e-ISSN: 0975-9506, p-ISSN: 2961-6093

Available online on http://www.ijpqa.com/ doi: 10.25258/ijpqa.16.3.3

International Journal of Pharmaceutical Quality Assurance 2025; 16(3); 09-18

Original Research Article

Point Prevalence Survey (PPS) Of Antimicrobial Use in Hospital Using WHO Methodology - Findings and Implications for Antimicrobial Stewardship Program

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Received: 25-09-2024 / Revised: 31-12-24 / Accepted 02/01/2025
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Conflict of interest: Nil

Abstract:

Background & Objectives: Inappropriate antimicrobial use leads to antimicrobial resistance (AMR) resulting in increased morbidity and mortality with a significant economic burden. Because of the increasing concern about AMR, World Health Organization (WHO) instituted Point Prevalence Survey (PPS) methodology to collect data to help formulate hospital interventions to optimise antimicrobial use. The objective was to analyse the prevalence of antimicrobial use among hospitalized patients at a point of time.

Material & Methods: This cross-sectional point prevalence survey modified from the WHO PPS protocol was conducted among hospitalized patients who received antibiotics before 9AM on the survey date. Data were collected from case files using a pre-structured and validated google form based on the WHO Methodology under the guidance of the National Centre for Disease Control (NCDC).

Results: The prevalence of antimicrobial use was 81.39% of which 98.9% were empirical. 40% of patients received one, 36% received two and 24% received more than two antimicrobials. 47% of all antimicrobials prescribed were from the "Access" group, 51.8% from the "Watch" group, and 1.2 % from the "Reserve" group. The most frequently prescribed antimicrobial was ceftriaxone (76%), followed by Metronidazole (41.7%) and amoxiclav (21%).

Conclusion: Overall hospital antimicrobial use prevalence is high with preference for empirical prescription from the Watch group. The antimicrobial prescribing behaviour must adhere to the standard treatment guidelines, and prescribe preferably from the Access group of antibiotics so as to promote antimicrobial stewardship.

Keywords: Point Prevalence Survey, Antimicrobial Resistance, Antimicrobial Stewardship, AWaRe, Ceftriaxone.

Introduction

Inappropriate antimicrobial use leads to antimicrobial resistance (AMR), which is a major threat to public health. Resistance occurs when bacteria, viruses, fungi, or parasites are exposed to antimicrobials but are not killed by them, rendering antibiotics ineffective. Infection with resistant organisms leads to longer illnesses, increased morbidity, and mortality, and incurs significant economic costs [1]. As per the World Bank report, by 2050 AMR could cause a global economic crisis [2]. It is estimated that 20–50% of antibiotic use is inappropriate in hospitals [3].

The key contributors to the spread of AMR include inappropriate use of antimicrobials, over-prescription, incomplete course of antimicrobials, prescription without culture sensitivity tests/antibiograms, sparse data on antimicrobial use, and lack of surveillance systems [4]. Other factors influencing AMR

are poor infection prevention and control in healthcare facilities, poor hygiene and sanitation, and limited discovery of new antimicrobials [5]. For this reason, varied strategies have been developed to combat this problem, like an emphasis on the rational use of antibiotics, optimizing infection control, and promoting the development of newer antimicrobials [6]. In view of the increasing concern of AMR, the World Health Organization (WHO) instituted a methodology to assess antimicrobial use in low- and middle-income countries (LMIC) while maintaining comparability with data obtained from high-income countries (HIC) by Point Prevalence Survey (PPS) [7]. The WHO PPS methodology is a standardized tool that collects basic information from medical records of hospitalized patients relevant for the treatment and management of infectious diseases regardless of whether these patients are on antibiotic therapy or not. It collects data about the quantity (prevalence) and quality of antimicrobials prescribed, recognizes barriers, identifies targets for improved antibiotic use, and helps to formulate interventions to improve antimicrobial use [8]. Assessment of the appropriateness of antimicrobial use is done with the help of quality indicators (QIs), which are measurable elements and are evidence-based. The quality assessment indicators include prescription patterns, investigations requested, adequacy of empirical treatment according to guidelines, time to initiation of appropriate antimicrobial therapy, and switch from intravenous to oral therapy. [9–11].

