Original Article

Drug Utilization Pattern and Adverse Drug Reaction Monitoring of Antibiotics use in Ear, Nose and Throat Infection at Tertiary Care Hospital, Lucknow, India

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Abstract:

Objective: To investigate the ENT department's (OPD, IPD) antibiotic prescribing practices at a tertiary care hospital in Lucknow, India. **Material and Methods:** A prospective, cross-sectional, non-experimental (observational) study was performed in (OPD, IPD) department of Ear, Nose and Throat (ENT) over a period of 6 months. **Result**: In this study, 100 ENT patients (51 male, 49 female) were selected based on inclusion and exclusion criteria. Ear infections were the most common reason for visits (86 patients), followed by nose (7 patients) and throat infections (5 patients). The most commonly prescribed antibiotics were β-lactam antibiotics, with penicillin's (amoxicillin with clavulanic acid) and cephalosporin's (cefixime) being the most commonly used. Combination therapy was used in 100 patients, with an average of 1.9 antibiotics per patient per course. A total of 40 antibiotics were prescribed, with oral being the most common route of administration. Only one adverse drug reaction was reported, with a suspected link to cefixime causing an increase in rashes in one patient. The study population had comorbid conditions of anxiety, epilepsy, and anaemia. **Conclusions:** To conclude, our study in the university teaching hospital (IIMSR) highlighted lesser utilization of antibiotics in ENT infections, as some of the ENT infections are not due to bacteria. The majority of ENT patients admitted to the hospital appear to have bacterial infections, and most of them reacted favourably to antibiotic treatment. Majority of the patients used the regimen in accordance with the current guidelines.

Keywords: Antibiotic agents, drug utilization, adverse drug reaction, ENT infection.

Introduction:

Adults and children generally are affected by diseases of the ear, nose, and throat (ENT), which can cause severe impairment in patients' daily lives [1]. With the growing global population, infections are expected to remain the leading cause of disease, with upper respiratory tract infections (URTIs) causing hearing loss and learning disabilities. The World Health Organization (WHO) reported in its World Health Report that respiratory infections caused 94.6 disability adjusted life years lost worldwide and were the fourth leading cause of death, accounting for 4.0 million fatalities or 6.9% of all deaths.

In a general hospital, acute respiratory infections account for 20-40% of outpatient visits and 12-35 percent of inpatient stays. URTIs, which include nasopharyngitis, pharyngitis, tonsillitis, and otitis media (OM), account for 87.5 percent of all respiratory infection episodes. They are a major cause of morbidity and workplace absenteeism. Viruses cause the great majority of acute URTIs. In most cases, a common cold is caused by viruses and does not require the use of antimicrobials unless it is accompanied by acute OM with effusion, tonsillitis, sinusitis, or a lower respiratory tract infection. Because most occurrences of rhino sinusitis are viral, they recover on their own without the need for antibiotics [2]. Antibiotics were mostly administered for respiratory and ENT diseases having a viral aetiology, like rhino-pharyngitis and severe bronchitis. Antibiotic prescriptions are written in around 40% of all consultations for rhino-pharyngitis and in about 80% of those for acute bronchitis, according to the findings of the various surveys. Antibiotics were administered in more than 90% of pharyngitis cases, regardless of the patient's age. In contrast, the frequency of consultations for acute middle ear infections has stayed essentially stable over the last ten years, while antibiotic prescriptions have climbed dramatically, reaching 80 percent of consultations. Antibiotic prescription diversity is due to true variances in infecting organisms and antimicrobial susceptibility from country to country or even region to region, but other factors may also be at play, such as physician choice, local policy, costs, and a lack of local guidelines [3]. The current global rise in antibiotic-resistant bacteria, along with a lower trend in new antibiotic discovery, has major health and economic ramifications. Antibiotics are widely misused, including use based on false medical grounds, as well as misuse involving the improper agent, administration method, dose, and treatment duration. Antibiotic use results in the development of resistance as a natural biological process. “Poor patient adherence to dose regimens and the administration of substandard antibiotics result in suboptimal concentrations that fail to treat infection and may promote the formation of resistant bacterial populations; hence, underuse, irrational use, and overuse may both play a role in promoting resistance.” At this time, there is no such thing as an ideal antibiotic, and the overuse of broad-spectrum antibiotics in respiratory infections leads to resistance development in pathogenic bacteria as well as the patient's normal bacterial reservoir [4]. Asia is one of the regions with the

