Positive	16	29.62	3	5.55	1	1.85	0	0
Gram Negative	9	16.66	2	3.70	0	0.00	1	1.85
Gram Positive And Gram Negative	12	22.22	3	5.55	2	3.70	0	0.00
Mycobacterium Tuberculosis	4	7.40	1	1.85	0	0.00	0	0.00

Al Shimemeri et al found that most commonly isolated organism in their institution were gram positive cocci (60%) compares our result, which is similar to our study that the patients had infections from gram positive organisms such as streptococcus species, lactobacillus etc... This result can be vary with other studies. These differences could be influenced by the types of infections seen in each study. The high prevalence of resistant gram negative isolates has been attributed to several factors including easy availability of broad-spectrum antibiotics, lack of antimicrobial stewardship programs, old architectural design preventing proper isolation of infected or colonized patients , lack of strong infections controlled programs and a lack of well-trained specialist and clinical pharmacist in infectious disease field.[5]

4.7 Tests for antibiotic sensitivity and resistance

230 patients received antimicrobials without testing antibiotic sensitivity and resistance; only 4 patients did antibiotic sensitivity and resistance test.

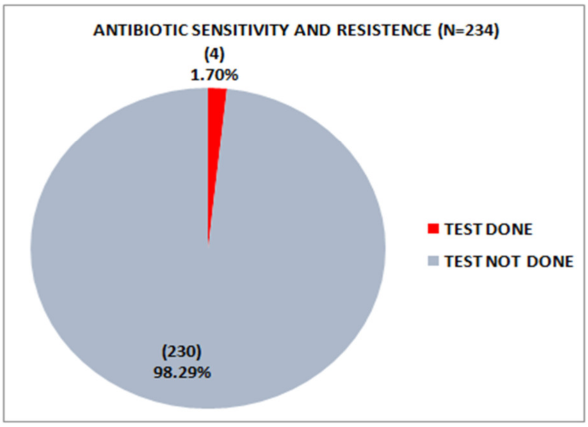

Fig 1. Test for Antibiotic Sensitivity and Resistance (N=234)

4.8 *Class of antibiotics prescribed*

Among the study population widely prescribed class of antibiotics were Cephalosporins (24.78%) and the least were penicillin/macrolide, penicillin/betalactamase inhibitors/tetracycline, nitroimidazole, macrolide/cephalosporins, lincosamide/penicillin antibiotic, fluoroquinolones/beta lactamase, fluoroquinolones/lincosamide, cephalosporin/glycopeptides, cephalosporin/fluoroquinolones, beta lactamase inhibitors/lincosamide which is 0.42%. Ceftriaxone was the most commonly prescribed antibiotic in the drug class of third generation cephalosporins with excellent activity against much gram negative and reasonable activity against gram positive microorganisms.

Table 7: Class of Antibiotics prescribed (N=234)

Class Of Antibiotics	Number Of Patients	Percentage (%)
Cephalosporins	58	24.78
Penicillin Antibiotics	31	13.24
Penicillin/Beta Lactamase	31	13.24
Fluoroquinolones	23	9.82
Anti-Tuberculosis	14	5.98
Beta-Lactamase Inhibitors	14	5.98
Lincosamide	9	3.84
Penicillin Antibiotic/Beta Lactamase Inhibitors/Fluoroquinolones	8	3.41
Cephalosporin/Macrolide	6	2.56
Aminoglycosides	5	2.13
Macrolide	5	2.13
Penicillin Antibiotic/Beta Lactamase Inhibitors/Aminoglycosides	4	1.70
Beta-Lactamase Inhibitors/Tetracyclines	3	1.28
Cephalosporin/Aminoglycosides	3	1.28
Cephalosporin/Beta Lactamase	3	1.28
Macrolide/Fluoroquinolones	3	1.28
Macrolide/Penicillin Antibiotic	3	1.28
Tetracycline	2	0.85
Beta-Lactamase Inhibitors/Lincosamide	1	0.42
Cephalosporin/Fluoroquinolones	1	0.42
Cephalosporin/Glycopeptide	1	0.42
Fluoroquinolones/Lincosamide	1	0.42
Fluoroquinolones/Beta-Lactamase	1	0.42
Lincosamide/Penicillin Antibiotic	1	0.42
Macrolide/Cephalosporin	1	0.42
Nitroimidazole	1	0.42
Penicillin/Beta Lactamase/Tetracycline	1	0.42
Penicillin/Macrolide	1	0.42

In Iran study conducted by Safaeian et al, penicillin were the most prescribed antibiotic.[6] Borade S et al reported among his study population, mostly prescribed antimicrobial agents to neonates admitted in NICU were cefotaxime (35.8%).[7]

4.8 *Number of antibiotics per prescription*

Most of the patients were on single therapy (76%) followed by double therapy (17.85%), quarter therapy (5.55%), and the least of the prescription contained Triple therapy (5.55%). Results of R.Selvaraj et al[8], Kumar Abhijith et al[9], Borade S et al[7] revealed majority of their study population were also on Monotherapy.