Surveillance of antimicrobial use is an integral part of the strategy to contain antimicrobial resistance. In April 2017, the National Centre for Disease Control (NCDC) developed and implemented the National Action Plan on Antimicrobial Resistance (NAP-AMR) in alignment with the Global Action Plan for containing AMR and proposed strategies to optimize the use of antimicrobial agents by developing a methodology to estimate their consumption in hospitals. It focuses on reducing the quantity of antimicrobial consumption and improving the quality of antimicrobial prescription. Other measures to counter AMR include unhindered access to antimicrobials in health centers, developing and promoting new rapid diagnostic tools to reduce unnecessary use of antibiotics, providing financial and technical support to develop new medicines and vaccines, and improving global surveillance of drug resistance [12]. India is a major manufacturer of antibiotics and is also a leading consumer, and most of it is without prescription. In this scenario, it is likely that inappropriate use of antibiotics is widespread. Data on the prevalence of antimicrobial use and its appropriateness is available for most developed countries; but is scarce from this region.

Dr. BRAM Hospital, associated with Pt. JNM Medical College, is a national antibiotic consumption network site under the NCDC. The microbiological diagnostic and susceptibility test facility is functional in the hospital, and infection prevention control practice is also implemented to reduce antimicrobial resistance. This point prevalence survey was conducted as part of the multicentric PPS conducted by NCDC to analyze the prevalence of antimicrobial use, indication for prescription, prescribing practice according to AWaRe (Access, Watch and, Reserve) classification, and other information relevant to treatment and management of infectious diseases in hospitalized patients.

This study will support policymakers and practitioners for rationalizing antibiotic prescriptions, raise awareness, and identify targets for interventions to improve antibiotic use, which will be a step towards antimicrobial stewardship.

Aim and Objectives

This PPS aimed to analyze both the quantity and quality of antimicrobial use. The primary objective was to analyze the prevalence of antimicrobial use among hospitalized patients of different wards/clinical specialties and different infections at a point in time. The secondary objective was to analyze their appropriateness in terms of indication, adequacy of empirical treatment according to guidelines, susceptibility testing, and antibiotic use according to WHO AWaRe classification. Subsequently, the results can be used to identify targets for intervention and implement a sustainable antimicrobial stewardship program.

Materials and Method

This cross-sectional point prevalence observational study was conducted over two days among inpatients admitted to the wards at Pt. JNM Medical College associated with Dr. BRAM Hospital, Raipur, C.G. (tertiary care teaching hospital) in central India, on 3rd January and 23rd February 2022. The wards covered on the first day were not included for the survey on the second day. Pt JNM Medical College is a National Antimicrobial Consumption Network (NAC-NET) site under NCDC for the National Programme on AMR containment. This hospital has 1429 beds with an occupancy rate of 42.25% in January and 48.39% in February.

PPS implementation: To ensure successful conduction of the PPS, clinical specialties with frequent prescription of antimicrobials like Medicine, surgery, ENT, respiratory medicine, orthopedics, pediatrics, and obstetrics and gynecology departments were included. Hospital authorities, clinicians, medical officers, and nursing staff on duty were explained about the survey to streamline it. A PPS team was constituted, which included a nodal officer for antimicrobial consumption, faculty, postgraduate residents from the pharmacology department, and second-year MBBS students who volunteered to

be surveyors. The team was trained by the NCDC to conduct the survey and was imparted knowledge about the importance of AMR. A mock drill was conducted one day prior to the survey to acquaint the investigators with the details of the protocol, practice for filling the questionnaire completely, and identify gaps, if any, and resolve them. The team was divided into working groups consisting of 3-4 individuals for each ward, and the duty doctor of the ward was available to assist in completing the survey.

PPS Protocol: All hospitalized patients admitted before 9:00 am on the survey date and not scheduled for discharge and admitted for at least 24 hours before the survey were included for the survey. Casualty wards, or emergency wards, were excluded as the patients are not admitted there for more than 24 hours. ICU beds were excluded as they were converted to COVID beds.

Details were collected from case files using a pre-structured Google form validated by NCDC based on the WHO Methodology for Point Prevalence Survey on Antibiotic Use in Hospitals (Version 1.1).

