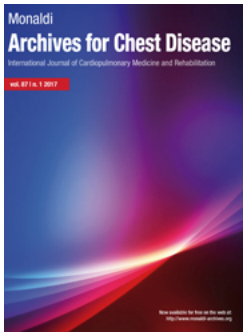

Monaldi Archives for Chest Disease

eISSN 2532-5264 https://www.monaldi-archives.org/

Monaldi Arch Chest Dis 2023 [Online ahead of print]

To cite this Article:
Nyamagoud SB, Swamy AHMV, SP A, et al. **Prescription analysis emphasizing medication adherence of antibiotics in lower respiratory tract infections.** *Monaldi Arch Chest Dis* doi: 10.4081/monaldi.2023.2527

Prescription analysis emphasizing medication adherence of antibiotics in lower respiratory tract infections

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Contribution: Acknowledgement that all authors have contributed significantly and that all authors agree with content of manuscript. Dr. Sanatkumar Bharamu Nyamagoud and AHM Viswanath Swamy worked on concept and design, Anchu S P and Sonia S Gaitonde did the data collection, Jaison M Johnson and Vishwanath Hegadal worked on analysis and interpretation of results. All the authors have read and approved the final version of the manuscript and agreed to be accountable for all aspects of work.

Conflict of interest: The authors declare that they have no conflict of interests, and all authors confirm accuracy.

Availability of data and materials: All data generated or analyzed during this study are included in this published article.

Ethics approval and consent to participate: The study protocol was approved by the Institutional Ethical Committee of KLE College of Pharmacy Hubballi, A constituent unit of KLE Academy of

Higher Education and Research, Belagavi, Karnataka, India (KLECOPH/IEC/2021-22/03 dated 26/11/2021).

Informed Consent: Written informed consent was obtained from a legally authorized representative for anonymized patient information to be published in this article. The manuscript does not contain any individual person's data in any form.

Acknowledgements: The authors are thankful to the Vice-Chancellor, Registrar and Dean of Pharmacy, KLE Academy of Higher Education and Research, Belagavi. We would also like to thank the medical and hospital staff of Vivekanand General Hospital, Hubballi for providing necessary support.

Abstract

Antibiotics are choice of drugs in patients with respiratory infections. Irrational use of antibiotics is an important public health issue faced on daily basis by the community and the individual. Keeping this in consideration, the current study investigates the prescription pattern of antibiotics in lower respiratory tract infections in general population. The aim of the study includes prescription pattern analysis of antibiotics for LRTIs in the general population and to evaluate adherence to antibiotic treatment. This was a hospital-based retrospective observational study conducted between November 2021 to April 2022 in the Department of General Medicine and Pediatrics. Compliance with various antibiotics was scrutinized by using MMAS 4 scale. Patient demographics, laboratory details, prescribed antibiotics, and duration of hospital stay were gathered over a period of 6 months. A total of 200 patients were involved in the study, out of which 53% were males and 47% were females. A total of 2127 drugs were prescribed to 200 patients (10.6 drugs/prescription). Ceftriaxone was the most commonly used antibiotic followed by azithromycin and piperacillin/tazobactam. The most frequently diagnosed disease was bronchopneumonia (41%) followed by A/E COPD (28%). Evaluation of medication adherence resulted in 58% high and 11% poor adherence. The number of antibiotics prescribed was found to be rational, but the prevalence of polypharmacy should be prevented. Medication adherence decreases as the frequency of antibiotics increases, so it is recommended to lower the frequency of drugs as possible to enhance compliance.

Key words: prescription pattern; medication adherence; lower respiratory tract infections; antibiotics.

Introduction

Infectious diseases pose a serious hazard to public health regardless of an individual's age, gender, socioeconomic level, or lifestyle. In India, one million people die each year from respiratory tract infections, with acute lower respiratory tract infections accounting for 10-15% of all deaths [1]. A respiratory tract infection (RTI) is described as an infection that affects both the upper and lower respiratory tracts and is divided into two categories: URTI and LRTI [2].

