

A Cross Sectional Study of Antibiotic Usage in a Tertiary Care Hospital and Health Center in a North Maharashtra District

Shyam V Ashtekar¹, Sanjukta V Shenoy², Prerana S Gosavi³, Ratna S Ashtekar⁴

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Author's Affiliation:

¹Associate Professor; ²Student; ³Tutor, Dept. of Community & Medicine, SMBT IMS & RC, Dhamangaon; ⁴Medical practitioner, Sanjivan Hospital, Dindori, Nashik

Correspondence

AshtekarShyam Vinayak
ashtekar.shyam@gmail.com

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ABSTRACT

Introduction: Appropriate use of antibiotics is important for (a) Better therapeutic results (b) Saving costs (c) Minimize resistance to antibiotics. This is a descriptive cross-sectional study of prescriptions in a tertiary hospital and health center. Objective was to evaluate antibiotic usage in a teaching institute.

Methodology: For a sample size of 220, 256 prescriptions from IPD and OPD, containing any antimicrobial, at the pharmacy and another 240 prescriptions from the peripheral Health Centre were collected over a fortnight in 2018. Prescriber identity was concealed and protected. Prescriptions were assessed by two independent raters based on the AMR National Guidelines on antibiotics. Rater 1 and Rater2 had fair agreement (quadratic kappa 0.3348, 95%CI 0.2207-0.4489). Data were compiled and analyzed on excel and EPI info.

Results: Hospital pool yielded 203 medical and 53 surgical cases, of which 60% prescriptions were rated appropriate, 35% borderline and 5% un-acceptable. Health center data (n=240) showed 89% had no diagnosis. Amoxicillin+Clavulinic acid, ceftriaxone, azithromycin, Ofloxacin topped the hospital usage, while Amox+CA and Cefixime topped the health center usage.

Conclusions: Hospital prescriptions nearly conformed to guidelines, the Health center prescribing called for adherence to protocols. Cost-reducing options and minimizing resistance to higher antibiotics.

Key words: Antibiotics, prescriptions, AMR guidelines, GARP

INTRODUCTION

Globally, rational approach to use of antibiotics/antimicrobials has been on agenda. Appropriate and judicious use antimicrobial medicines is important for three reasons (a) Better therapeutic results (b) Saving costs (c) Minimize emergence of resistance to antibiotics.

Antibiotics/antimicrobials constitute a major tool against infectious diseases in India especially due to host and environment factors like malnutrition, multiple vitamin deficiencies, overcrowding, illiteracy, poverty, poor sanitary facilities, low standards of personal hygiene and inadequate vector control. Improper usage of antibiotics also entails substantial wastage of resources and therapeutic

failure is yet another problem. Simple antibiotics often work better than new generation antibiotics, but the latter are abused by most practitioners due to lack of regulation, poor knowledge, desire to give magical cures in private sector and neglect of possibility of developing resistance. The low-cost antibiotics are in disuse because of small margins earned by pharmacists. Adding to this chaos is the preferences by quacks and pharmacists for high priced antibiotics. In India, legally only allopathic doctors are allowed to prescribe antibiotics. But non-allopathic doctors are prescribing them as well. Antibiotics are also dispensed as Over-the-Counter (OTC) in many pharmacies. Antibiotic usages also tend to change as new drugs and brands

hit the market. Antibiotics are also used in dairy and poultry. This widespread use has led to emergence of resistance of some bacteria to certain drugs from region to region. Years ago, a multi-drug resistant 'Superbug' had caused a furor¹. In India national media quoted ICMR stating that 50% antibiotics usage in India is inappropriate, and this should be a call for action from all stakeholders.² There are now guidelines about use of antibiotic/antimicrobial drugs at Global and national level. The Government of India has published National Treatment Guidelines for Antibiotic Use in Infectious Diseases.³ In the developed health systems antibiotics are used cautiously and responsibly. WHO EU has published a list of critically important antimicrobials for human use.⁴ In fact, they are used mostly after culture sensitivity tests. This is possible because of laboratory facilities in all settings, proper documentation and much better access to health facilities. Indian Out-Patient-Departments (OPDs) in teaching hospitals and health Centers are overcrowded and have no scope for culture sensitivity tests before prescribing antibiotics in the general settings. It is, therefore, all the more necessary to exercise diligence and follow protocols for diagnosis and appropriate selection of antibiotics thereafter.