Data were collected in Google form, from case records of patients who fulfilled the above criteria, irrespective of whether an antimicrobial was prescribed or not. Details of patient demographics (gender, age, weight), admission dates, diagnosis at the time of admission, total number of antimicrobials prescribed during the hospital stay, their class, dose, frequency, route of administration, and duration (start date and end date) were noted. Indications/infection types according to pre-defined categories: community-acquired infection (CAI), hospital-acquired infection (HAI), and medical and surgical prophylaxis were entered in the survey protocol. Choice of antibiotics in compliance with treatment guidelines and information regarding empirical or definitive treatment based on culture sensitivity tests was noted. Antimicrobials included antibiotics for systemic use but excluded topical antibiotics, antifungals, antitubercular drugs, antimalarials, and antiviral drugs. The two-day data were pooled and completely anonymized; no unique identifiers were recorded. The surveyors did not have any direct contact with the patients, so patient consent was not required. Ethical clearance for the study was provided by NCDC, and institutional approval for conducting the survey was obtained.

Data Analysis: Data were entered and analyzed in MS Excel and checked for completeness and correctness. An analysis was done to assess the quantity of antimicrobial use: the number of patients on antimicrobial agents and the number of antimicrobials prescribed per patient.

Quality of antimicrobial use included the indication of antimicrobial use and adherence to national/local antimicrobial treatment guidelines related to antimicrobial use, which were analyzed. Antimicrobial use is defined as the receipt of at least one antibiotic per patient. Antimicrobials prescribed were classified as per W.H.O. AWaRe classification 2021 [13]. All data were presented in frequency and percentage. The Department of Microbiology was involved in the interpretation of the data.

Table 1: PPS Survey details

No. of wards surveyed	**7**
Wards surveyed	Medicine Orthopaedics ENT OBG Respiratory Medicine Surgery Paediatric
Total number of patients admitted in the wards on the survey dates	344
Patients eligible for a survey	215 Male: 115 Female:100 Adult: 198 Paediatric 17
Patients on at least one antibiotic	175
Antimicrobial agent's prescriptions	338
Number of antibiotics prescribed	19

Table 2: Ward-wise Prevalence of antibiotics use, break up of total antibiotic prescriptions according to AWaRe category

Wards	Total patients admitted	Eligible patients	Patients on antibiotics	Prevalence of antibiotics use	Antibiotics prescribed	Access (%)	Watch (%)	Reserve (%)
Medicine	134	77	60	77.9%	134	58 (43.28)	76 (56.71)	0
Surgery	94	50	44	88%	94	50 (53.19)	43 (45.74)	1 (1.06)
Obstetrics and gynaecology	47	27	90	70.3%	45	28 (62.22)	16 (35.55)	1 (2.22)
Paediatrics	6	6	5	83.3%	6	0	6 (100)	0
Others (ENT, Orthopaedics, Respiratory medicine)	63	55	47	85.45%	59	23 (38.98)	34 (57.62)	2 (3.38)
Total	344 patients	215	175	81.39%	338 antibiotics	159 (47.04)	175 (51.77)	4 (1.18)

(Note: One patient might have received more than one antibiotic. It is a coincidence that the numbers of admitted patient and number of antibiotics prescription are same in all wards except "others" wards, and should not be confused.)

Results

The PPS survey details, as shown in Table 1, were done in a single hospital with 1429 beds. On the day of survey 344 patients were admitted in the wards surveyed, 215 patients were eligible, and 175 patients were on antibiotics and received 338 antimicrobial prescription encounters with 19 different antibiotics. The prevalence of antimicrobial use is 81.39% (175/215), and ward-wise prevalence of antimicrobial use is shown in Table 2.(Prevalence of antibiotic use is calculated as the number of patients on antibiotics divided by the number of eligible patients multiplied by 100). The mean age of the patient admitted in the pediatric ward was 5.16±3.31 years, and in adult wards, the mean age was 39.77±16.71 years. The proportion of males was 54.48%. The date of admission, diagnosis, and start date of antimicrobial therapy was mentioned in all case files. Of the 175 patients receiving antibiotics, 40% received only one antimicrobial, 36% received 2 antimicrobials, and 24% received more than two antimicrobials. Measurable quality indicators are shown in Table 3. A request for blood culture was sent in 6.3% (11/175) of cases, and only 2 (1.14%) patients received antimicrobial treatment directed to the culture report; the remaining 98.9% received empirical therapy. The major therapeutic indications as classified by the NCDC project protocol are surgical prophylaxis, medical prophylaxis (e.g., pancreatitis, alcoholic liver disease, and severe anemia), community-acquired infection, and hospital-acquired infections, which accounted for 45.1%, 21.1%, 29.1%, and 4.6% of cases, respectively. 91.4% of patients received antimicrobials parenterally, 18.3% received double gram-negative cover, and 12.6% received double anaerobic cover. The frequency of parenteral antibiotic use in different wards and the stop date/review date mentioned are shown in Table 4. The proportion of prescribed antimicrobials is ceftriaxone 39.3%, metronidazole 21.6%, and amoxiclav 10.9%, as shown in Figure I. Ward-wise, three frequently prescribed antimicrobials are shown in Figure 2. 47% of all antimicrobials prescribed were from the Access Group of W.H.O. AWaRe classification for antibiotic stewardship, while 51.8% were from the Watch Group and 1.2% from the Reserve Group. Ward-wise break up of total antibiotics prescriptions and their AWaRe category is depicted in Table 2.