most serious resistance issues. The prevalence of resistant pneumococci in Asian countries, in particular, have been worrying. In India, bacteria resistant to ampicillin, trimethoprim, nalidixic acid, and chloramphenicol are found in nearly every healthy person [5]. Despite the fact that antibiotics have been used in clinical practice for many years, little is understood about how they should be used best in the clinic. How antibiotics should be delivered clinically to reduce resistance development while maintaining safety and efficacy is a crucial and largely unresolved subject. There is a need for data on both antibiotic use and determinants of use from all regions in the world. In too many countries there is no adequate surveillance of prescribing, of drug quality, or of the resistance problem. Through European surveillance of antimicrobial consumption (ESAC) project, significant improvements in the surveillance of antibiotic use in Europe have been achieved. However, a global approach is needed where comparable data are generated [6]. Therefore, studies reflecting drug utilization are required, as they assess the appropriateness of drug therapy. Drug use evaluation is an ongoing, authorized, and systemic quality improvement process that is designed to review the drugs that are prescribed to patients, provide appropriate feedback to clinicians/other relevant groups, develop criteria and standards that describe optimal drug use, and educate and counsel patients on appropriate drug use. Prospective drug utilization studies can directly influence patient treatment and outcome. Pharmacovigilance of antibiotics for its safer use is also essential; the overall purpose of pharmacovigilance is improvement in the safety of medicines (WHO, 2004). The estimation of the probability that a drug caused adverse clinical event is usually based on clinical judgment. Using the conventional categories and the criteria of definite, probable, possible and doubtful adverse drug reaction generates wide variability scales (Naranjo's and WHO's probability scale). The Naranjo's scale categorizes the reaction as highly probable, probable, possible and unlikely; this probability scale is based on simple questionnaire that can be answered rapidly [7], this scale is easier and time saving as compared to WHO's probability scale.

Hence, the present prospective study was aimed to evaluate drug utilization pattern and adverse drug reaction monitoring of antibiotics use in ear, nose and throat infections.

Methodology:

Study design

The present study is a prospective study, which utilizes a Medication Utilization Pattern formulated according to the WHO format. The study was conducted at a tertiary care and teaching hospital in Lucknow, encompassing both the IPD and OPD facilities of the 500-bedded institution. The duration of the study spanned a period of six months.

The study population consisted of 100 patients who willingly participated and were enrolled based on predefined inclusion and exclusion criteria.

Inclusion criteria encompassed patients of any age and gender visiting the OPD and IPD, prescribed with at least one antibiotic for ENT (Ear, Nose, and Throat) infection. On the other hand, exclusion criteria included patients who were not being treated for ENT infection, patients unable to comply with the study requirements, as well as mentally retarded and unconscious patients. The sources of data for the study included physician prescribing records and the patients' medication profiles.

Method and Materials used

Medication Utilization and Suspected Adverse Drug Reaction Monitoring (MUADRM) form and CDSCO Suspected ADR Reporting Form. The data will be collected in a predesigned proforma from the medical record sheets, drug charts, and laboratory investigations of patients. The enrolled patients will be 100 observed from admission till discharge. Descriptive statistics will be applied to the collected data and analysed using Microsoft Excel software.

Data collection

The following data were collected based on the questionnaire:

Patient profile including age, sex, weight, patient address, and marital status; drugs prescribed, both generic and brand names; drugs dose and frequency; as well as demographics, current diagnosis, and medical history.