Teaching hospitals are in a special position to guide antibiotic usage in the locality and at least within the district. But since the faculty is in a flux, institutional policies need to be developed and doctors informed about it regularly. The emergence of antibiotic resistance in In-Patient-Department (IPD) settings can be life-threatening. They can result in increased incidence of morbidity, complications and mortality. These nosocomial infections require periodic culture sensitivity studies. For this, the current patterns of usage of antibiotics need to be studied and reviewed by the institute at regular intervals and appropriate actions planned. This descriptive cross sectional study is an attempt to fill the gap of studies on antibiotic usage in Maharashtra and India.

AIMS AND OBJECTIVES

The objective of the study is to obtain and analyze the antibiotic usage patterns in a Medical College Hospital and a Health Centre.

METHODS

This is a descriptive cross-sectional study on a convenience sample of prescriptions containing antibiotics.

The study was done in a medical college Hospital in North-Western Maharashtra functioning in a

tribal block, with the health center in the same block 30 km away.

A recent report from Selvaraj in similar settings in India estimates that about 47% use of antibiotics was inappropriate⁴. The sample size was calculated using this proportion with the standard statistical formula as follows: Sample size (n) = $[(DEFF * Nap (1-p)) / [(d^2 / Z_{1-\alpha/2}^2 * (N-1) + p * (1-p))]]$, where mean proportion of unjustifiable prescriptions $p=50$ at 95% CL, accepting 5% allowable error and 1.2 as design effect for non-random sample of two clusters). The sample size calculation was done on Open Epi stat-Cal application⁵. The estimated sample size was 182 at 10% error and 99% confidence limits. This was rounded by adding 20% for any exclusion or rejection, and hence was 220 hospital and health centre each. The data was collected from 1st August, 2018 to 28th September, 2018.

The hospital records from OPD and some from IPD were collected on 15 days in September between 12 to 1pm time slot for convenience and the required sample size (say 250) was fulfilled. The prescriptions were photographed concealing name of prescriber physician for confidentiality. The hospital had a daily OPD of about 800 in various departments, but the daily tally of antibiotic prescriptions in the 2hr time slot was about 30-35. About 250 prescriptions, containing any antibiotic, were collected from the hospital pharmacy as per inclusion criteria. They were screened and analyzed as per recommended standard indications for antibiotic usage. Criteria like clinical diagnosis; laboratory investigations, preferred brands, cost, regimen, dosage etc. were noted in excel. Some 240 prescriptions from an associated Health Centre 30km away were collected over five days, and compiled and studied using the same criteria. All brand names were converted into generic names with help labels, and if necessary Internet search and the help of institutional pharmacist.

Antibiotic usage for stated conditions was assessed by a doctor-student team with the help of National Treatment Guidelines for antibiotic usage in infectious diseases 2016 (R). Grade A, B, C were used for Appropriate, Borderline and Un-acceptable use respectively. A second evaluation was obtained from Rater 2 independently and quadratic kappa analysis done for degree of agreement. (6,7) Excel and Epi-Info were used for data entry and analysis.

RESULTS

For a sample size of 220, 256 prescriptions from IPD and OPD, containing any antimicrobial, at the pharmacy and another 240 prescriptions from the peripheral Health Centre were collected over a fortnight in 2018. Out of 256 prescriptions from

Table 1: Medical and Surgical Diagnosis Mentioned on Prescriptions in the Hospital

Medical diagnosis	N	Surgical diagnosis	n
URTI	59	Umbilical hernia	4
Not mentioned	51	Fibroadenoma	3
Dengue fever	17	Fissure in ano	3
UTI	17	Otomycosis	3
LRTI	12	Acute appendicitis	2
Acute Gastroenteritis	10	Benign PHT	2
AFI	7	Cholelithiasis	2
Acute GE & dehydration	5	CSOM	2
Febrile convulsions	2	Inguinal hernia	2
Malaria	2	IT Fracture	2
Pneumonia	2	Renal calculi	2
Viral fever	2	Tonsillitis	2
Other medical	17	Other surgical	24
Total medical	203	Total surgical	53

