



Received on 06 June, 2017; received in revised form, 13 August, 2017; accepted, 29 August, 2017; published 01 March, 2018

ANALYSIS OF ANTIMICROBIAL USAGE PATTERN: A RETROSPECTIVE OBSERVATIONAL STUDY

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Keywords:

Drug utilization, Prescription, Antimicrobials, Retrospective

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ABSTRACT: Objective: Antimicrobials have become one of the most misused therapeutic agents resulting in resistance. Present study was carried out to evaluate the antimicrobial drug utilization pattern. **Method:** A retrospective, observational record based study was done in hospitalized patients from medicine and surgery department of tertiary care hospital of central India over a period of one year. **Result:** Among 385 patients, 53.25% were females and 26.75% were in 41 - 50 years age group. Amongst 775 antimicrobials prescribed, 75% were injectables. Average number of antimicrobials per prescription was 2.01 ± 0.6 . Use of antimicrobial monotherapy (39.74%) was common and 25.71% had more than two antimicrobials. About 33.16% drugs were prescribed by generic names and FDCs were prescribed in 37.14%. Culture and sensitivity tests were done in 35.6% cases. Cephalosporins (65.19%) were the most preferred antimicrobials followed by penicillins, aminoglycosides and antiamoebics. Ceftriaxone, amikacin and metronidazole were the most commonly prescribed antimicrobials. Prescribed daily dose (PDD) was greater than defined daily dose (DDD) for ceftriaxone, amikacin, amoxicillin, metronidazole and levofloxacin indicating their wide usage. **Conclusion:** Antimicrobials' prescribing in our hospital is empirical; there is a need for strict antibiotic prescription policy. Generic drug prescribing should be encouraged. Such type of studies should be carried out regularly to evaluate the changes in the pattern and its rationality.

INTRODUCTION: Antimicrobial drugs are the greatest contribution of 20th century to therapeutics. They are one of the few drugs which can cure and not just palliate disease. Their importance is magnified in the developing countries, where infective diseases predominate. Today, almost one third of the patients receive one or the other antibiotic during their course of hospital stay¹. However, antibiotics have become one of the most misused therapeutic agents available to the medical profession.

Their indiscriminate use has resulted in the emergence of resistant strains contributing significantly towards rise in the escalating health care costs and patient morbidity and mortality². It is the responsibility of the doctors to develop good prescribing habits which will help in reducing the intensity of the problem. Drug utilization evaluation is a tool to improve the rationality in prescribing *i.e.* it helps in monitoring the drug efficacy, cost constraints and other factors related to patient safety³. It also plays a key role in minimizing adverse drug effects⁴.

WHO has developed a unit of drug use measurement called defined daily dose (DDD). The methodology used in these studies mainly consists of comparison of consumption using DDD, which is the assumed average maintenance dose per day for a drug used for its main indication in adults.

	QUICK RESPONSE CODE DOI: 10.13040/IJPSR.0975-8232.9(3).1231-36
	Article can be accessed online on: www.ijpsr.com
DOI link: http://dx.doi.org/10.13040/IJPSR.0975-8232.9(3).1231-36	

The DDD does not necessarily reflect the recommended or actual dose used. The other way of expressing drug consumption is prescribed daily dose (PDD)⁵. In this context, we felt that there is a need to do an audit of antibiotic prescribing patterns which could be an important indicator of the quality and standard of clinical practice. So, the study was carried out to evaluate the pattern of antimicrobial drug use at a tertiary care teaching hospital of the central India.

MATERIALS AND METHODS: Present study was carried out in indoor patients of Chirayu medical college and hospital, Bhopal after the permission from Institutional Ethics Committee. It was a retrospective, observational record based study carried over a period of one year. Patients admitted in department of medicine and surgery were randomly selected and included in the study. Case records of the patients were collected from the medical record department (MRD) of the hospital. Total 500 patients' data was screened and 385 patients who received antimicrobial therapy were selected.

A specially designed case record form was used to collect the required information. Patient related information such as age, sex, diagnosis and date of admission and discharge was noted. Drug related information contained details such as number of antimicrobials prescribed, name and category of antimicrobial agent, dosage form, route of administration, antimicrobials prescribed by generic or brand name and use of fixed dose combinations (FDC). Prescribed drugs were classified according to the Anatomical Therapeutic Chemical (ATC) – Defined Daily Dose (DDD) classification. DDDs were obtained from the WHO ATC/DDD website 2017⁶. Prescribed Daily Dose (PDD) was calculated by taking the average of the daily doses of the antimicrobial drugs. The PDD to DDD ratio was then noted. Data was analyzed using Microsoft Excel 2010 and values were presented as average or percentage, as applicable.