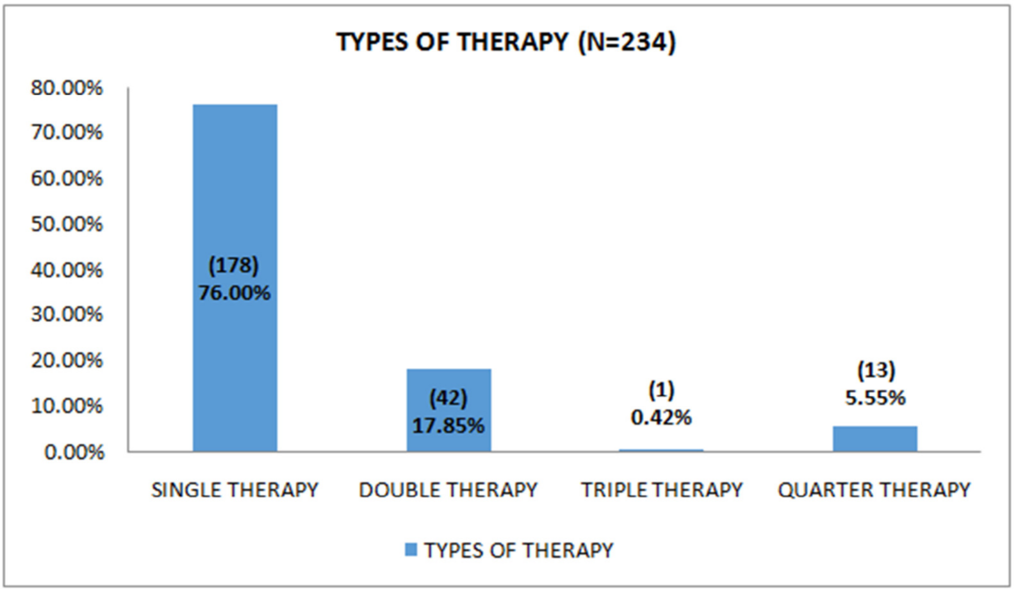

Fig 2. Number of antibiotics per prescription. (N=234)

4.10 *Drug distribution pattern*

Table 8 shows details of prescription containing monotherapy.178 patients were on Monotherapy, among that ceftriaxone was the highest prescribed Antibiotic (20.51%) and the less common drugs were Gentamicin, cefpin, metronidazole, ofloxacin, streptomycin, clarithromycin and cefepime-tazobactam which is 0.42%.

Table 8. *Details of prescription containing Monotherapy.*

Drugs Prescribed	Number Of Patients	Percentage (%)
Ceftriaxone	48	20.51
Amoxicillin-Clavulanic Acid	29	12.39
Piperacillin –Tazobactam	29	12.39
Cefoperazone –Sulbactam	14	5.99
Levofloxacin	11	4.71
Clindamycin	10	4.27
Moxifloxacin	10	4.27
Cefotaxime	7	2.99
Amikacin	3	1.28
Erythromycin	3	1.28
Ceftriaxone- Sulbactam	3	1.28
Ampicillin	2	0.85
Doxycycline	2	0.85
Gentamicin	1	0.42
Cefpin	1	0.42
Metronidazole	1	0.42
Ofloxacin	1	0.42
Streptomycin	1	0.42
Clarithromycin	1	0.42
Cefepime-Tazobactam	1	0.42

Table 9 shows details of prescription containing dualtherapy. 42 patients were on dual therapy, among that piperacillin + tazobactam+levofloxacin was the highest prescribed Antibiotic (4.27%) and the less common drugs were ceftriaxone+metronidazole, Clindamycin + penicillin, Ceftriaxone+vancomycin, Cefotaxime+levofloxacin, Ciprofloxacin+clindamycin, Cefoperazone+sulbactam + doxycycline, Cefoperazone+sulbactam+clindamycin which is 0.42%.