Evaluation of parameters

- The following parameters were evaluated in the research study: types of antibiotics prescribed, the average number of antibiotics per prescription, the average age range of patients utilizing antibiotics, a comparison of antibiotics prescribed in monotherapy versus fixed-dose combination therapy, a comparison of antibiotics prescribing by generic versus brand name, compliance or adherence assessed using Weekly Diary Cards, with a criterion for noncompliance defined as less than 80% of the recommended intake of prescribed drugs. Additionally, the mode of administration of drugs, concomitant diseased conditions, and the most commonly used agents of a particular class, the most common diagnosis, the average cost of drug per prescription, and the occurrence and severity of adverse drug reactions due to antibiotics were examined.
- There are some examples of suspected adverse drug reactions due to antibiotics mentioned in the table [Table A].

Table A: Some suspected ADRs due to antibiotics

Class	Drugs	Adverse reaction
Beta - Lactams		
A. Penicillins	Amoxicillin, Amoxicillin + Clavulanic acid Piperacillin +Tazobactum	Nausea, vomiting, diarrhoea, erythematous maculopapular rashes, erythema multiforme, hypersensitivity vasculitis, urticaria, Anaphylaxis, Stevens-Johnson syndrome, Diarrhoea/loose stools, skin rashes, urticaria, vaginitis
B. Cephalosporins	Cefadroxil , Cefpodoxime, Cefixime, Cefixime , Ceftriaxone, cefoperazone + salbactum, cefepime + Tazobactum	Nausea, vomiting, diarrhea, rash, urticaria, angioedema, pruritus, erythema multiforme, Stevens-Johnson syndrome, Anaphylactic reaction, Diarrhoea, nausea, abdominal pain, vomiting, diaper and skin rash, headache, pruritus, Anaphylactic reaction
C. Carbapenems	Meropenem, Imipenem, Doripenem	Gastrointestinal upset and diarrhea, Nausea, Seizures, Headache, Rash and allergic reactions, Hypokalemia
Glycopeptides	Vancomycine , Teicoplanin	Hypersensitivity reactions (eg. Anaphylaxis, redman syndrome), AKI, hearing loss, vertigo, fever, chills.
Aminoglycoside	Amikacin, Gentamycin, Streptomycin	Ototoxicity, Nephrotoxicity, Vertigo
Quinolones	Ciprofloxacin, Norfloxacin Ofloxacin, Levofloxacin Moxifloxacin	Nausea (rare), irreversible damage to central nervous system (uncommon), tendinosis (rare)
Macrolides	Azithromycin, Clarithromycin	Nausea, vomiting, and diarrhea (especially at higher doses), Jaundice

Statistical analysis

- Descriptive statistics were applied to the collected data using Microsoft Excel software. Results are expressed in percentages and mean-standard deviation (SD).
- ANOVA / Student's T- test was applied on the collected data to evaluate the statistical significance.

Ethical considerations

The study was complied fully with the WHO guidelines and done after obtaining approval from Institutional Research and Ethics Committee with approval no IEC/IIMS&R/2021/58.

Informed Consent Form

An oral and written consent was obtained from the patient before participation of subject in the study.

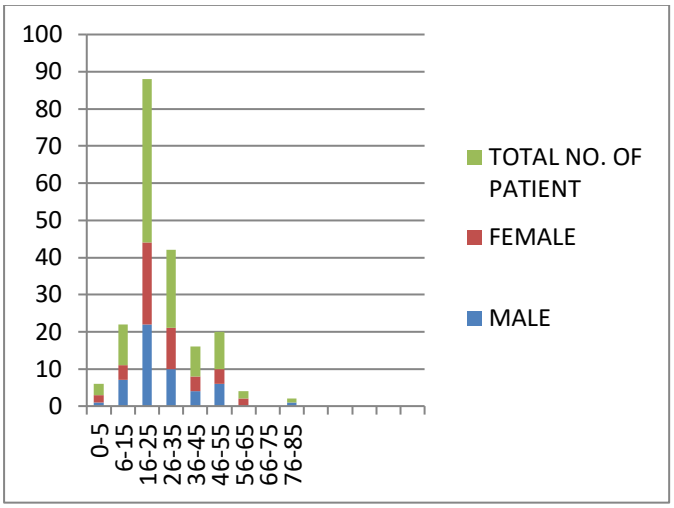
RESULT

Demographic Character of Study Population

A total of around 700 patients visited the ENT OPD and IPD, over a period of 6 months. On the basis of inclusion and exclusion criteria, 100 patients were selected for the present study. Among the 100 ENT patients, 51 were male and 49 were female. The highest numbers of patients were in the age group 16–25 years and the lowest percentage was geriatric patients (Table 1, Graph 1).