RESULTS: Out of 385 cases analyzed, 53.25% were females and 46.75% were males. Most of the cases were in the age group of 41 to 50 years (26.75%) followed by 31 to 40 years (22.86%) as shown in **Table 1**.

TABLE 1: DEMOGRAPHIC DETAILS OF STUDY POPULATION

Age in years	Male	Female
< 20	17	18
21-30	31	36
31-40	37	51
41-50	48	55
51-60	32	18
> 60	15	27
Total	180 (46.75%)	205 (53.25%)

A wide spectrum of clinical diagnoses was observed including chest infection, urinary tract infection, febrile illness, malaria, head injury, appendicitis, hemorrhoids, CVS related disorders and sepsis. Average duration of hospitalization in our study population was around 5 days. A total of 775 antimicrobials were prescribed, out of which 577 were injectables. Average number of the drugs per prescription was 2.01 ± 0.6 . About 33.16% drugs were prescribed by generic names and FDC were prescribed in 37.14% cases. **Fig. 1** show the distribution of the number of antimicrobial drugs per prescription which ranges from 1 to 6.

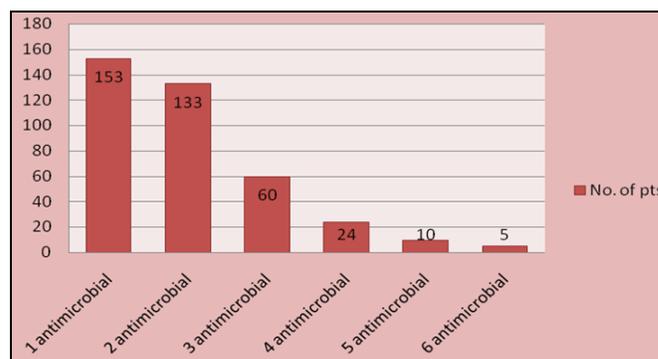


FIG. 1: DISTRIBUTION OF ANTIMICROBIAL DRUGS PER PRESCRIPTION

Cephalosporins (65.19%) were the most preferred antimicrobials followed by penicillins, aminoglycosides and antiamoebics as shown in **Fig. 2**

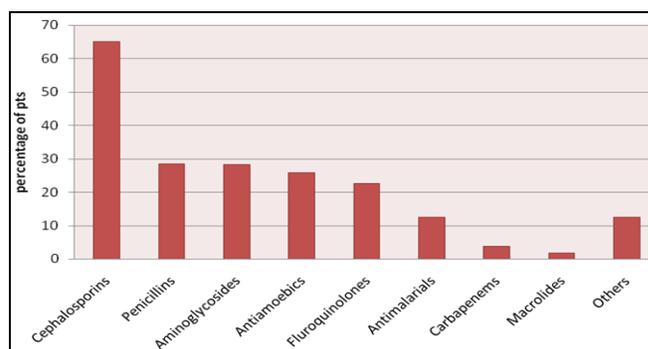


FIG. 2: PRESCRIBING FREQUENCY OF ANTIMICROBIALS

Usage of each antimicrobial is shown in **Table 2**. Ceftriaxone was the most common drug amongst all the antimicrobial agents used in 32.47% patients followed by amikacin (24.94%), metronidazole (22.08%) and amoxicillin with clavulanic acid (19.48%).

TABLE 2: PRESCRIBING FREQUENCY OF INDIVIDUAL ANTIMICROBIALS

Drug group	Subgroup	Prescribing frequency (%)
Cephalosporins (n=251)	Ceftriaxone	32.47
	Cefotaxime	16.10
	Cefoperazone	6.49
	Cefixime	4.42
	Cefuroxime	3.90
	Cefpodoxime	1.30
	Cefepime	0.52
Penicillins (n= 110)	Amoxicillin	19.48
	Piperacillin	7.27
Aminoglycosides (n= 109)	Ampicillin	1.82
	Amikacin	24.94
	Gentamicin	3.38
Antiamoebics (n= 100)	Metronidazole	22.08
	Tinidazole	3.90
Quinolones (n= 87)	Ciprofloxacin	10.39
	Levofloxacin	6.49
	Norfloxacin	3.12
	Moxifloxacin	1.82
	Ofloxacin	0.78
Antimalarials (n=48)	Artesunate	9.87
	Chloroquine	2.08
	Primaquine	1.30
Carbapenems (n=15)	Meropenem	3.38
	Imipenem	0.52
Macrolides (n=7)	Azithromycin	1.30
	Clarithromycin	0.52
Others (n=48)	Fluconazole	3.38
	Doxycycline	3.12
	Clindamycin	2.08
	Albendazole	1.30
	Teicoplanin	0.78
	Aztreonam	0.52
	Aciclovir	0.52

Pattern of antimicrobial drug use as per the ATC/DDD classification is shown in **Table 3** and **4** denotes the comparison of PDD & DDD values.

