International Journal of One Health
Available at www.onehealthjournal.org/Vol.9/No.2/14.pdf

RESEARCH ARTICLE
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Generating evidence on antibiotic use across human and animal health sectors using the World Health Organization's Access, Watch, Reserve (AWaRe) classification: Exploratory pilot study in rural Pune, India

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Received: 11-07-2023, **Accepted:** 16-11-2023**, Published online:** 22-12-2023

doi: www.doi.org/10.14202/IJOH.2023.166-171 **How to cite this article:** Kudale AM, Hiralkar SS, Sawant PA, Hulsurka YP, Fatate NR, Waghmare PP, Randive AP, Phutane MS, Pawar P, and Mhase P (2023) Generating evidence on antibiotic use across human and animal health sectors using the World Health Organization's Access, Watch, Reserve (AWaRe) classification: Exploratory pilot study in rural Pune India, *Int. J. One Health*, 9(2): 166–171.

Abstract

Background: Human antibiotic formulations in animal feed for therapeutic and non-therapeutic purposes have contributed to antimicrobial resistance worldwide; however, little evidence is available in low- and middle-income countries. We aimed to generate evidence of antibiotic use across the human and animal health sectors by investigating the overlap in antibiotic use in community settings in rural blocks of Pune District, India, following the World Health Organization's (WHO) Access, Watch, Reserve (AWaRe) classification.

Materials and Methods: An exploratory pilot study using a cross-sectional design in two randomly selected rural blocks of the Pune district included 138 interviews with general physicians (GPs, n = 62), pharmacists (n = 60), and veterinary practitioners (n = 16) using semi-structured interview schedules and the WHO AWaRe classification. IBM-Statistical Package for the Social Sciences, Version 21.0 software was used for descriptive statistics and to calculate the proportions of the different antibiotic groups. The WHO AWaRe classification was used to describe antibiotic use by the study participants and to assess the overlap in antibiotic use.

Results: Our study provides evidence of an overlap in human and animal antibiotic use in rural community settings across the human and animal health sectors. Amoxicillin (access group), penicillin (access group), and ofloxacin (watch group) were used in both human and animal health. Amoxicillin and penicillin were used to treat common bacterial infections, ofloxacin was used to treat skin infections in humans and animals, and ofloxacin was used to treat pneumonia in animals and urinary bladder infections in humans. In contrast, azithromycin (watch group), cefixime (watch group), and amoxicillin (Access Group), with or without other antibiotics, were the most commonly used antibiotics by GPs in humans.

Conclusion: We confirmed the overlap in antibiotic use across the human and animal health sectors in rural community settings, suggesting the need for interventions following the One Health approach. Further, research is required to assess the patterns of this overlap, as well as behavior, knowledge, and potential solutions to help avoid this overlap and prevent the rampant use of antibiotics in the animal and human health sectors in rural community settings.

Keywords: antimicrobial resistance, antibiotics use, overlap, rural India, WHO AWaRe.

Introduction

Antibiotics are used as preventive and curative measures against infectious diseases [1–3]. Antibiotics are widely used in human medicine and animal husbandry. However, the indiscriminate use of antibiotics has contributed to the development of antimicrobial resistance (AMR) among microbial species [3–5]. According to the World Health Organization (WHO), AMR is one of the top ten global public health threats. Anthropogenic factors such as indiscriminate prescribing of antibiotics by physicians and over-the-counter (OTC) dispensing are growing threats to public health [6–8]. The WHO states that approximately half of antibiotic consumption is attributed to non-human applications [9, 10].