Table 9: Details of prescription containing Dual phase therapy (N= 234)		
Drugs Prescribed	**Number Of Patients**	**Percentage (%)**
Piperacillin+Tazobactam+Levofloxacin	10	4.27
Piperacillin+Tazobactam+Amikacin	4	1.70
Azithromycin+Ceftriaxone	4	1.70
Azithromycin+Levofloxacin	3	1.28
Azithromycin+Amoxicillin	3	1.28
Ceftriaxone+Amikacin	3	1.28
Moxifloxacin+Cefoperazone	2	0.85
Cefoperazone+Sulbactam+Levofloxacin	2	0.85
Cefixime+Ceftriaxone+Sulbactam	2	0.85
Ceftriaxone+Azithromycin	2	0.85
Ceftriaxone+Metronidazole	1	0.42
Clindamycin+Penicillin V	1	0.42
Ceftriaxone+Vancomycin	1	0.42
Cefotaxime+Levofloxacin	1	0.42
Ciprofloxacin+Clindamycin	1	0.42
Cefoperazone+Sulbactam+Doxycycline	1	0.42
Cefoperazone+Sulbactam+Clindamycin	1	0.42

Table 10 shows, only 1 patient was on triple therapy, and that was penicillin +Erythromycin+Amoxicillin and 13 patients were on quarter therapy, and that was Rifampicin+isoniazid+ethambutol+pyrazinamide.

Table 10: Details of prescription containing Multi therapy (N=234)		
Drugs Prescribed	**Number Of Patients**	**Percentage (%)**
Rifampicin+Isoniazid+Ethambutol+Pyrazinamide	13	5.55
Penicillin V+Erythromycin+Amoxicillin	1	0.42

Abdulrahman Al- Yamani et al (2016) conducted a similar study which states that piperacillintazobactam.[4]

4.11 *Dosage form prescribed*

Injections were most commonly prescribed 174 (74.35%)

Table 11: Dosage form prescribed (N=234)		
Dosage Form Distribution	**No.Of Patients**	**Percentage (%)**
Tablets	60	25.64
Injection	174	74.35

In Gujarat, Nishita H et al conducted a prescription audit in the inpatients of a tertiary care hospital attached with medical colleges says that oral dosage (69.54%) were mostly prescribed than injections.[10]

4.12 Drug interaction

Drug interaction was present in 15 prescriptions. 219 prescriptions did not have drug interactions.

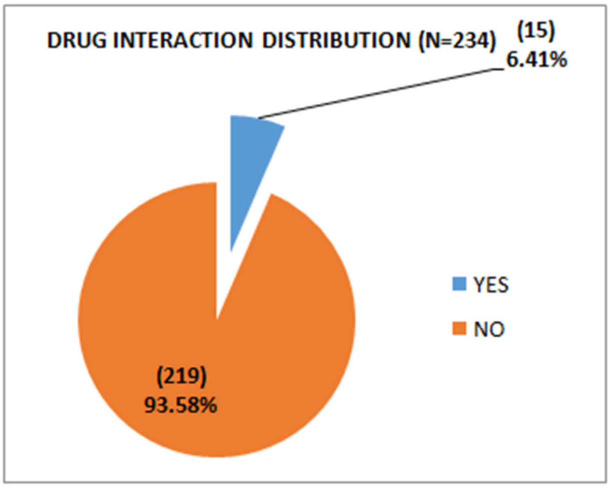

Fig 3. *Drug Interaction (N=234)*

4.13 Drug interactions

Table 12: Drug Interactions found

Primary Drug	Secondary Drug	Reaction
Pantoprazole	Rifampin	Rifampin decrease the level of effect of pantoprazole by affecting hepatic enzyme CYP2C19 metabolism[11]
Rabeprazole	Rifampin	rifampin decreases the level or effect of rabeprazole by affecting hepatic enzyme CYP3A4 metabolism[11]
Acetaminophen	Isoniazid	Isoniazid increases toxicity of acetaminophen by unknown mechanism[11]
Acetaminophen	Rifampin	Rifampin decreases the level of acetaminophen by increasing metabolism[11]
Heparin	Ceftriaxone	ceftriaxone will increase the level or effect of heparin by anticoagulation[11]
Levofloxacin	Hydrocortisone	both increases by other.increases the risk of tendon rupture[11]
Levofloxacin	Azithromycin	both increases QTC interval[11]
Amikacin	Piperacillin-tazobactam	pharmacodynamic synergism[11]
Isoniazid	metronidazole	metronidazole will increase the level or effect of isoniazid by affecting hepatic enzyme CYP2E1 metabolism.[11]
Prednisolone	Rifampin	rifampin decreases the level or effect of prednisolone by hepatic or intestinal enzyme CYP3A4 metabolism.[11]

4.14 Drug interaction pattern

Drug interaction based on severity, among 234 patients 10 (43.47%) suffered from major interactions, there were no moderate interactions found and 13 (56.52%) patients suffered from minor interactions.