Table 1 (Demographic Character of Study Population)

Age	Male	Female	Total
0-5	1	2	3
6-15	7	4	11
16-25	22	22	44
26-35	10	11	21
36-45	4	4	8
46-55	6	4	10
56-65	0	2	2
66-75	0	0	0
76-75	1	0	1
TOTAL	**51**	**49**	**100**



Graph 1 (Demographic Character of Study Population)

Type of ENT Infection

During the study, it was observed that 87 patients visited for treating ear infection, 7 for nose infections, 5 for throat infections and 1 for combination of ENT infections (Table 2).

Table 2 (Type of ENT Infection)

Type Of Ent Infection	No. Of Patients
Ear	87
Nose	7
Throat	5
Combination (ENT)	1

Average Number of Antibiotics per Prescription

During the study, it was observed that the most commonly prescribed antibiotics were β-Lactam (penicillin's and cephalosporin's)–107, followed by Quinolones- 2, Macrolides- 2, Chloramphenicol – 43, Tetracycline – 2 and Aminoglycosides -43 (Table 3).

Table 3 (Average Number of Antibiotics Per Prescription)

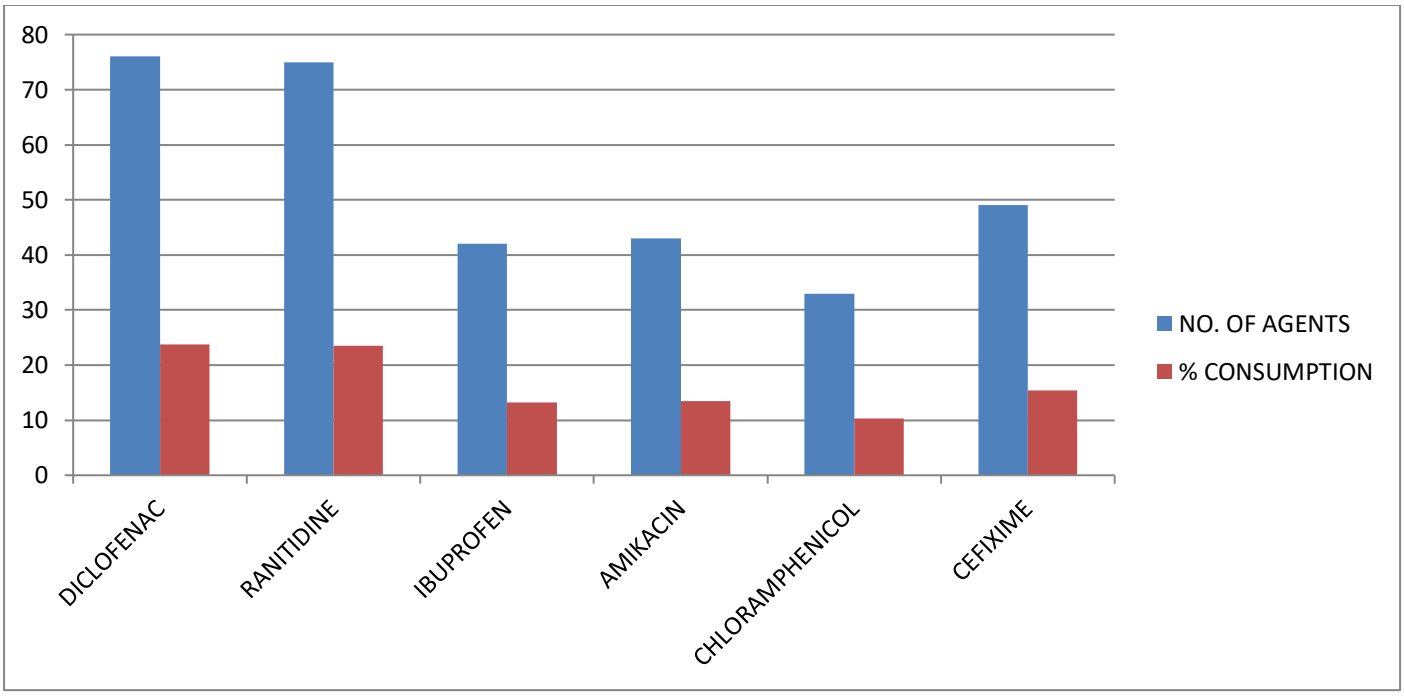
Antibiotics	No. Of Agents	% Consumption
Amoxiclav	39	25
Clavulanic Acid	11	7.05
Cefuroxime	2	1.28
Cefixime	45	28.84
Ceftriaxone	6	3.84
Doxycycline	1	0.64
Chloramphenicol	2	1.28
Amikacin	43	27.56
Azithromycin	3	1.92
Clathromycin	4	2.56