BPH= Prostate HyperTrophy

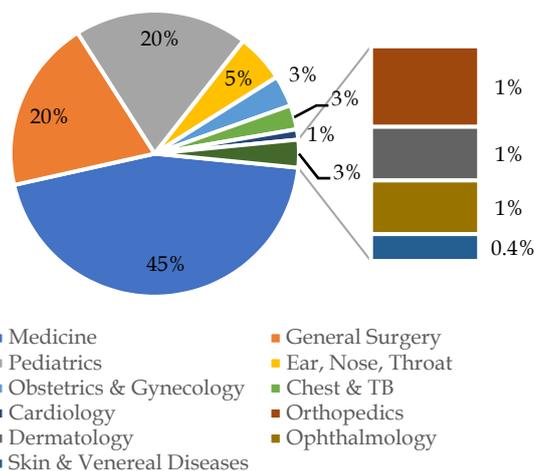


Figure 1: Share of various departments in prescriptions (hospital n=246)

Table 2: Assessment of the Antibiotic Usage by Clinical Departments (Rater 1)

Unit	A	B	C	Total	Percentage
Medicine	64	40	11	115	45%
Pediatrics	37	11	2	50	20%
General Surgery	23	27	0	50	20%
Ear, Nose, Throat	11	3	0	14	5%
Obs & Gynec	3	6	0	9	4%
Chest & TB	7	0	0	7	3%
Orthopedics	3	0	0	3	1%
Cardiology	0	2	1	3	1%
Dermatology	2	0	0	2	1%
Ophthalmology	1	1	0	2	1%
Skin & VD	1	0	0	1	0%
Total	152	90	14	256	

A: Appropriate, B:Borderline, C: unacceptable
VD= Venereal Diseases

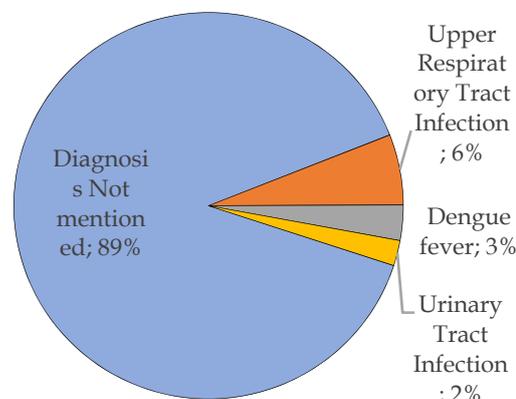


Figure 2: Conditions mentioned in 240 health center case papers

Table 3: Agreement between Rater 1 and Rater2

Rater2	Rater 1			TOTAL
	A	B	C	
A	108	41	4	153
B	32	32	1	65
C	12	17	9	38
TOTAL	152	90	14	256

hospital, OPD (n=172) and In-Patient Departments (IPD) (n=84) and 240 from health center.

Table 1 shows medical and surgical diagnostic conditions found in the 256 prescriptions from IPD and OPD of the Hospital.

Use of Antibiotics in Institutional Setup

In the Hospital data the rate of use of antibiotics was 1.15 per patient, with only 40 out 256 case records showing second antibiotic, out of which 28 belonged to IPD, thus the use of a second antibiotic in OPD was mere 7%. Further the use of 3rd antibiotic was only in 3 cases out of 84 IPD cases.

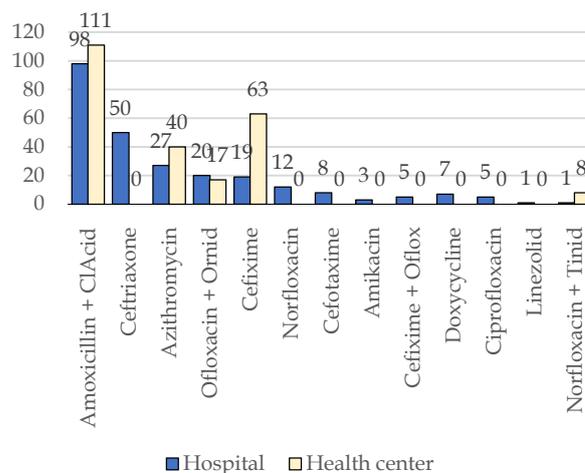


Table 3: Antimicrobial use by hospital and health center

A study of 240 prescriptions/case papers showing antibiotic use obtained from the Health Centre was

done. It was noted that 89% (n=211) case papers out of 240 studied did not mention any clinical diagnosis, though symptoms were written in a few. The use of second antibiotic was found only in one case. This rate of antibiotic use/prescription was just about 1.