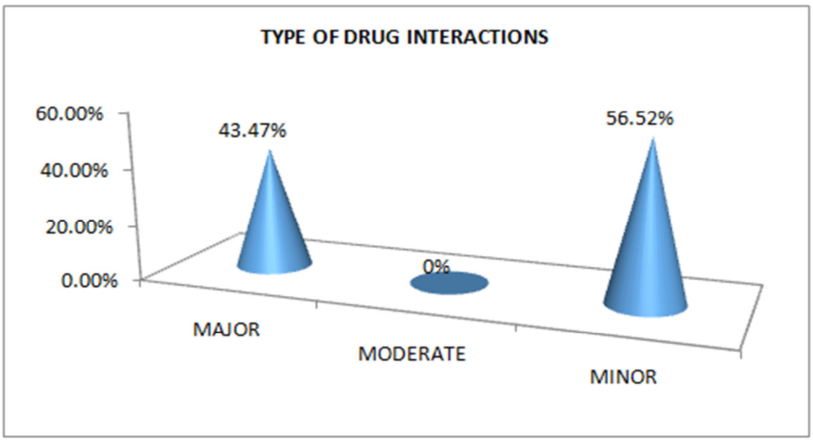

Fig 4. Drug interaction pattern

4.15 *Type of therapy*

Among the total study population Majority of the patients were under (69.65%) empirical therapy and the rest were under targeted therapy (30.34%).

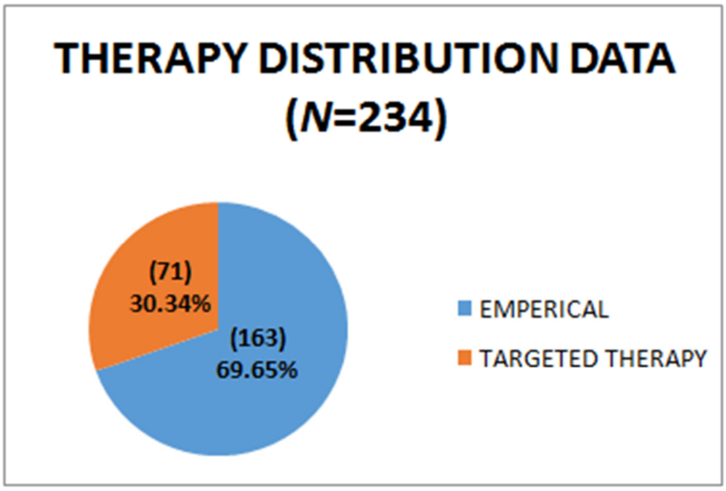

Fig 5. Type of therapy (N=234)

4.16 *Medication error*

Inappropriate drug selection 88 (29.23%), inappropriate dose selection 100 (33.22%), inappropriate duration of antibiotics 103(34.21%), allergic medication prescribed 4 (1.32%) and omission of the dose 6 (1.99%) were found in our study (Fig 6).

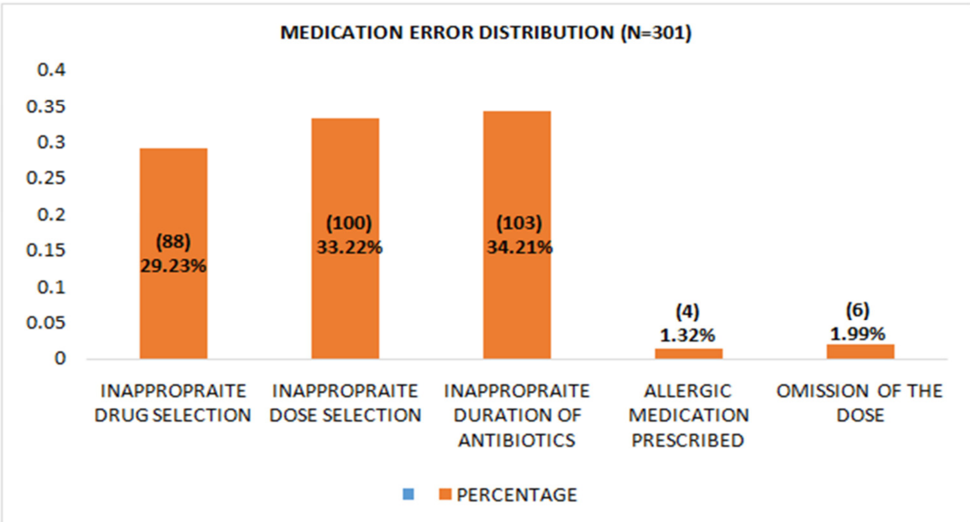

Fig 6. Medication Error (N=301)