Table 3: Quality indicators related to antimicrobial prescriptions.

Item	Number (N=175)	Percentage
Diagnosis documented	175	100 %
Request sent for blood culture	11	6.3%
Antimicrobial treatment directed to culture report	2	1.1%
Antimicrobials prescribed as Empirical therapy	173	98.9%
Therapeutic indications-		
Surgical prophylaxis	79	45.1%
Community-acquired infection	51	29.1%
Medical prophylaxis	37	21.1%
Hospital-acquired infection	08	4.6%
Oral route	15	8.6%
Parenteral route	160	91.4%
Empirical therapy Compliant with National/Local guidelines	121	69.1%
Patients receiving double anaerobic cover	22	12.6%
Patients receiving double Gram-negative cover	32	18.3%

Table 4: Frequency of Each Antimicrobials Prescribed & AWaRe Category

Antimicrobial Class	Antimicrobial	Aware Classification	Prescriptions N=338	Percentage
Ant-amoebic	Metronidazole	Access	73	21.6%
Penicillin	Ampicillin	Access	17	5.0%
	Amoxiclav	Access	37	10.9%
Aminoglycosides	Amikacin	Access	17	5.0%
	Gentamycin	Access	6	1.8%
Tetracycline	Doxycycline	Access	8	2.4%
	Clindamycin	Access	1	0.3%
Cephalosporin	Ceftriaxone	Watch	133	39.3%
	Cefixime	Watch	7	2.1%
	Cefotaxime	Watch	2	0.6%
Penicillin	Piperacillin + Tazobactam	Watch	7	2.1%
Fluroquinolones	Ciprofloxacin	Watch	3	0.9%
	Levofloxacin	Watch	2	0.6%
	Ofloxacin	Watch	1	0.3%
Macrolides	Azithromycin	Watch	11	3.3%
Rifamycin	Rifaximin	Watch	7	2.1%
Carbapenems	Meropenem	Watch	1	0.3%
Steroidal Antibacterial	Fusidic Acid	Watch	1	0.3%
Oxazolidinones	Linezolid	Reserve	4	1.2%
Antimicrobials prescribed AS PER W.H.O. AWaRe Classification (n=338)				
Access			159	47 %
Watch			175	51.8%
Reserve			4	1.2 %

