









Shweta Kumar<sup>1</sup> Pankaj Shukla<sup>2</sup> Pramod Goel<sup>2</sup> Vivek Mishra<sup>2</sup> Ayush Gupta<sup>3</sup> Tadepalli Karuna<sup>3</sup> Rakesh Srivastava<sup>4</sup> Amit Gupta<sup>5</sup> Deepak Baharani<sup>6</sup> Parijat Pansey<sup>7</sup> Sunil Chandiwal<sup>8</sup> Sandeep Shrivastava<sup>9</sup> Ankur Gupta<sup>10</sup> Shailendra Singh Rajpoot<sup>11</sup> DebaDulal Biswal<sup>12</sup> Mehrunnisa Ansari<sup>13</sup> Kamini Walia<sup>14</sup> Sagar Khadanga<sup>1</sup>

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Address for correspondence Sagar Khadanga, MBBS, MD, Section of Infectious Diseases, Department of General Medicine, All India Institute of Medical Sciences, Bhopal, 462020, Madhya Pradesh, India (e-mail: drsagarkhadanga@gmail.com).

# **Abstract**

# **Keywords**

- ► antibiotic consumption
- antibiotic usage
- antimicrobial resistance
- antimicrobial stewardship program
- ► point prevalence study

Objective Indian hospitals (especially government-run public sector hospitals) have a nonexistent antimicrobial stewardship program (AMSP). After successfully initiating AMSPs in tertiary care hospitals of India, the Indian Council of Medical Research envisages implementing AMSP in secondary care hospitals. This study is about the baseline data on antibiotic consumption in secondary care hospitals.

Materials and Methods It was a prospective longitudinal observational chart review type of study. Baseline data on antibiotic consumption was captured by a 24-hour point prevalence study of antibiotic usage and bacterial culture rate. The prescribed antibiotics were classified according to the World Health Organization (WHO) Access, Watch, and Reserve classification. All data were collated in Microsoft Excel and summarized as percentages.

**Results** Out of the 864 patients surveyed, overall antibiotic usage was 78.9% (71.5%) in low-priority areas vs. 92.2% in high-priority areas). Most of the antibiotic usage was

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Thieme Medical and Scientific Publishers Pvt. Ltd., A-12, 2nd Floor, Sector 2, Noida-201301 UP, India

<sup>&</sup>lt;sup>1</sup> Department of General Medicine, All India Institute of Medical Sciences, Bhopal, Madhya Pradesh, India

<sup>&</sup>lt;sup>2</sup>Department of Quality Assurance, National Health Mission, Government of Madhya Pradesh, Bhopal, Madhya Pradesh, India

 $<sup>^{3}</sup>$  Department of Microbiology, All India Institute of Medical Sciences, Bhopal, Madhya Pradesh, India

<sup>&</sup>lt;sup>4</sup>Department of General Medicine Govt. J.P. Hospital, Bhopal, Madhya Pradesh, India

<sup>&</sup>lt;sup>5</sup> Department of Critical Care, Bansal Hospital, Bhopal, Madhya Pradesh, India

<sup>&</sup>lt;sup>6</sup> Jabalpur Hospital & Research Centre, Jabalpur, Madhya Pradesh, India

<sup>&</sup>lt;sup>7</sup>Department of Pulmonology, Anant Hospital, Jabalpur, Madhya Pradesh, India

<sup>&</sup>lt;sup>8</sup> Department of Medical Services, Choithram Hospital, Indore, Madhya Pradesh, India

<sup>&</sup>lt;sup>9</sup>Department of Surgery, Medanta Hospital, Indore, Madhya

<sup>&</sup>lt;sup>10</sup>Department of Critical Care, Rajshree Apollo Hospital, Indore, Madhya Pradesh, India

<sup>&</sup>lt;sup>11</sup> Department of Critical Care, Metro Hospital & Cancer Research Centre, Jabalpur, Madhya Pradesh, India

<sup>&</sup>lt;sup>12</sup>Department of Medical Oncology, Balco Medical Centre, Raipur, Chhattisgarh, India