Lower respiratory tract infections (LRTI)are infections that affect the airway below the larynx including Trachea and Alveolar sacs. The diseases included in the study are acute bronchitis, bronchiolitis, acute exacerbation of COPD, bronchopneumonia and tuberculosis. Appropriate antibiotic selection based on the infecting organism is critical for assuring the safety and efficacy of a particular medication as well as preventing the emergence of resistance [3]. Antibiotics are microorganism-produced chemicals that selectively restrict or kill the growth of other bacteria at very low concentrations [4].

The prescription pattern describes the volume and profile of prescription use, as well as trends, drug quality, and adherence to standard treatment guidelines. Prescription pattern monitoring studies (PPMS) is concerned with monitoring, evaluating, and advising changes to the prescribing pattern in order to provide safe, effective, and cost-efficient patient treatment [5]. The WHO prescribing indicators could be used to examine prescription patterns [6]. In this project, the current version of the WHO 22nd Essential Medicines List (EML) is used to refer essential drug list for prescription pattern analysis.

Patient compliance is the extent to which patient follow their medications as prescribed by healthcare providers. Treatment failure and poor clinical outcomes are caused by non-compliance with antibiotic regimens. Antibiotic adherence is one of numerous actions that must be taken to prevent antibacterial resistance [7]. Poor medication adherence is believed to be the cause of at least 33% of all drug-related hospital admissions in underdeveloped nations. Adherence to antibiotics is critical not just for preventing antibiotic resistance, but also for treating and preventing secondary infections [8]. This study employs the Morisky medication adherence questionnaire-4 (MMAS-4) to assess medication adherence to a discharged antibiotic regimen for lower respiratory tract infections [9].

Materials and Methods

This was an observational study carried out for a period of 6 months from November 2021 to April 2022, conducted on inpatients from the General Department in Vivekananda General Hospital, Deshpande Nagar, Hubballi, a tertiary care hospital in Hubballi over a period of 6 months. The hospital caters to both urban and rural populations. Most of the patients belong to the lower and middle strata of the society. A total of 200 inpatient case records of the general population with LRTI were analyzed.

Inclusion criteria

Patients with lower respiratory tract infections, patients admitted to the Inpatient General Medicine Department, patients of all age groups, both genders, and patients with comorbidities.

Exclusion criteria

Intensive care unit patients, obstetrics and gynecology patients, cases from the Outpatient Department, patients with COVID-19, and patients who are not willing to participate in the study.

Data analysis

Each patient's information was gathered on a form made specifically for case records. The demographic information, diagnosis, hospitalization, drug type, dosage regimen (form, route, frequency, and duration), average number of drugs per encounter, ratio of encounters with an antibiotic prescription, and group-wise antibiotic prescription were all examined in the inpatient case records. Descriptive analysis was performed after pooling the data. Results were analyzed using MS Excel 2019 and SPSS 25.0. Chi- square and Pearson’s correlation tests were carried out to determine the significance and associations among variables.

Results

A total of 200 inpatient case records admitted with LRTI were observed and analyzed. All the inpatient case records had complete documentation of information, including the patients’ demographic characteristics, provisional diagnosis, drug name, dose route and dosage. In this study, the analysis of demographic data showed the majority of patients with LRTI belonged to the 61-75 age group accounting for about 26%. About 53% of the study participants were male