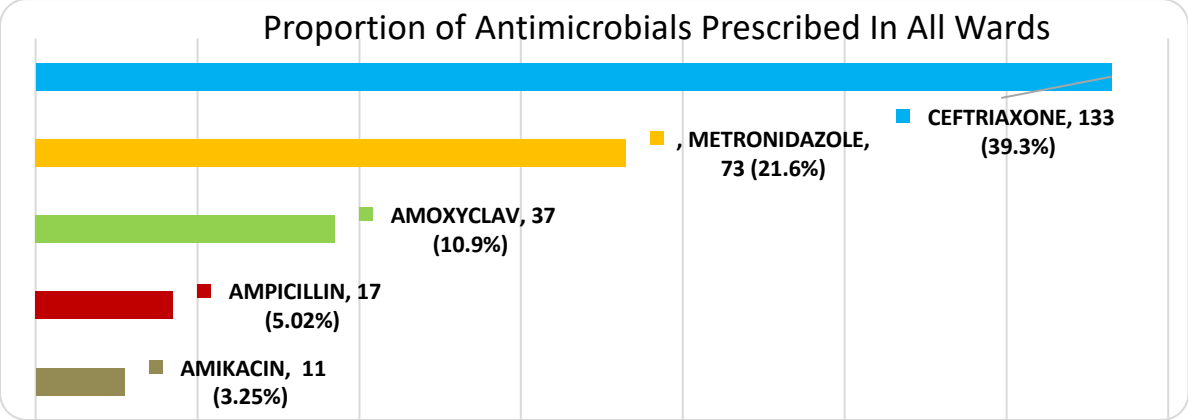

Figure 1: Proportion of Antimicrobials Prescribed In All

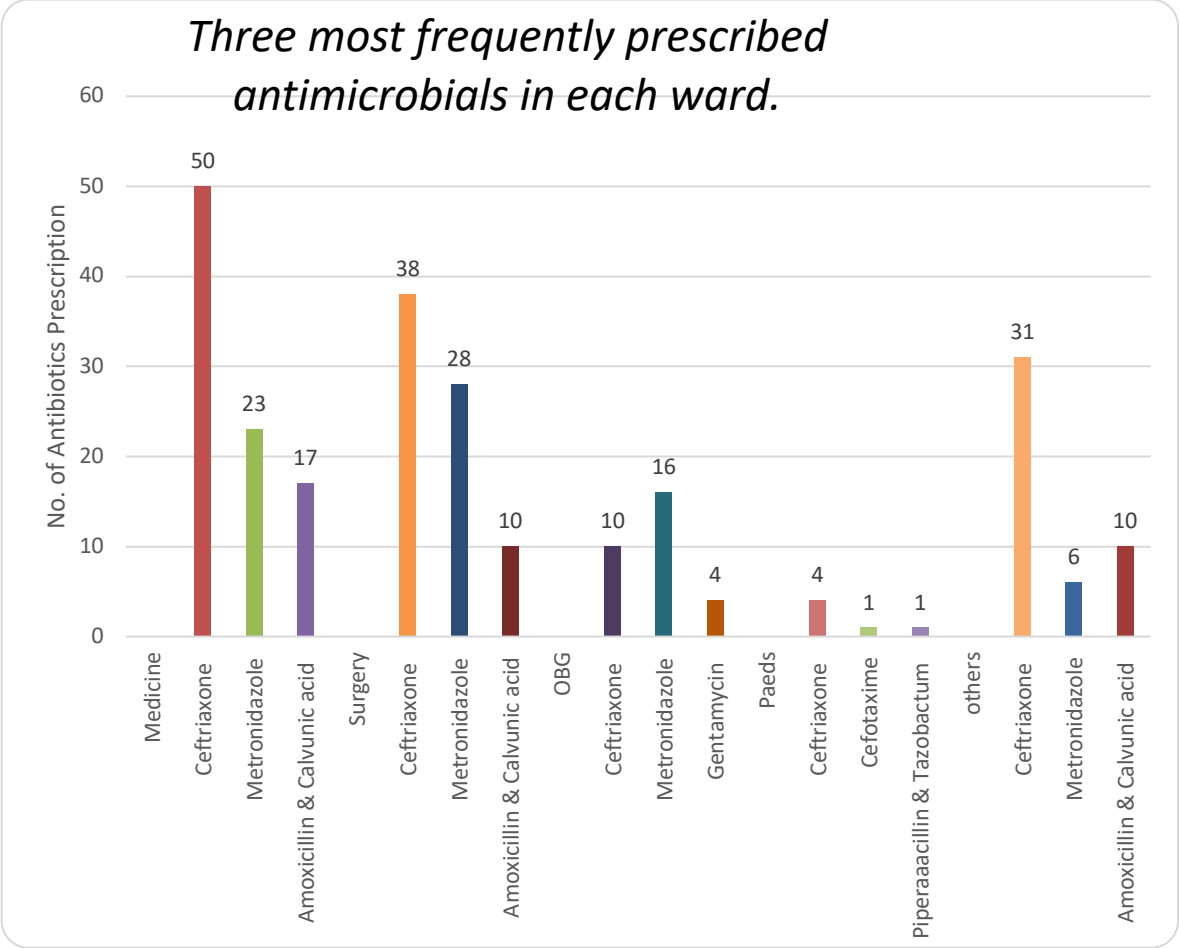

Figure 2: Three most frequently prescribed antimicrobials in each ward

Discussion

India is the largest manufacturer and consumer of antimicrobial agents, but there is no data available on the level of AMR. The government of India launched the National Action Plan on Antimicrobial Resistance in 2017 to contribute towards the global effort to tackle this silent pandemic. This point prevalence survey on antimicrobial consumption is a part of the national initiative to address the pressing challenge of inappropriate antimicrobial prescription and resultant antimicrobial resistance. It was conducted using WHO methodology, which is a simple tool to monitor the effectiveness of antibiotic policies and generate useful data on the prevalence and the pattern of antibiotic use and guide antibiotic stewardship programs. The prevalence of antimicrobial use was 81.4% among the hospitalized eligible patients on the days of the survey. This is high compared to Ethiopian hospitals (72%), Latin America (54%), and other Indian hospitals (64.7%), all belonging to LMIC, and is much higher than antimicrobial use in European PPS

2016-17 (28%) and USA PPS 2015 (46%), which are high-income countries (HIC) [14–18]. Higher use of antimicrobials in hospitalized patients may be attributed to the physician's antibiotic prescribing practice, less importance to antibiotic guidelines, poor utilization of microbiology facilities, and easy/ample accessibility of antimicrobials in the hospital pharmacy. Fear of treatment failure because of the presence of resistant organisms in the community and a higher infection rate due to poor sanitation and hygiene facilities also forces clinicians to prescribe higher and multiple antibiotics to hospitalized patients. Surgery wards have the highest prevalence of antimicrobial consumption, which may be to prevent surgical site infection, which is a frequent postoperative complication.

A request for blood culture at the time of initiation of therapy was sent only in 6.3% of cases, and treatment based on AST results was done only in 1.1% of cases, which is extremely low as compared to other studies [6, 15]. This underutilization of microbiological services and a preference for empirical prescribing, which is like other LMICs [14,19,20], but contrasts with HICs [18,21] and is a major contributor to AMR. This calls for an urgent need to raise awareness among the clinicians to refrain from