TABLE 3: ATC CODE, DDD, PDD AND PDD/DDD RATIO OF ANTIMICROBIALS

S. no.	Drug	ATC code	DDD (gm)	PDD (gm)	PDD / DDD
1	Ceftriaxone	J01DD04	2	3	1.5
2	Cefotaxime	J01DD01	4	4.5	1.13
3	Cefoperazone	J01DD12	4	4	1
4	Cefixime	J01DD08	0.4	0.43	1.07
5	Cefuroxime	J01DC02	0.5	0.45	0.9
6	Cefpodoxime	J01DD13	0.4	0.39	0.98
7	Cefepime	J01DE01	2	1.78	0.89
8	Amoxicillin	J01CA04	1	1.68	1.68
9	Piperacillin	J01CA12	14	14.2	1.01
10	Ampicillin	J01CA01	2	1.76	0.88
11	Amikacin	J01GB06	1	1.24	1.24

12	Gentamicin	J01GB03	0.24	0.18	0.75
13	Metronidazole	J01XD01	1.5	1.76	1.17
14	Tinidazole	J01XD02	1.5	1.35	0.9
15	Ciprofloxacin	J01MA02	1	0.8	0.8
16	Levofloxacin	J01MA12	0.5	0.75	1.5
17	Norfloxacin	J01MA06	0.8	0.7	0.88
18	Moxifloxacin	J01MA14	0.4	0.30	0.75
19	Ofloxacin	J01MA01	0.4	0.45	1.13
20	Artesunate	P01BE03	0.28	0.30	1.07
21	Chloroquine	P01BA01	0.5	0.5	1
22	Primaquine	P01BA03	0.015	0.015	1
23	Meropenem	J01DH02	2	1.8	0.9
24	Imipenem	J01DH51	2	1.75	0.875
25	Azithromycin	J01FA10	0.3	0.3	1
26	Clarithromycin	J01FA09	0.5	0.45	0.9
27	Fluconazole	J02AC01	0.2	0.2	1
28	Doxycycline	J01AA02	0.1	0.15	1.5
29	Clindamycin	J01FF01	1.2	1	0.833333
30	Albendazole	P02CA03	0.4	0.4	1
31	Teicoplanin	J01XA02	0.4	0.35	0.875
32	Aztreonam	J01DF01	4	3.75	0.9375
33	Acyclovir	J05AB01	4	4	1

TABLE 4: COMPARISON OF PDD AND DDD

PDD > DDD	PDD < DDD	PDD = DDD
Ceftriaxone	Cefepime	Cefoperazone
Amoxicillin	Ampicillin	Azithromycin
Metronidazole	Ciprofloxacin	Chloroquine
Amikacin	Gentamicin	Primaquine
Levofloxacin	Aztreonam	Albendazole
Cefotaxime	Cefpodoxime	Flucanazole
Cefixime	Cefuroxime	Acyclovir
Piperacillin	Tinidazole	
Ofloxacin	Norfloxacin	
Artesunate	Moxifloxacin	
Doxycycline	Meropenem	
	Imipenem	
	Clarithromycin	
	Clindamycin	
	Teicoplanin	

DISCUSSION: Antibiotics being the most commonly prescribed group of drugs, the problem of its overuse is a global phenomenon. Drug utilization studies are powerful exploratory tools to ascertain the role of drugs in the society. By monitoring the antimicrobial pattern in a particular geographical area, we can improve the quality of health care system by proper intervention. Present study was carried out to evaluate the antimicrobial drug utilization pattern in our institute.

The average number of antimicrobials per prescription came out to be 2.01% which is in the range of 1.3 - 2.2 found in similar studies in other countries⁷. These findings suggest limited incidence of polypharmacy. It is preferable to keep the number of drugs per prescription as low as possible since polypharmacy leads to increased risk of drug interactions, increased hospitalization cost and errors of prescribing.

Out of the 385 prescriptions, use of antimicrobial monotherapy (39.74%) and 2 drug therapies (34.55%) was common and 25.71% had more than two antimicrobials. This could be expected since many patients were having mixed type of infection, so two or more antimicrobials had been used to cover the pathogens. Drugs covering gram +ve, gram -ve and in certain situation anaerobes as well were given together.

The most common route of antimicrobial administration was parenteral that accounted for 74.45% and oral for 25.55%. This is because ceftriaxone, amikacin, & metronidazole which are mainly used parenterally contributed to the large section of the prescription sample. Parenteral to oral shift was practiced in 1.5% cases.