<sup>&</sup>lt;sup>13</sup>Department of Microbiology, Govt. P.C. Sethi Hospital, Indore, Madhya Pradesh, India

<sup>&</sup>lt;sup>14</sup>AMR Division of Epidemiology and Communicable Diseases, Indian Council of Medical Research, New Delhi, India

empirical with an extremely low bacterial culture rate (21.9%). Out of the prescribed drugs, 53.1% were from the WHO watch category and 5.5% from the reserve category. **Conclusion** Even after 5 years of the launch of the national action plan on AMR (NAP-AMR) of India, AMSP is still non-existent in small- and medium-level hospitals in urban cities. The importance of trained microbiologists in the health care system is identified as a fulcrum in combating antimicrobial resistance (AMR); however, their absence in government-run district hospitals is a matter of grave concern and needs to be addressed sooner than later.

### Introduction

Since the discovery of the first antibiotic over a century ago, antibiotics have saved millions of lives from infectious diseases and increased the life expectancy of humans. The link between antibiotic usage and the emergence of resistant organisms has been well recognized.<sup>1</sup> Between the years 2000 and 2015, global per-capita antibiotic consumption increased by 39%, primarily due to an increase in income and hence consumption of antibiotics. India was identified to have a drastic increase in the consumption of antibiotics in 2018.<sup>2</sup> With the unrestricted overuse and misuse of these life-saving antibiotics, we are witnessing, never seen before, antimicrobial resistance (AMR). Identifying the increased incidence of multidrug resistant organisms (MDROs), World Health Organization (WHO) developed the global action plan on AMR in 2015.3 India launched its national action plan on AMR (NAP-AMR) in 2017 and advocated each of its states for an actionable plan on the blueprint of NAP-AMR.<sup>4</sup> The state of Madhya Pradesh is situated in the central region of India and is the second state in the country to roll out the Madhya Pradesh State Action Plan for containment of antimicrobial resistance (MPSAPCAR).

Improved access to antibiotics and yet avoiding irrational usage is critical for improving health outcomes. A thorough understanding of antibiotic consumption globally and in each geographical region is a critical component of anti-AMR strategies. Sustainable development goals call for everyone to have access to safe, effective, high-quality, and affordable essential medicines and vaccines. Balancing the easy access to antibiotics and ensuring their appropriate use is a global challenge.<sup>5</sup> As part of the Essential Medicines List (2017), WHO introduced categorizing the drugs into the Access, Watch, and Reserve (AWaRe) classification of antibiotics. AWaRe divides antibiotics used to treat common infections into categories: Access, Watch, Reserve, and unclassified. Access groups of antibiotics are typically used as first or second-line therapies, and they should be widely available and reasonably priced, whereas the "Watch and Reserve" group of antibiotics are used as the last line of the resort and should be utilized at the bare minimum.<sup>6</sup>

Indian Council of Medical Research (ICMR) has established a nationwide "Antimicrobial Resistance Surveillance and Research Network" (AMRSN).<sup>7,8</sup> All India Institute of Medical Sciences, Bhopal (AIIMS Bhopal) is one of the regional centers

of ICMR AMRSN. After the successful initiation of the antimicrobial stewardship program (AMSP), in the participating tertiary care hospitals, the AMRSN is currently working with the feeding secondary care hospitals in small cities of India, generating data on the consumption of antibiotics usage and subsequent advocacy for AMSP. This study is about the baseline data of antibiotic consumption in secondary care hospitals of central India. This is one of its types of study, consolidating Indian data on antibiotic usage and bacterial culture rate (BCR) in secondary care hospitals.

### **Materials and Methods**

This is a prospective longitudinal observational chart review type of study. A total of 10 sites were nominated by National Health Mission in three cities of Madhya Pradesh. Out of the total 52 districts of Madhya Pradesh, only two districts hospitals (DHs) had microbiological culture facilities and were included in the study. The rest of the 8 study sites were smaller nursing homes in urban cities with in-house microbiology laboratories. The study was initiated with due approval from the Institute Human Ethics Committee (IHEC) vide letter of permission number-LOP/2020/EF0157 dated February 24, 2020. As the study was only an observational chart review without any patient identifier, waiver of consent was granted by IHEC.