empiric prescription to decrease antibiotic consumption. At present this institute is working to create its own institutional antibiogram, which will help the clinicians to prescribe more rationally. Among therapeutic indications for prescriptions, surgical prophylaxis (45.1%) was the leading indication, and an antimicrobial was administered for a duration more than the recommended single pre-operative dose. Prolonged use of unnecessary antibiotics even after aseptic precautions is associated with an increased rate of AMR and side effects [14]. The hospital-acquired infection (HAI), as mentioned in case sheets, was seen in 8 cases (4.6%), which is like other studies [14,17,18]. These patients were prescribed 4 or more antimicrobial agents, mostly from the Watch group, which has high resistance potential. HAI can be due to surgical site infection, hospital-acquired pneumonia, catheter-associated urinary tract infection, and central line-associated septicemia and usually is an outcome of inadequate sanitation in hospital settings with non-adherence to strict aseptic precautions, limited susceptibility testing, and preferential use of second-line agents from the watch category [21]. HAIs are usually caused by multi-drug-resistant organisms and may disseminate from healthcare settings to the community, further amplifying the burden of AMR [22].

Individual case record analysis shows that 12.6% and 18.3% of patients received double antibiotic cover for anaerobic and gram-negative infections, respectively. The addition of a second antimicrobial agent to treat Gram-negative infections that are susceptible to a single agent may amplify antimicrobial resistance by increasing selective pressure on pathogens and increasing the incidence of adverse effects [23]. Patients on double anaerobic coverage (12.6%) received amoxicillin/clavulanic acid along with metronidazole empirically, which should be avoided as amoxiclav itself has coverage against gram-positive and gram-negative anaerobic organisms. Double anaerobic cover is recommended only in a few instances, like Clostridium difficile infection or necrotizing fasciitis [24]. The route of drug administration is an important quality indicator for antimicrobial stewardship. 91.4% of patients received antimicrobials intravenously, like studies from other countries [6, 14-17, 21]. Antibiotic stewardship intervention recommends switching to oral antibiotics as early as possible based on microbiology results, as it has better outcomes in terms of complications, adverse effects, resistance, and cost [25].