Most Commonly Used Agents

The most commonly used agent of these classes, i.e., β-lactam was penicillin's (amoxicillin with clavulanic acid-50) and cephalosporin's (cefixime-49) followed by quinolones (chloramphenicol-43), macrolides (azithromycin-3), tetracycline's (doxycycline-1) and aminoglycoside (amikacin-43) (Table 4, Graph 2).

Table 4 (Most Commonly Used Agents)

Commonly Used Agents	No. Of Agents	% Consumption
Diclofenac	76	23.8
Ranitidine	75	23.5
Ibuprofen	42	13.2
Amikacin	43	13.5
Chloramphenicol	33	10.3
Cefixime	49	15.4



Graph 2 (Most Commonly Used Agents)

Comparison of Antibiotics Prescribed in Monotherapy VS Fixed-Dose Combination Therapy

The prescription of patients showed that a total of 8 patients received antibiotics as monotherapy, whereas 12 patients were on multiple drug therapy. Among those who were treated with drug combinations, 25 received two drugs, 43 received three drugs and 17 received four drug regimens (Table 5). The average number of antibiotics agents prescribed per patient per course was found to be 19.894%

Table 5 (Comparison of Antibiotics Prescribed in Monotherapy VS Fixed-Dose Combination Therapy)

Antibiotics Prescribed	No. Of Prescription	% Of Prescription
Single	8	8
Two	25	25
Three	41	41
Four	14	14
Multiple	12	12

Mode of Administration of Drugs

A total of 40 antibiotics (this calculation is from both IPD and OPD and post- operative and pre-operative medications from day 1 to date of discharge of 100 patients) were prescribed. Their routes of administration were oral (30), intravenous (6) and ear drop (4) (Table 6).

Table 6 (Mode of Administration of Drugs)

Mode of Administration	No. Of Drugs
Oral	30
IV	6
Otic (Ear Drop)	4

Concomitant Disease Conditions

The comorbid condition of the study population was found was anxiety, epilepsy, anaemia.

Occurrence and Severity of ADR due to Antibiotics

Overall 1 ADRs were reported during the study. Increase in no. of rashes in 1 patients due to suspected drug cefixime.(Table 7)

Table 7 (Occurrence and Severity of ADR due to Antibiotics)

Medicine	Diarrhoea	Headache	Dizziness	Eosinophilia	Gi Upset	Itching	Rashes	Nausea & Vomiting
Amoxiclav	0	0	0	0	0	0	0	0
Cefixime	0	0	0	0	0	0	1	0
Chloramphenicol	0	0	0	0	0	0	0	0
Amikacin	0	0	0	0	0	0	0	0
Ranitidine	0	0	0	0	0	0	0	0
Ibuprofen	0	0	0	0	0	0	0	0
Diclofenac	0	0	0	0	0	0	0	0
Nitrofurantoin	0	0	0	0	0	0	0	0

Discussion

Prescription by a doctor may be taken as a reflection of physician's attitude to the disease and role of the drug in treatment. It also provides an insight into the nature of health care delivery system. Little information exists about the prescriptive behaviour of physicians and the misuse of antibiotics in the management of outpatient and inpatient with ENT infections.