The hospitals identified their intensive care unit (ICU) and high-dependency care unit (HDU) as high-priority areas (HPA) for AMSP implementation. Some low-priority areas (LPA) like general wards were also identified for comparison. The study was initiated on April 1, 2021, and is still ongoing. Baseline point prevalence study (PPS) was conducted at the implementation of AMSP in the hospital using an in-house developed tool. Data was captured from 8 AM of the day till 8 AM of the next day. BCR was calculated by dividing the number of cases in which any form of the sample was sent for aerobic bacterial culture by the total number of patients who were on an antibiotic. All patients admitted to AMSP implementation areas were considered. Data collection was entrusted to the on-duty nursing officers (NO). Data accuracy was checked by the senior NO and medical records department. The final data was checked and compiled by the quality managers of the hospital. The formal sample size was not calculated and all cases who were hospitalized in the AMSP implementation areas of the hospitals were included in the

**Table 1** Baseline antibiotic consumption in the low-priority area

Hospital	Patients surveyed (N)	Patients on of oral/IV antibiotics, n/N (%)	Patients on intravenous antibiotics, n1/N (%)	Patients on oral antibiotics, n2/N (%)
H1	168	129/168 (76.8)	118/168 (70.2)	11/168 (6.5)
H2	35	21/35 (60.0)	21/35 (60)	0/35 (0)
Н3	52	41/52 (78.8)	41/52 (78.8)	0/52 (0)
H4	9	8/9 (88.9)	8/9 (88.9)	0/9 (0)
H5	76	66/76 (86.8)	66/76 (86.8)	0/76 (0)
Н6	52	31/52 (59.6)	29/52 (55.8)	2/52 (3.8)
H7	41	34/41 (82.9)	27/41 (65.9)	7/41 (17.1)
Н8	61	12/61 (19.7)	11/61 (18)	1/61 (1.6)
Н9	30	28/30 (93.3)	21/30 (70)	7/30 (23.3)
H10	32	28/32 (87.5)	27/32 (84.4)	1/32 (3.1)
Total	556	398/556 (71.5)	369/556 (66.3)	29/556 (5.2)

Abbreviation: IV, intravenous.

study. Compiled and collated data were entered in spreadsheets. The data were summarized as frequencies and percentages for categorical variables. The percentage was calculated to one decimal value.

## **Statistical Analysis**

All data were collated in Microsoft Excel for analysis. Categorical variables were summarized as percentages.

### Results

A total number of 864 in-patients (556 in LPA and 308 in HPA) were surveyed at 10 different hospitals for conduction of the PPS. Overall, 682 patients (398 in LPA and 284 in HPA) accounting for 78.9% of patients were on at least one antibiotic, that is, oral or intravenous (IV) in our study group. The detailed hospital-wide patient data in LPA is provided in ►Table 1 and that of HPA is mentioned in ►Table 2.

The mean percentage of patients with any form of antibiotic (oral/IV) was 71.5% in LPA with a range from 19.7 to 93.3% in various hospitals. In LPA, the mean percent of cases with IV antibiotic usage was 66.3% (18-88.9%). The mean percentage of patients with any form of antibiotic (oral/IV) was 92.2% in HPA, like ICU/HDU with a range from 84.8 to 100% of cases. In HPAs, the mean percent of cases with IV antibiotic usage was 85.7% (62.1-100%). Among all the patients who were on IV antibiotics (LPA = 369, HPA = 265), only 7% of cases in LPA versus 11.6% cases in HPA were initiated IV antibiotics on that day of PPS and 87.5% of patients were continued with the same antibiotics in LPA versus 72.8% in HPA.