Figure 1 shows Unit wise Distribution of Prescriptions in Hospital Sample. Figure 2 shows Diagnosis mentioned on prescriptions at health center. Figure 3 shows various Antibiotics used by hospital and health center. From the figure 3, it is evident that Amoxicillin + Clavulanic Acid, Ceftriaxone and Azithromycin are most preferred antibiotics in both setups.

Table 2 shows that maximum usage of antibiotics is by gen. Medicine, Pediatrics Department and General Surgery Departments. The difference between grade allocations is significant as shown by Chi square test.

The hospital data (256) on diagnostics was shared with rater 1 and rater 2 independently, and the kappa with quadratic results are as follows: Observed kappa: 0.3348 (0.95 confidence limits 0.2207-0.4489) SE 0.0582; Maximum possible quadratic-weighted kappa, given the observed marginal frequencies: 0.8927, 0.375 observed as proportion of maximum possible.

DISCUSSION

The study aimed at finding antibiotic usage patterns in the teaching institute and health center from prescriptions sampled in pharmacy. Broadly the hospital usage was seen as conservative, as nearly 60% usage was rated A by both raters, while B was at 35-25%. The health center usage was problematic since 88% prescriptions were without stated diagnosis.

Antibiotics usage in the Hospital

First of all, it seems that from a daily OPD workload of 800+, the researcher could get only 25-30 cases in an hour's time-slot each day. A rough estimate of 5 hours of OPD and 800 cases suggests an hourly workload of 150 cases. A yield of 30 antibiotic prescriptions out of 150 is about 20%. This crude estimate suggests that antibiotic usage was relatively sparse (about 20%) in the pool of OPD case papers. It was, therefore, necessary to extend the data collection from 2 days, as originally planned, to 10 days. This is the one positive indication of conservative use of antibiotics in the institute.

Table 1 shows that URTI (23%) leads the hospital list of diagnostic conditions (n=256) from the study

sample, while *diagnosis not mentioned* follows closely (at 20%). Dengue fever also featured for antibiotic prescription at 3rd position, along with UTI, followed by LRTI. This data should help focus on use of protocols for these problems on a priority, in the context of antibiotic usage. URTIs are often viral, but are commonly treated with antibiotics. The leading departments in the hospital for entries in this study are General Medicine, followed by Pediatrics and General Surgery. Since these have the maximum case load and crowded OPDs, these departments can be focused first fine tuning antibiotic usage. Table 2 shows that close to 59% prescriptions in the hospital setting are appropriate by rater 1, while 35% are borderline in the context of diagnostics mentioned. Only 6% antibiotic prescriptions were un-acceptable. The rater 2 counts are 59.77%, 25.39% and 14.84%. There is a fair agreement between the two raters. Seen in the context of low use of antibiotics in OPD cases in the hospital and a small rate of (6%) un-acceptable use, and minimal use of second antibiotic, the hospital practices for antibiotic usage are appreciably good. However the 35% in category B also need to be audited further by respective departments for improvement.

The rate of prescription of antibiotic medicines was 1.15/prescription in the hospital data suggesting conservative approach. The economical use of a second antibiotic and rare use of the third antibiotic suggested a systematic and rigorous approach based on clinical criteria. This conservative use compares well with several other studies. This practice needs reinforcement.

Most of the entries from the case papers mentioned a five days' use of antibiotics and patients were expected to return for follow-up. However, the five-day prescription is a reasonable thumb rule. This said, the compliance of patients for the five-day consumption is beyond the scope of this study. Hence this study ignored the dose and duration factors for deciding rational use.

Antibiotic Usage in Health center

In contrast to above picture of conservative use, the Health Centre sample showed high usage of antibiotics; about 30-40 each day in an OPD workload of 80-100 cases. Further, a similar use of Amoxicillin + Clavulanic Acid in the Health Centre OPD (Fig 3) is striking and needs review. The health center OPD is run by two AYUSH doctors with help of visiting consultants, and the latter may have reduced the portion of non-diagnosis in this sample, which stands at 88%. In the larger public health system, the Primary Health Centre OPDs are often run by AYUSH doctors and the conditions there need a similar review. It is necessary that a standard protocol is used by Primary Health Centre for

antibiotic usage. The use of Trimethoprim+Sulfa, Doxycycline, plain amoxicillin need to be the bulk of use at primary level facilities. These drugs are still there in the Standard treatment Guidelines (STG) and must be employed as first line choice. This is in great contrast with primary care study from Botswana reporting better usage (8).