In 1990, Aswapokee et al conducted a study in nine medical wards in one of the hospitals in Thailand. The author reported that 44% of admitted patients had been prescribed antibiotics, but only 8% received an appropriate antimicrobial agent. Antibiotics were used without evidence of infection in 35% of the patients. A survey of inpatient antibiotic use in a teaching hospital in south Africa in the medical, surgical and gynaecological wards showed that 27-32% of patients were prescribed antibiotics and 22% of antibiotics were used inappropriately.[12] Borade S et al (2014) conducted a study on the topic evaluation of antimicrobial prescription pattern in Neonatal Intensive Care Unit of a tertiary care teaching hospital. In this study they closely scrutinized the accuracy of antimicrobial administration on the basis of dose and frequency. AMA were administered 145 (59.67%) times with appropriate dose and frequency. In the remaining 40% times either dose or frequency was inappropriate. In our study 301 medication error were reported which include inappropriate drug selection 88 (29.23%) inappropriate dose selection 100 (3.22%), and an inappropriate duration 103(34.21%), allergic medication 4 (1.32%) and omission of dose were 6 (1.99%).

4.17 *Rationality monitoring*

Among 234 patients 109 (46.58%) were rationally prescribed and 125 (53.41%) were irrationally prescribed.

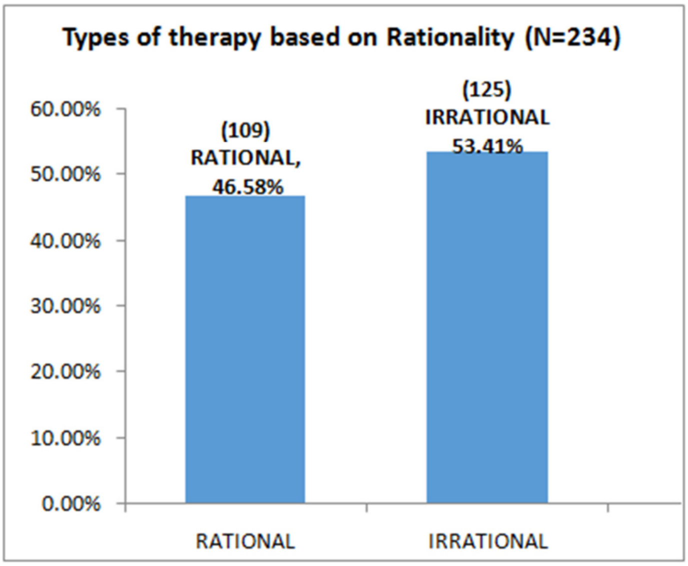

Fig 7. Rationality monitoring (N=234)

Borade S et al (2014) conducted a study on evaluation of antimicrobial prescription pattern in Neonatal Intensive Care Unit of a tertiary care teaching hospital. Number of neonates received antimicrobial agents out of 118 neonates, 66 (56%) were treated rationally. In this study most of the studies and literatures define rationality on the basis of dose, frequency and duration but nothing is mentioned regarding the appropriate drug selection but in our study it is also taken into consideration.

5 CONCLUSION

Antibiotic usage is increasing day by day with or without proper prescription. Antibiotic resistance is at an alarming rate leading to increased morbidity and mortality worldwide. Irrationality in the usage, negligence of standard guidelines and Antimicrobial resistance are increasing complexity in the therapy and Outcome. This study found that irrational use of medication was high (53.41%) and a highly significant medication errors had also been reported; Clinical pharmacist can solve these issues by providing proper drug based counseling to patients and through proper prescription monitoring and a better future of antibiotic therapy can be ensured. Public awareness and sensitization of medical practitioner are the needs of the time, for better future of antimicrobial therapy. Clinical pharmacist- based patient counseling can ensure the involvement of patients in the therapy and in building up a better relationship with medical care team, which is a gateway to the medication adherence, rationality and appropriate usage of antibiotics. So, clinical pharmacist- initiative patient education and periodic revision of certain drug policies can play a vital role in better medical practice.

6 AUTHORS CONTRIBUTION STATEMENT

Mr K C Arul prakasam guided and divided the entire work. Ms. Pooja Chandran conceived the presented idea. Ms. Abhirami Jayachandran, Ms. Asmina sherin H and Ms. Archana M Nair designed the data collection form and worked for getting approval from pulmonologist. The entire team was involved in collecting and compiling the data required for the study. Ms. Abhirami Jayachandran prepared the manuscript with others under the guidance of Mr. K C Arul prakasam.

7. CONFLICT OF INTEREST

Conflict of interest declared none.

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