WHO AWaRe classification was conducted among all the patients who were on IV antibiotics. Out of the total number of 634 patients who were on IV antibiotics, 269 (42.4%) cases belonged to the Access category, 337 (53.1%) cases to the Watch category, and 35 (5.5%) cases to the Reserve category

Table 2 Baseline antibiotic consumption in the high-priority area

Hospital	Patients surveyed (N)	Patients on of oral/IV antibiotics, n/N (%)	Patients on intravenous antibiotics, n1/N (%)	Patients on oral antibiotics, n2/N (%)
H1	66	56/66 (84.8)	41/66 (62.1)	15/66 (22.7)
H2	14	13/14 (92.9)	13/14 (92.9)	0/14 (0)
Н3	37	37/37 (100)	35/37 (94.6)	2/37 (5.4)
H4	14	14/14 (100)	14/14 (100)	0/14 (0)
H5	24	24/24 (100)	24/24 (100)	0/24 (0)
H6	22	19/22 (86.4)	19/22 (86.4)	0/22 (0)
H7	26	24/26 (92.3)	22/26 (84.6)	2/26 (7.7)
Н8	8	8/8 (100)	7/8 (87.5)	1/8 (12.5)
Н9	89	81/89 (91)	81/89 (91)	0/89 (0)
H10	8	8/8 (100)	8/8 (100)	0/8 (0)
Total	308	284/308 (92.2)	264/308 (85.7)	20/308 (6.5)

Abbreviation: IV, intravenous.

Table 3	Point prevalence of	antibiotic usage and	BCR
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LPA			НРА			
Hospital	Patients on any antibiotics, N	Patients for whom any culture was ordered, n <sub>1</sub>	BCR, n <sub>1</sub> /N (%)	Total no. of patients on any antibiotics, N	Total no. of patients for whom any culture was ordered, $n_2$	BCR, n <sub>2</sub> /N (%)
H1	129	2	2/129 (1.6)	56	0	0/56 (0.0)
H2	21	21	21/21 (100.0)	13	13	13/13 (100.0)
H3	41	8	8/41 (19.5)	37	12	12/37 (32.4)
H4	8	0	0/8 (0.0)	14	3	3/14 (21.4)
H5	66	26	26/76 (39.4)	24	13	13/24 (54.2)
H6	31	7	7/31 (22.6)	19	11	11/19 (57.9)
H7	34	0	0/34 (0.0)	24	4	4/24 (16.7)
H8	12	8	8/12 (66.7)	8	2	2/8 (25.0)
H9	28	4	4/28 (14.3)	81	12	12/81 (14.8)
H10	28	3	3/28 (10.7)	8	1	1/8 (12.5)
Total	398	79	79/398 (19.8)	284	71	71/284 (25)

Abbreviations: BCR, bacterial culture rate; HPA, high-priority area; LPA, low-priority area.

of IV antibiotics. On subcategorization, 55.6% of IV antibiotics were from the Watch category in LPA versus 49.8% in HPA, and 3.3% of IV antibiotics were from the Reserve category in LPA versus 8.7% in HPAs.

The overall BCR was 21.9% (150/682) and 19.8% (79/398) in LPA versus 25% (71/284) in HPA. Five out of ten hospitals had BCR less than 25% in both LPA and HPA. Blood was the most common specimen sent for culture 53/150 (35.3%), followed by urine (24%), respiratory samples (19.3%), pus (6.6%), and others (13.3%). Among the total number of specimens sent for microbiological culture, the overall culture positivity rate was 33.3% (50/150). The culture positivity rate for different specimens was as follows: pus (70%), respiratory samples (51.7%), urine (38.8%), and blood (16.9%) as in **Table 3**.