Clinicians prescribed a significant number of antimicrobials (33.16%) by generic names but majority were used by brand (proprietary) names. This is similar to some previous studies where brand name drugs were commonly prescribed^{8, 9}. This is an issue of concern and can be readdressed to some extent by prescribers' education.

The development of FDC has become important from public health perspective. In our study FDCs were used in 37.14% amongst them 1% were not from rational medicine list of WHO whereas Laveesh *et al.*, reported that FDC were used in 35 % patients among which 66.66% were irrational¹⁰. We considered FDCs rational or irrational as per the FDCs notified by DCGI, India in July 2016¹¹. Commonly used FDC were amoxicillin + clavulanic acid, piperacillin + tazobactam, ceftriaxone + sulbactam and cefoperazone + sulbactam.

Among the antimicrobials, cephalosporins were found to be prescribed to the largest number of patients (65.19%) followed by penicillins (28.57%) and aminoglycosides (28.31%). Similar findings were observed in many studies^{12, 13, 14}. Amongst cephalosporins, third generation is the most commonly prescribed one. Cephalosporins are group of antibiotics with broad spectrum of activity, low rate of toxicity and ease of administration. Due to their activity against most gram-ve organisms and their availability, third generation cephalosporins are most commonly

used. This may put cephalosporins having wider action including activity against pseudomonas into danger of becoming ineffective.

Ceftriaxone was the most frequently prescribed antimicrobial drug in 32.47% of patients followed by amikacin (25%) and metronidazole (22%) similar to other studies^{15, 16}. Ceftriaxone has high antibacterial potency, wide spectrum of activity and low potential for toxicity. It is used to treat different types of bacterial infections including respiratory, bone, abdominal, urinary tract and skin infections. Gidamudi *et al.*, reported that ceftriaxone was the most common antimicrobial used for treatment of urinary tract infections¹⁷. Study done in pediatric patients in Ethiopia also showed that ceftriaxone was the most frequently prescribed antibiotic¹⁸.

When the PDD to DDD ratio is either less than or greater than one, it may indicate that there is either under or over utilization of drugs. Nevertheless, it is important to note that the PDD can vary according to patient and disease factors. For instance, amongst anti-infectives, PDD vary according to the severity of the infection. The DDDs for most anti-infectives are based on treatment of moderately severe infections. In hospital care, much higher doses are frequently used and this must be considered when using the DDD as a unit of measurement¹⁹. The PDDs can also vary substantially between different countries. Thus, WHO encourages countries to have their own DDD list based on indigenous data.

In our study PDD/DDD ratio was greater than 1 for the antimicrobials such as ceftriaxone, amoxicillin, amikacin, metronidazole and levofloxacin indicating their wide use. Culture and sensitivity tests were done in 35.6% cases and remaining were managed empirically. Culture and sensitivity is not always feasible due to cost factor, time constraint and also the antimicrobials are prescribed depending upon the clinical experience of the doctors. Thomas *et al.*,²⁰ in India observed that empirical use of antimicrobials in primary care centre was 100% and it was 78% in tertiary care centre. Studies done in Saudi Arabia and Nepal also indicated that empirical use of antimicrobial agents is common in developing countries^{21, 22}.

Prescription of antibiotics without being evidenced by culture and sensitivity tests result in emergence of multiple antibiotic resistant strains. Therefore, there is need for strict antibiotic prescription policies, which should be developed by collaborative efforts involving physicians, surgeons, pharmacologist and microbiologists.

CONCLUSION: The present study provides baseline data of prescribing pattern of antimicrobial agents in indoor patients of medicine and surgery department. Ceftriaxone and amikacin were found to be the first and second most commonly prescribed antimicrobials. Our findings are in line with what were reported by previous similar work. Antibiotic prescribing in our hospital is empirical, we would like to recommend that antibiotic selection should be based on the result of culture and sensitivity testing whenever possible. The percentage of drugs prescribed in generic form was found to be less in comparison to what WHO recommends and this issue must be addressed. This study is limited by the fact that we relied on relatively small sample size that may compromise the generalizability of the findings. Lastly, we recommend larger scope prospective study to emphasize on ensuring of rational use of antibiotics and hence fighting against the alarmingly increasing antimicrobial resistance.

ACKNOWLEDGEMENT: We acknowledge Dr. V.H. Bhavsar, Professor, Department of Pharmacology and Dr. Umesh Sinha, Associate Professor, Department of Community Medicine, Chirayu medical college and hospital, Bhopal for timely providing the appropriate research guidance.

CONFLICT OF INTEREST: There is no conflict of interest amongst the researchers.

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How to cite this article:

Rode S and Salankar H: Analysis of antimicrobial usage pattern: a retrospective observational study. *Int J Pharm Sci & Res* 2018; 9(3): 1231-36. doi: 10.13040/IJPSR.0975-8232.9(3).1231-36.

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