(Table 1). One hundred and thirty-five (135) patients with numerous co-morbidities were identified. Out of these, hypertension (21%), type 2 diabetes (16%) and anemia (9%) were the most frequently reported illnesses. The total number of drugs prescribed was 2127 and mean number of drugs per prescription was 10.6. The most common diagnosis was bronchopneumonia (n=84), the least being bronchiectasis (n=3). In our study, 99% (n=198) of prescriptions contain antibiotics among which 11% received mono antibiotic therapy, 43% dual antibiotic therapy, 22.5% triple therapy and 16% quadruple therapy. Among antibiotics, ceftriaxone was most frequently prescribed (26.5%; n=138), whereas ampicillin, cefpodoxime, gentamicin, clarithromycin, and cilastatin were the least (Figure 1). Most of the antibiotics were parentally administered (60%). Out of 521 prescribed antibiotics, 30% were given as once-daily regimen (n=154), 48%were given as a twice-daily regimen (n=251) and 19% were given as a thrice-daily regimen (n=99) and 3% were given as a four-times daily regimen (n=17) (Figure 2). According to WHO prescribing indicators polypharmacy, increased percentage of encounters with injections, decreased prescription of generic drugs and decreased use of essential medicines were noticed (Table 2). One hundred and forty-one (141) patients were surveyed to check their medication adherence to prescribed antibiotics. For this purpose, MMAS 4 questionnaire is used where "0" value is taken for "yes" and value "1" is taken for "no" (Table 3). With the aid of MMAS4, we discovered that 31% of patients (n=44) were marginally adhering to their drug regimens, while the remaining 11% of patients (n=15) were not adhering at all (Table 4). Using the chi-square test (with $p<0.05$) it was observed that age, educational status, economic status, and frequency of drug regimen had a significant correlation with medication adherence (Table 5).

Discussion

Lower respiratory infections are one of the combined leading infectious causes of death. Antibiotics are the first-line treatment for these infections except for viral infections. In recent years the widespread use of antimicrobials has resulted in an increase in the development of resistance to antibiotics. PPMS and medication adherence are effective ways to monitor prescriptions and analyze the factors influencing non-adherence.

After considering all these factors an attempt to study prescription pattern analysis of antibiotics and medication adherence is carried out. A total of 200 patients were enrolled in this study out of which the majority of subjects were males 105 (53%) compared to that females 95 (47%). A similar study was conducted by Beg *et al.* [1] were 56.41% of patients were male and 43.59% were female.

According to this study, the mean age of participants was found to be 50.12±21.65. This study also indicates that LRTI is more prevalent in elderly subjects belonging to the age group of 61-75 years (26%). These study results are in contrast with the study conducted by Shafinaz *et al*. [10] because in their study most of the patients were in the age group of 18-29 years (37.5%), followed by 30-39 years (27.2%).

Most patients presented with bronchopneumonia (41%) followed by A/E of COPD (28%). A similar study conducted by Ahmed *et al*. [11] had shown similar findings to the present study where 68% of the subject were diagnosed with A/E of COPD followed by CAP (24.0%).

In this study out of 200 patients, 135 of them presented with co-morbidities. Of which the majority of the co-morbidities were hypertension (21%) followed by T2DM (16%), anemia (9%). However, the study conducted by Panicker [12] had shown a similar finding where majority of co-morbidities were found to be diabetes mellitus (34%) followed by hypertension (32%).

In the current study, almost all patients were prescribed antibiotics (99%) and only 2 patients were prescribed without antibiotics. A similar study was conducted by Baby *et al.* [13]. The most widely used antibiotic in this study was amoxicillin + clavulanic acid (58%). A total of 521 antibiotics were prescribed for 200 patients. Out of which majority of participants received twice daily (48%) antibiotic regimens, followed by OD (30%), TID (19%), and QID (3%). Similarly, out of 198 antibiotic prescriptions most of the subjects received dual antibiotic therapy (43%), followed by triple therapy (22.5%). Similar results are shown in the study conducted by MB *et al.* [14] where 32.77% of patients received dual therapy and 39.49% received monotherapy.