# **Discussion**

This is a study of its kind to identify the spectrum of consumption of antibiotic usage among hospitalized patients in medium and small hospitals in central India. The overall point prevalence of antibiotic usage (PPAU) was found to be 66.3% for IV antibiotics. We have earlier reported a PPAU of 47.9% in the same region but in a large tertiary care institute.9 Our observations are similar to that of other studies from Pakistan (70.6%) and China (54.5%). 10,111 However, the PPAU is significantly low in European countries like Switzerland (23.6%),<sup>12</sup> Ireland (20.6%),<sup>13</sup> and Scotland (9.9%). 14 The BCR in this study was found to be extremely low (21.9%) in these secondary care hospitals. We have earlier reported the baseline BCR in the same region but in a large tertiary care institute as 47.3%. 15 The BCR from various other countries has been documented as follows: China (40.16%), <sup>16</sup> Italy (61.2%), <sup>17</sup> and Switzerland (69%). <sup>18</sup> We have also documented in our earlier study that BCR

improves significantly (47.3% to 77.6%) with the implementation of AMSP. This study emphasizes the need for urgent AMSP implementation at secondary care hospitals in India.

As per WHO recommendations, the "Access category" of antibiotics should be approximately 60% with a negligible amount of usage of the Reserve group of antibiotics. In our study, the ground reality was far more alarming. The mean usage of the "Access category" of antibiotics was only 42.4%. "Watch category" of drugs was used in 53.1%. The "Reserve category" that should be as minimal as possible was found to be up to 5.5%. A recently published study by ICMR among coronavirus disease 2019 (COVID-19) patients found that almost 75% of antibiotics are prescribed from "Watch and Reserve categories" of antibiotics. However, the study was published from tertiary care centers with high-end COVID-19 treatment facilities. A country-wise comparative usage of various categories of drugs is provided in - Table 4.

This study demonstrates the extremely high levels of usage of antibiotics (specifically IV antibiotics) in secondary care small and medium hospitals in India. The study further emphasizes the dismal state of microbiological identification and targeted antibiotic therapy. The reasons are multifold, namely nonavailability of trained clinical microbiologists and laboratory technicians, nonreliability of the laboratory, nonavailability of the laboratory  $24 \times 7$ , and cost burden to the poor patients. However, the orthodox attitude of the clinicians to send an appropriate sample for microbial identification is also an important factor. It was alarming to know that only 2 out of 52 government-run public DHs have in-house microbiological laboratory facilities. Even in those two DHs, trained clinical microbiologists were not available. Time is apt to develop an adequate number of reliable microbiology laboratories in public sector government-run hospitals for a successful practice of AMSP.

**Table 4** Antibiotic usage in different countries as per WHO AWaRe classification

Country	WHO AWaRe classification of drugs		
	Access	Watch	Reserve
Canada <sup>20</sup>	85.9	8.5	0.006
Australia <sup>20</sup>	84.3	8.8	0.003
USA <sup>20</sup>	86.7	11.9	0.1
UK <sup>20</sup>	73.2	12.1	0.05
Sri Lanka <sup>20</sup>	80.5	13.9	0.0
Russia <sup>20</sup>	79.4	19.8	0.002
China <sup>20</sup>	40.3	42.2	0.1
India <sup>20</sup> (earlier study)	35.0	47.3	0.2
India (current study)	42.4	53.1	5.5

Abbreviation: WHO AWaRe, World Health Organization (WHO) Access, Watch, and Reserve.

The limitations of the study are that hospitals were nominated by the state government machinery without randomization where at least some facilities of in-house microbiological laboratories were available. All the hospitals were nominated from four smaller cities in central India. The data was self-reported by the hospitals and hence the actual scenario might be darker.

### **Conclusions**

India developed its NAP-AMR in 2017 and MPSAPCAR was developed in 2019. The study documents the baseline characteristics of antibiotic usage in small and medium hospitals in central India. The extremely high rates of empirical usage of antibiotics (Watch and Reserve categories) with an extremely low incidence of BCR are bothersome and have the potential for community-level MDROs epidemics in India and subsequent pandemics in near future. It seems the COVID-19 scenario has augured a pandemic within a pandemic.

# **Ethical Approval**

The study was initiated with due approval from the Institute Human Ethics Committee (IHEC) vide letter of permission number-LOP/2020/EF0157 dated February 24, 2020.

Conflict of Interest None declared.

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