The sizeable portion of non-diagnosis in the health center OPD probably results from a crowded OPD run by consultants aided by AYUSH doctors. It is estimated that the availability of average time per patient in this setting is about 3-4 minutes, which should be adequate for putting down a probable diagnosis and appropriate prescription. However the redeeming feature is that the rate of antibiotics used in 240 cases was just about 1, in contrast to the Botswana study stating 2.5 antibiotics used per case⁸

Compared with developed countries, India has several constraints on establishing rational antibiotic use. It is often not possible to wait for culture sensitivity to start treatment in India situations, especially in rural and tribal settings. Hence the institute in the study will have to bank on syndromic clinical approach for rational selection of antibiotics. Yet the sensitivity patterns have to be established. Till then, it is possible to use private and public laboratory data on culture sensitivity of pathogens to arrive at working protocols, and the two recent studies mentioned from Nashik district can serve as pointers.^{9,10}

Use of Amoxicillin+Clavulanic Acid, a high cost FDC medicine at Rs 108 a pack of 10 tabs at 2018 prices, seems to top the hospital OPD usage (Table 1). This may be due to greater perceived efficacy of the antibiotic combination, broader spectrum and serious condition of the patients due to improper management by quacks or late referral. This may also be due to long-distance patients who may experience difficulties in travel for repeat visit. However this can be reviewed and cheaper options like Trimethoprim-Sulpha, Doxycycline and plain Amoxicillin.

Agreement by Raters

As per the methodology, it was seen that stated diagnostic conditions did not facilitate a very straight selection of antibiotics even from the antibiotic guidelines in the OPD settings. Clinical conditions like URTI, UTI, diarrhea, PUO do not suggest any particular microbe. Hence, one has to select from possible options with the help of personal knowledge and experience. Therefore, along with antibiotic guidelines, this study had to use the experience of a tutor-doctor from the department of PSM, based on the antibiotic guidelines. The initial rating was done on both hospital and health center data

by a student-tutor team. We then rated only hospital data by a non-institutional practitioner. This is subject to some variation due to personal and learned opinions. The quadratic kappa value of 0.3348 suggested only a fair agreement. Hence there is scope for hospital usage to differ from model usage as per AMR. This situation can be dealt with consensus building among respective units. However, the final word can only come from culture sensitivity tests and hospital epidemiological studies.

The health center settings need more scrutiny and protocol adherence for antibiotic use, for the triple goals stated (a) desired therapeutic effect (b) economy of drug usage (c) minimize emergence of antibiotic resistance.

The study findings need to be seen on the backdrop of antibiotic usage issues in the world, Indian guidelines and patterns of antibiotic usage.

Antibiotic usage: A Global concern

Use of antibiotics is a global concern, including developing countries. Underdeveloped countries are also reviewing antibiotic drug use. A Botswana study found that 87% of antibiotic usage was appropriate, underlining wider awareness and action even in developing countries and another African study presents difficulties in such settings even if culture sensitivity tests are available.^{8,11} The comprehensive guidelines published by Government of India should be useful to all levels of care.³

Gillian Porter and Nathan Hills have reviewed 115 articles from India and concluded that the misuse of medications is widespread. The factors involved all levels of the health system including regulation, enforcement and policy, healthcare providers and consumers.¹² A report from Delhi stated that 43% to 69% outpatient prescriptions for child diarrhea showed use of antibiotics in public and private facilities, ignoring that many incidents could be viral in origin. Many Indian studies are available including from tertiary medical institutes underlining need for major reforms. Some of these are quoted here. An Ujjain study from a teaching hospital and a non-teaching hospital, reported that lack of distinction between use for prophylaxis and therapy was a major factor for improvement.¹³ Another study of two Ujjain Hospital IPDs suggested that at the Teaching Hospital a significantly higher proportion of patients having fever without registered bacterial infection were prescribed antibiotics (82%) compared with the Non-teaching Hospital.¹⁴ A 2011 Delhi survey of outpatient prescriptions from public and private health facilities reported high use rate of antibiotics, with 43% prescriptions having at least one antibiotic and 39% of prescriptions collected in pharmacies carried an antibiotic.