338 antimicrobial prescriptions were issued to 175 patients with 20 different antibiotics for systemic use. The most frequently prescribed antimicrobial was ceftriaxone (39.3%), followed by metronidazole (21.6%) and amoxiclav (10.9%), which is similar to other studies in India and other LMICs [15,16,26]. This finding is different from PPS in high-income countries, where penicillin with a β-lactamase inhibitor (Amoxiclav) was the most prescribed antibiotic, followed by third-generation cephalosporins [15, 27]. National Treatment Guidelines recommend using third-generation cephalosporins (e.g., ceftriaxone) only when the first-line agents are ineffective [28,29]. The high empirical use of ceftriaxone as a first-line agent is largely because of its easy availability in the hospital pharmacy and the non-availability of cefazolin (first-generation cephalosporin with better infection clearance rate and lower cost). Although Amoxiclav was the third most prescribed antimicrobial, it is recommended as a first-line agent from the access group with high susceptibility against community pathogens [29].

According to the WHO AWaRe classification, antimicrobials prescribed should be more than 60% from the Access group, less than 40% from Watch, and less than 4% from the Reserve group [13]. Use of second-line drugs (watch group) empirically as the first drug of choice can lead to not only a higher rate of resistance but also an increase in ADR. Irrational use leads to mutations among the commensals, which may become reservoirs of AMR genes and may fuel the "resistance gene pool" of pathogenic bacteria through horizontal gene transfer. These resistant organisms may disseminate, leading to the spread of multi-drug-resistant pathogens into the community [30]. In a study on antibiotic-associated adverse drug effects,

cephalosporins were most implicated for causing ADRs, with ceftriaxone being the leading individual offender [31]. Therefore, the use of ceftriaxone for empirical therapy should be discouraged. In this survey, 46.9% of antimicrobials were from the Access group, 51.9% from the Watch group, and 1.2% from the Reserve group. This prescribing is better than in West and Central Asian countries, where 66.1% of prescriptions were from Watch and only 28.4% from the access group [32]. The use of "watch" antibiotics was high in lower-middle and upper-middle-income countries, and this may be ascribed to easy access to these antibiotics and rising levels of resistance to Access Group.

Conclusion

Most of the responsibility of reducing the AMR lies with the physician. This study shows that the prevalence of antimicrobial prescriptions was 81.39% and only 1.1% after susceptibility testing, indicating the underutilization of microbiological services. The high prevalence of antibiotic consumption in surgical wards (88%) and higher use (51.8%) from the "Watch" group with ceftriaxone as the most frequently prescribed antimicrobial agent suggests a pressing need on the part of the clinicians to follow standard treatment guidelines to prevent antimicrobial resistance. The results of this survey will motivate greater action on AMR by highlighting targets for antimicrobial stewardship interventions and ensuring safer prescribing practices.

Recommendations: AMR is a dynamic and rapidly evolving field. As “selective antibiotic pressure” mounts, newer, highly resistant pathogens will continue to emerge, posing new challenges to clinicians. So, we recommend the antimicrobial prescribing behavior must preferably be from the Access group, should adhere to standard treatment guidelines of infectious diseases after performing susceptibility testing, and follow the hospital/local antibiogram. Double antimicrobial for gram-negative or anaerobic infection must be used only in recommended infections. Periodic surveillance should be conducted to monitor antimicrobial use and implement interventions to prevent the spread of AMR.

Limitations: This study was done at a single tertiary care center and is not representative of primary and secondary care centers. Certain quality indicators, like a request for culture from the site of infection, time taken for sequential antimicrobial therapy (shifting from IV to oral to reduce the cost and complications of parenteral therapy), antibiotic de-escalation (shifting from empirical to definitive therapy after susceptibility testing), dose adjustment for renal functions, and therapeutic drug monitoring, were not included in the survey, which would have given a better insight about the prescribing behavior and would guide the stewardship program better. Though antimicrobial susceptibility testing facilities exist in the institute and the reports are generated in a timely manner, they are inadequately used. The findings of this survey will certainly aid the hospital antibiotic policy and will be a step toward AMR containment.

Technical support: National Centre for Disease Control, DGHS, Ministry of Health and Family Welfare, Govt. of India

Acknowledgment: All Faculty and Residents, Department of Pharmacology, Medical student volunteers from 2nd year MBBS, Ms. Apoorva Gupta Pharmacist for the NAC-NET site: for survey and manuscript compilation, Mr. Piyush Sharma, Data Entry Operator, Ms. Preeti Singh Pharmacovigilance Associate (PvPI) Pt. JNM Medical College, Raipur for manuscript bibliography.

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