On the other hand, antibiotics are used to improve the health and productivity of dairy animals and poultry birds [11, 12] in livestock husbandry. The use of antimicrobials for both therapeutic and non-therapeutic purposes, such as the metaphylactic treatment of animals for short-term success, leads to more widespread issues, such as the emergence of

AMR species that are no longer medically curable [13]. Globally, bacterial AMR is known to cause 1.27 million deaths each year, and 4.95 million deaths are associated with bacterial AMR [14]. In India by 2050, a 7.5% decline in livestock populations is predicted as a direct result of bacterial AMR [14]. India is known as "The AMR Capital of the World" due to the significant burden of drug-resistant pathogens [15]. In 2015, the World Health Assembly developed a global action plan on AMR as a response to a serious AMR crisis that has recently emerged. This global AMR action plan outlines five main objectives and addresses the need for a practical "one health" approach. The competing interests of multiple organizations involved in human medicine, animal, and environmental sectors pose a challenge in completely accepting a single health approach [16]. Some of the critical challenges in implementing antibiotic stewardship interventions include a lack of awareness and motivation among prescribers regarding discriminant practices in an antibiotic prescription, lack of adequate controls on antibiotic availability, including OTC availability, pressure from the livestock production industry for unnecessary prescribing of antibiotics, and lack of reliable data on antibiotic consumption [17, 18]. In 2017, the WHO Expert Committee developed an Access, Watch, Reserve (AWaRe) classification system of antibiotics to facilitate antibiotic stewardship efforts at each level [3, 19]. The AWaRe classification of antibiotics is expected to facilitate the discriminatory use of antibiotics and prevent their systematic misuse and overuse. Antibiotics are classified into three categories based on their spectrum of activity and potential to develop resistance: Access, first- and second-line treatment for infections; Watch, broad-spectrum antibiotics; and reserve, last-resort antibiotics [19].

Many antibiotics such as growth promoters or prophylaxis are used in livestock management for therapeutic and non-therapeutic purposes [16, 20–22]. Although earlier studies suggest an overlap in antibiotic use between humans and animals, which depletes the efficacy of antibiotics [6], there is less documentation in Indian setting, particularly in rural areas.

Against this background, we designed an exploratory pilot study to assess the extent of overlap in antibiotic use within and across human and animal health sectors by documenting the antibiotics prescribed by human general practitioners termed as general physicians (GPs), veterinary practitioners, and pharmacists using the WHO AWaRe classification, which has proven to be a user-friendly monitoring tool to classify and organize antibiotics, as well as promoting responsible use [3].

Materials and Methods

Ethical approval and Informed consent

Ethical guidelines (ICMR 2018 guidelines) for health and social sciences research were strictly followed throughout this study. Written informed consents were obtained from GPs, veterinary practitioners, and pharmacists. The study was approved by the Institutional Ethics Committee of Savitribai Phule Pune University (Ref. No. SPPU/IEC/2020/84).

Study period and location

The study was conducted from January 2021 to March 2023 in villages of the Junnar and Mulshi blocks of Pune District, Maharashtra, India.

Study sites

Fifteen blocks were divided into five district subdivisions in Pune district. Except for Pune, all four of these five district subdivisions, Baramati, Bhor, Pune, Shirur, and Maval, are predominantly rural. Of these four rural subdivisions, two were selected. Shirur, which encompasses Junnar, Ambegaon, Khed, and Shirur talukas and is more distant from urban Pune, and Maval, which encompasses Maval and Mulshi talukas, was selected as the study sites.

Study design, sampling approach and sample size

This was an exploratory pilot cross-sectional study. Two blocks were randomly selected from these two rural subdivisions of Pune District, Junnar and Mulshi. These blocks included 23 villages, 12 from Junnar and 11 from Mulshi, with human and livestock populations, which were then randomly selected using a proportionate human and animal population sampling approach. All GPs (n = 62), veterinary practitioners (n = 16), and pharmacists (n = 60) who were available and willing to participate at the time of the study were purposively selected for this study.

Data collection and analysis

Three predesigned and pretested semi-structured interview schedules were used for GPs, veterinary practitioners, and pharmacists. In addition to profile characteristics, the interview schedules included details of antibiotic use through which they were administered, prescribed, sold, and dispensed for common infections. The Statistical Package for the Social Sciences software (version 21.0, IBM SPSS Statistics, NY, USA) was used for descriptive statistics and to compute the proportions of the different antibiotic groups. The 2021 WHO AWaRe classification describes antibiotic use by the study participants, as assessed by the variations between AWaRe group antibiotics.