¹⁵ A south India study of attitudes of 286 practicing physicians showed that the majority felt that antibiotics were overprescribed. ¹⁶ A Pune study dating back to 1998, quoting irrational use to the extent of 30%. ¹⁷ Various reports from tertiary institutes state the irrational use ranging from 30% to 60%. ^{4,14,18-20} Thus the problem calls for action at the very root of the system-the medical colleges.

Reports from Nashik region about antibiotic-resistance

A recent study from Nashik in western Maharashtra reported that "the proportions of MDR and ESBL-producing *Acinetobacter* spp. isolates ranged from 89.4% to 95.9% and from 87.9% to 94.0%; respectively. The proportions of non-susceptible isolates to aminoglycosides; carbapenems; antipseudomonal penicillins/lactamase inhibitors; cephalosporins; folate pathway inhibitors; or Penicillins/lactamase inhibitors exceeded 77.5%. Proportions of fluoroquinolone and tetracycline non-susceptible isolates ranged from 65.3% to 83.3% and from 71.3% to 75.9%; respectively". ⁹

Another study from the same region reported that "for the extended-spectrum cephalosporins, the proportions of non-susceptible *E. coli* and *Klebsiella* spp. isolates were above 78.4% and 84.9% throughout the study period, respectively. *E. coli* and *Klebsiella* spp. isolates exhibited carbapenem non-susceptibility levels as high as 76.9% and 84.1% respectively". ¹⁰ This level of high antibiotic resistance warrants that syndromic approach to use of antibiotics, without culture sensitivity patterns to guide, is not helpful. Since this hospital institute was relatively new in its 4th year, a local protocol for antibiotic use is awaited, based on Culture and Sensitivity Studies in OPD and IPD settings. Thus we have a long way to go any rational use of antibiotics even in tertiary institutes.

GARP guidelines

The Global Antibiotic Resistance Partnership (GARP)-India Working Group has been working to rationalizing antibiotic use to limit antibiotic resistance in India. ¹² The GARP-IWG recommendations made in 2011 aim at " (i) reducing the need for antibiotics; (ii) lowering resistance-enhancing drug pressure through improved antibiotic targeting, and (iii) eliminating antibiotic use for growth promotion in agriculture". further it says "the highest priority needs to be given to (a) national surveillance of antibiotic resistance and antibiotic use - giving better information to underpin decisions on standard treatment guidelines, education and other actions, as well as to monitor changes over time; (b) increasing the use of diagnostic tests, which necessitates behavioral changes and improvements in microbiology laboratory capacity;

(c) setting up and/or strengthening infection control committees in hospitals; and (d) restricting the use of antibiotics for non-therapeutic uses in agriculture" ¹². These interventions should help to reduce the spread of antibiotic resistance, improve public health directly, benefit the populace and reduce costs and lessen pressure on the healthcare system.

LIMITATIONS

This study was not focused on departments or disciplines; hence the proportion of IPD-OPD or departments in the sampled prescriptions can change the usage statistics. Thus the study gives only a ball park estimate of rational or irrational use. Secondly we have not been able to analyze the use of second and third antibiotic along with the first one. Thirdly, though raters have referred to standard treatment guidelines, the final allocation of ABC grades was based on individual judgment. Hence there is bound to be weak agreement in two raters. The usage by hospital should be seen against this limitation.

CONCLUSION

1. The teaching hospital has an overall low utilization and satisfactory use of antibiotics in the OPD settings (60%), while 35% entries seem borderline in the given situation. The use of high cost FDC should be reviewed for replacement by effective low cost options.
2. The Health Centre OPD practices demand major improvement in diagnostic efforts and rational use of antibiotics. This makes a general case for training non-allopathic doctors working in primary care facilities in public and private sector.
3. Developing a culture sensitivity data base for hospital OPD and IPD is essential to bring further improvement in antibiotic usage

REFERENCES

1. Padhi S. New Delhi metallo-beta-lactamase-1: A weapon for the newly emerging drug-resistant bacteria. *Indian J Med Sci.* 2017;69 (1):29. accessed online 29 September 2018 <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3657891>
2. Poor awareness of antibiotic misuse in India a major concern [Internet]. *The New Indian EXpress.* Hyderabad; 2018 [cited 2019 Mar 30]. Available from: <http://www.newindianexpress.com/thesundaystandard/2018/may/13/poor-awareness-of-antibiotic-misuse-in-india-a-major-concern-1813877.html>
3. National Treatment Guidelines for Antimicrobial Use in Infectious Diseases; 2016 vol: 0 (2016) pp: 1-64 accessed online 2 Oct 2018 http://pbhealth.gov.in/AMR_guideline