The content of a prescription is influenced by a prescriber's training, their attitude towards the disease being treated, and the type of healthcare system within which they work. As per the prescribing indicators developed by WHO, the percentage of encounters with antibiotics was found to be 24.5%, which was within the optimal range. The average number of drugs per patient encounter was found to be 10.6 which was much higher than the optimum range. This value points out the extent of polypharmacy. The percentage of drugs prescribed by generic names was 37.9% and the percentage of drugs prescribed from the WHO essential drug list 2021 22nd edition was 75.9%. Both values suggest that prescription writing using brand names was common and usage of drugs from NLEM was not optimal. A similar study conducted by Kumar *et al.* expresses that an average of 5.59 drugs were prescribed per encounter. The percentage of encounter with antibiotics prescribed was 94% and percentage of drugs from NLEM was 40.09% **[15].**

Medication adherence is one of the major factors which determine the efficacy of the treatment provided. Out of 200 patients enrolled in this study, 141 were prescribed antibiotics during discharge. Since antibiotics are taken for the short-term course, a survey was taken after the discharge of the patients which was assessed using a self-reported MMAS 4 questionnaire. In the present study majority of patients had high (58%) Medication adherence and moderate adherence was shown by 31%. However, in a study by Llor *et al*. [16] it was stated that antibiotic compliance measured by the self-reported compliance questions was exceptionally greater than that objectively determined, indicating that self-reporting is prone to overestimation of true compliance. Hence, there could be a possibility that even in this study; the compliance rate was overestimated [8]. Using MMAS 4, the possible reasons for medication non-adherence were found to be; Omission of single doses of antibiotics in 41% cases, 20% of patients faced problems with remembering to take their medications, 25% stopped their medications because they felt better after taking medications and 23% stopped taking medications because they felt worse after taking the medications. Similar results were shown by studies conducted by Mathew *et al.* where 40% of patients discontinued their therapy when they felt better [17]. Analysis of medication adherence based on the frequency of antibiotics was done by Llor [16]. They found that as higher the number of daily doses of antibiotics the worse the compliance. Likewise in our study patients with a thrice-daily regimen (TID) forgot to take their medication more often than patients with a once-daily or twice-daily antibiotic regimen.

The role of demographics in medication adherence has been depicted in many previous studies using statistical analysis. It was reported that there is a significant relationship between demographics and medication adherence. In our current study, Pearson's chi-square correlation is used to check the significance considering $p<0.05$ as statistically significant. According to our study, it was proven that age, educational background, economics, and frequency of antibiotic use had a significant relation to the medication-taking behavior of the patient. It was found that frequent consumption of antibiotics and polypharmacy can reduce patient adherence to medications which results in unwanted complications like resistance to antibiotics, treatment failure, prolongation of hospital stay, and decreased health-related quality of life.

Conclusions

Prescription pattern monitoring studies help to improve the rational use of medicines and ensure the sagacious use of available resources. This study expresses the overview of the prescription

pattern of antibiotics in lower respiratory tract infections in the general population. Almost all patients were treated with antibiotics despite the presence of viral infections. Rationality of prescription pattern was analyzed using WHO prescribing indicators and it revealed that the prevalence of polypharmacy in hospitals were much higher than we thought. The cautious and judicious use of medications will lower the burden of multidrug resistance and thereby limiting the morbidity and mortality rates [5]. There is a need for conducting educational and training programs among prescribers in order to bring rational use of antibiotics. Adherence to national guidelines should be improved especially for respiratory infections.

Clinical pharmacist plays an important role in early detection and prevention of medication errors and they can also involve in prescription pattern analysis to provide feedback to physicians about the current prescribing trends. Our study highlights the percentage of medication adherence among patients towards prescribed antibiotics; 58% had high adherence, 31% had moderate and 11% had poor adherence. The adherence scores were significantly worse with the thrice-daily antibiotic regimen and better with the once-daily regimen. So, it is recommended to lower the frequency of drugs as possible to enhance compliance. Patient compliance could be improved with a good relationship between patient and provider and should communicate effectively with the patients to improve their knowledge and attitudes.

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Table 1. Socio-demographic distribution of study participants (n=200).