In general practice, the therapeutic approach for ENT infections is nearly empirical and the main aim of physicians is to treat as specifically as possible, while covering the most likely pathogens. The present descriptive study indicates general trends of prescribing in the OPD and IPD of ENT department

Demographic characteristics showed that percentage of males suffering from ENT infections was more than females. Many other studies showed that females are more sensitive to ENT infections than males; the reason might be their exposure to kitchen smoke. In our study, the observed percentage of males was predominant which might be due to the occupational reasons.

Further, it was found that a majority of the patients were in the age group of 16–25 years and the lowest percentages were in geriatric group. It indicates that ENT infections are more prevalent in young adults. Few studies have reported that majority of patients fell in different age groups like 35 - 55 years.

Patients suffering from various acute and chronic ENT infections were treated with different antibacterial agents. In our study, the number of patients with OM was maximum, however the cases of acute and chronic suppurative OM (ASOM and CSOM) observed. The cases sinusitis, DNS (DEVIATED NASAL SPETUM), allergic rhinitis predominate in nose-infected patients, Thyroglossal Fistula and Chronic Rhinosinusitis Polyposis. However, sore throat, acute pharyngitis were the maximum cases of throat-infected patients. It was an interesting observation that a significant number of patients with combination of ENT patients suffered from URTIs alone or along with OM and other infections.

Most commonly prescribed categories of antibiotics were found to be β-lactam (32.05%), followed by cephalosporin's (36.53%), Aminoglycosides (27.56%) and macrolides (1.92%). The chloramphenicol and tetracyclines constituted only 1.28 and 0.64%, respectively. Among the individual antibiotic drugs, maximum patients received a combination of amoxicillin with clavulanic acid (25%), followed by Cefixime (28.84%), amikacin (27.56) chloramphenicol (1.28%), azithromycin (2.56%), clarithromycin (1.92%) ceftriaxone (3.84%) and doxycycline (0.64%). So, the use of azithromycin and clarithromycin should be indicated only when their broad coverage is required or when other antibiotic use is prohibited due to allergy, etc.

However, a change in the prescribing patterns from a small spectrum to penicillin to amoxicillin/clavulanate, as indicative in our study, could be due to an increase in antibiotic resistance which encourages physicians to choose a broader and safer option. Further, 7.61 %patients received

antibacterial monotherapy; whereas 91.8 % patients were on multiple drug therapy.

Limitation of Study

Our study has many limitations. The study was carried out over a six-month period, and the seasonal variations in disease pattern and drug utilization were not considered. Furthermore, the no of patients was low and the study was restricted only one hospital, hence the result cannot be considered representatives of the whole country. However, in spite of all these limitations, our study highlighted some rational prescribing practices. Continuing education on rational drug use and development of easy to use treatment guidelines for common disease suggested. In our future endeavours, we plan to study the effect of regulatory and educational interventions on drug use patterns in the management of Ear, Nose and Throat Infections.

Conclusion

To conclude, our study in the university teaching hospital (IIMSR) highlighted lesser utilization of antibiotics in ENT infections, as some of the ENT infections are not due to bacteria. It appears that majority of the ENT patients visiting the hospital have infections primarily due to bacteria and most of the patients responded well to the use of antibiotics. Majority of the patients used the regimen in accordance with the current guidelines.

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Author contributions

All authors have accepted responsibility for the entire content of this manuscript and approved its submission.

Competing interests: Author states no conflict of interest.

Confidentiality of data

The data identifying each subject by name was kept confidential and accessible to the study personnel.

Data Availability

The patient's data have not been made public. They are kept with all the authors. If anyone need this data then request to corresponding author via e-mail.

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