- 7001495889.pdf
4. Selvaraj R. Prospective assessment of antimicrobial prescribing pattern at a tertiary care hospital. *Al Ameen J Med Sci.* 2015;8 (4):276-80.
 5. Open Epi- Sample Size [Internet]. 2017. Available from: <https://www.openepi.com/SampleSize/SSPropor.htm>
 6. Lowry R. Kappa as Measure Concordance in Categorical Sorting. 2011;1-4. accessed online 24 March 2019; <http://vassarstats.net/kappa.html>
 7. Padhyegurjar SB, Padhyegurjar MS; Technique of calculation of kappa statistics by category modification method. *Indian J Med Spec.* 2012;3 (2):178-82.
 8. Sepako E, Masseur A, Mashalla Y, Setlhare V, Chuma M, Tiroyakgosi C, et al. Assessment of prescribing practices at the primary healthcare facilities in Botswana with an emphasis on antibiotics: Findings and implications. *Int J Clin Pract [Internet].* 2017;71 (12):e13042. Available from: <https://www.ncbi.nlm.nih.gov/pubmed/29178350>
 9. Odsbu I, Khedkar S, Khedkar U, Nerkar SS, Tamhankar AJ, Lundborg CS. High proportions of multidrug-resistant acinetobacter spp. Isolates in a district in Western India: A four-year antibiotic susceptibility study of clinical isolates. *Int J Environ Res Public Health.* 2018;15 (1):1-13.
 10. Odsbu I, Khedkar S, Lind F, Khedkar U, Nerkar SS, Orsini N, et al. Trends in resistance to extended-spectrum cephalosporins and carbapenems among escherichia coli and klebsiella spp. Isolates in a district in Western India during 2004-2014. *Int J Environ Res Public Health.* 2018;15 (1): 1-15.
 11. Anyanwu NC, Arigbe-osula ME. Pattern of antibiotic use in a tertiary hospital in Nigeria. *Eur J Hosp Pharm.* 2012;19 (2): 195.2-195.
 12. Ganguly NK, Arora NK, Chandy SJ, Fairoze MN, Gill JPS, Gupta U, et al. Rationalizing antibiotic use to limit antibiotic resistance in india. *Indian J Med Res.* 2011;134 (9):281-94.
 13. Landstedt K, Sharma A, Johansson F, Stålsby Lundborg C, Sharma M. Antibiotic prescriptions for inpatients having non-bacterial diagnosis at medicine departments of two private sector hospitals in Madhya Pradesh, India: A cross-sectional study. *BMJ Open.* 2017;7 (4): e012974.
 14. Mahadik K, Sharma A, Pathak A, Lundborg CS, Dhaneria SP, Eriksson B. Surveillance of Antibiotic Consumption Using the "Focus of Infection" Approach in 2 Hospitals in Ujjain, India. *PLoS One.* 2012;7 (6):e38641.
 15. Kotwani AH. Trends in antibiotic use among outpatients in New Delhi, India. *BMC Infect Dis [Internet].* 1999;11, 2011.:99. Available from: <https://www.ncbi.nlm.nih.gov/pubmed/21507212>
 16. Sivagnanam G, Thirumalaikolundusubramanian P, Mohanasundaram J, Raaj AA, Namasivayam K, Rajaram S. A survey on current attitude of practicing physicians upon usage of antimicrobial agents in southern part of India. *MedGenMed [Internet].* 2004;6 (2):1.
 17. Kshirsagar MJ, Langade D, Patil S, Patki PS. Prescribing patterns among medical practitioners in Pune, India. *Bull World Health Organ.* 1998;76 (3):271-5.
 18. Manjhi PK, Mishra H, Dikshit H, Mohan L, Kumar M. Prescription pattern of antimicrobial drugs in paediatric outpatient department in a tertiary care teaching hospital. *Int J Pharm Sci Rev Res.* 2016;
 19. Thomas M, Govil S, Moses B V., Joseph A. Monitoring of antibiotic use in a primary and a tertiary care hospital. *J Clin Epidemiol.* 1996;49 (2):251-4.
 20. Vipul G, Bhatt P. Evaluation of rational usage of antimicrobial agents in the medicine department at tertiary teaching care hospital. *Int J Pharm Sci Res.* 2014. 5 (3): 865-873.