Characteristics	Subclass	Number	Percentage (%)
Gender	Female	95	47
	Male	105	53
Age	<15	20	10
	16 to 30	15	7.5
	31 to 45	41	20.5
	46 to 60	50	25
	61 to 75	52	26
	>75	22	11
Educational status	Educated	76	38
	Uneducated	124	62
Economical status	Above poverty level	60	30
	Below poverty level	140	70

Table 2. The drug utilization evaluation using WHO prescribing indicators.

Prescribing indicators	Total drugs encounters	Average percent	Standard / ideal
The average number of drugs per encounter	2127	10.6	1.6-1.8
Percentage of encounter of antibiotics	521	24.5%	20.0-26.8%
Percentage of encounters with injection	1119	52.6%	13.4-24.1%
Percentage of drugs prescribed by generic name	808	37.9%	100%
Percentage of drugs from EDL	1616	75.9%	100%

Table 3. Medication adherence using MMAS-4 Questionnaire.

MMAS 4 questionnaire	YES		NO	
	No. of patients	%	No. of patients	%
Do you ever forget to take your medications?	82	41	118	59
Do you ever have problems remembering to take your medications?	40	20	160	80
When you feel better, do you sometimes stop taking your medications?	50	25	150	75
Sometimes if you feel worse when you take the medicine, do you stop taking it?	47	23	153	77

Table 4. Outcomes of medication adherence.

Medication adherence	Number of patients	%
Poor	15	11
Moderate	44	31
High	82	58
Total	141	100

Table 5. Factors affecting the outcomes of medication adherence (n=141).

Variables	Medication adherence			p-value
	Poor	Moderate	High	
Age				0.052
<15	1	2	13	
16-30	0	1	9	
31-45	3	8	21	
46-60	4	11	29	
>60	7	22	19	
Gender				0.681
Male	7	26	44	
Female	8	18	38	
Education				0.000*
Educated	3	5	46	
Uneducated	12	39	36	
Economy				0.007
APL	1	9	33	
BPL	14	35	49	
Frequency of Antibiotics				0.001*
Once a day	10	33	55	
Twice a day	9	43	71	
Thrice a day	15	18	33	

*Level of significance at $p<0.005$.

Figure 1. Distribution of prescribed antibiotics for LRTI (others*: linezolid-6, moxifloxacin, vancomycin- 4, clindamycin-2, ampicillin, cefpodoxime, gentamicin, clarithromycin, cilastatin - 1).

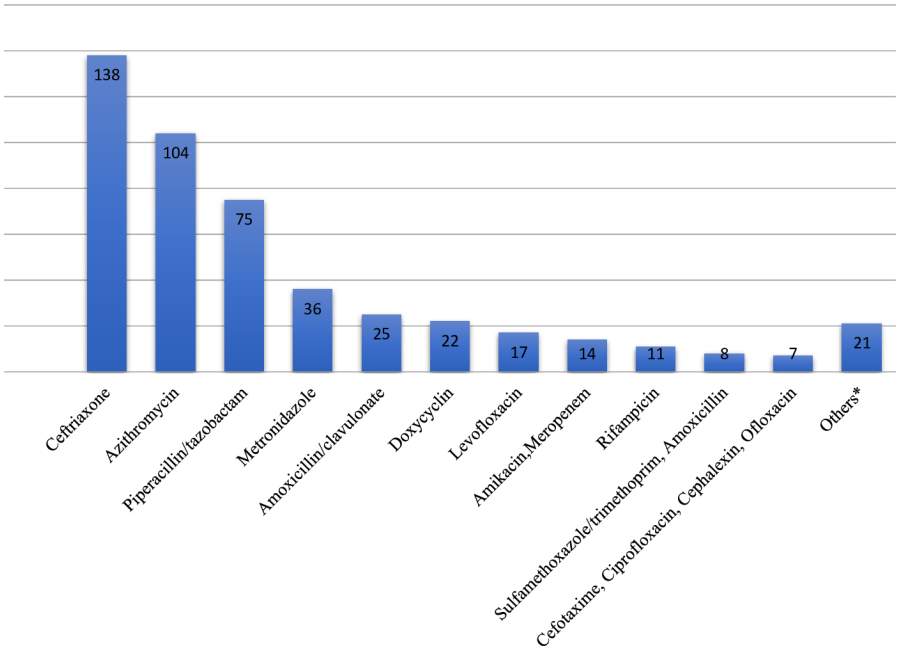
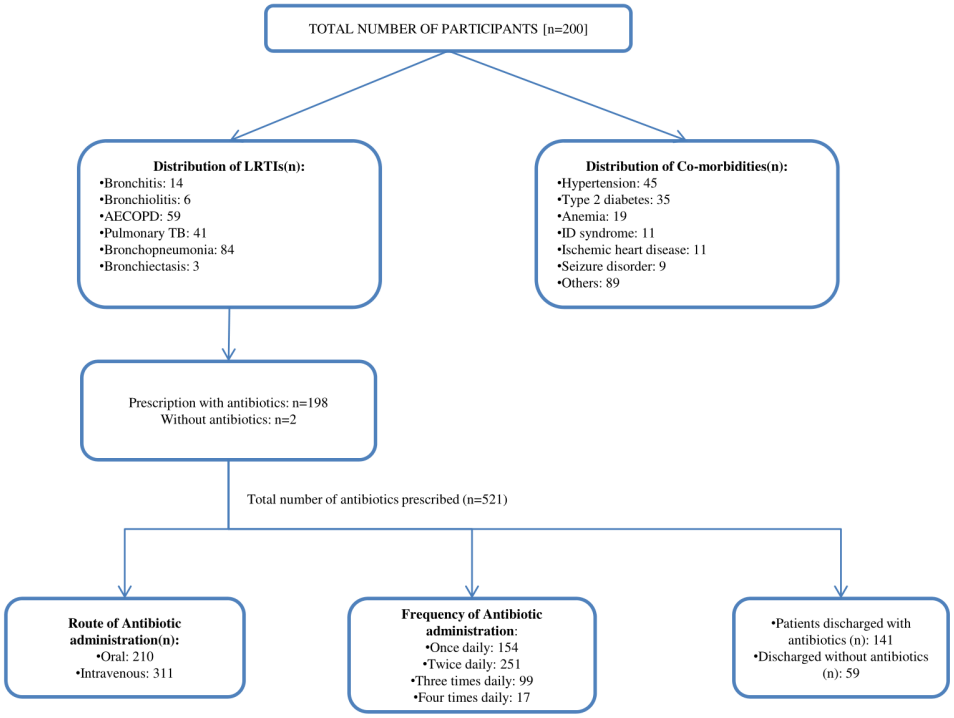


Figure 2. A brief summary of prescription pattern of antibiotics for lower respiratory tract infections.


TOTAL NUMBER OF PARTICIPANTS [n=200]
Distribution of LRTIs(n):
•Bronchitis: 14
•Bronchiolitis: 6
•AECOPD: 59
•Pulmonary TB: 41
•Bronchopneumonia: 84
•Bronchiectasis: 3
Distribution of Co-morbidities(n):
•Hypertension: 45
•Type 2 diabetes: 35
•Anemia: 19
•ID syndrome: 11
•Ischemic heart disease: 11
•Seizure disorder: 9
•Others: 89
Prescription with antibiotics: n=198
Without antibiotics: n=2
Total number of antibiotics prescribed (n=521)
Route of Antibiotic administration(n):
•Oral: 210
•Intravenous: 311
Frequency of Antibiotic administration:
•Once daily: 154
•Twice daily: 251
•Three times daily: 99
•Four times daily: 17
•Patients discharged with antibiotics (n): 141
•Discharged without antibiotics (n): 59