Results

Profile of the study participants

A total of 138 interviews were conducted with study participants from Junnar and Mulshi blocks, including GPs (n = 62), veterinary practitioners (n = 16), and pharmacists (n = 60).

Profile of GPs

Of the 62 GPs, 50 (81%) were men and 12 (19%) were women with ages ranging from 24 to 68 years with a median of 39.5 years. A majority 30 (49%) of the participants had completed the bachelor of ayurvedic medicine and surgery, followed by 16 (27%), 11 (18%), and 5 (6%) from other backgrounds, including bachelor of dental surgery, licentiate in the court of examiners in homeopathy, and bachelor of Unani medicine and surgery graduates. Overall, clinical experience (in years) of the study participants ranged from a minimum of 1 year to a maximum of 44 years (median: 13.5 years).

Profile of veterinary practitioners

Out of a total of 16 veterinary practitioners, 15 (94%) were male, and one (6%) was female, ranging in age from 25 to 67 years with a minimum age of 25 years and a maximum age of 67 years with a median of 42.5 years. Eight (50%) of the veterinary practitioners had a bachelor of veterinary sciences and master of veterinary sciences educational background, five (31%) had a dairy diploma in management and animal husbandry, and three (19%) were livestock supervisors and livestock development officers.

Profile of pharmacists

All 60 pharmacists were from the Junnar and Mulshi Blocks of the Pune district, with 72% (n = 43) of pharmacy qualifications and 28% (n = 17) of pharmacists from other educational backgrounds, respectively. The duration of pharmacy establishment ranged from 1 to 34 years, with a median of 5.5 years.

Antibiotics prescribed, sold, and dispensed by study participants according to the WHO AWaRe classification

The study participants were asked about their use of antibiotics, and their responses were assessed according to the WHO AWaRe classification.

General Physicians

Table-1 shows the distribution of antibiotics prescribed by GPs for a suspected illness vis-à-vis WHO AWaRe classification. General Physicians reported using six antibiotics from the access group, seven from the watch group, and one from the reserve group.

Top three antibiotics prescribed by general practitioners for routine use

The top three antibiotics prescribed by the GPs were azithromycin, cefixime, and amoxicillin (Figure-1). More than half of the GPs reported prescribing these three antibiotics in their routine practice; some GPs also prescribed other antibiotics. However, 58% of the patients received azithromycin, cefixime, and amoxicillin for specific diseases, such as bacterial infections, chronic diseases, and high fever. Few GPs have reported that they use other treatments other than antibiotics as their first choice of medicine.

Pharmacists

When classifying antibiotics sold or dispensed by pharmacists according to the AWaRe classification, five antibiotics in the access group and three antibiotics in the watch group were reported. The pharmacists in the reserve group did not report any antibiotic use. Table-2 compares the distribution of antibiotics sold or dispensed by pharmacists for a particular disease according to the WHO AWaRe classification.

Veterinary practitioners

The data obtained from veterinary practitioners included six antibiotics from the access group, four from the watch group, and none from the reserve group (Table-3).

Antibiotic use overlap

Table-4 illustrates the overlap in antibiotic use according to the WHO AWaRe classification in the human and animal health sectors.

Discussion

Our study followed the WHO AWaRe classification of antibiotics and found an overlap in the use of amoxicillin, penicillin (access group), and ofloxacin (watch group) in both human and animal health and medicine. Meropenem was the only reserve group antibiotic used in our study, as reported by GPs in their practice. Our study findings suggest that amoxicillin, cefixime, and azithromycin are the antibiotics most commonly prescribed by GPs, which means that a higher percentage of antibiotics were used in the Watch group than in the access group. Our study findings resemble a qualitative cross-country comparison conducted in Uganda, Tanzania, and India on the crossover use of human antibiotics in livestock, where penicillin, amoxicillin, and tetracycline have been reported as used in all three countries [23]. The study findings suggest that eight out of the 26 antibiotics found to be used in animals were from the

Table-1: Antibiotics prescribed by the GPs classified as per WHO AWaRe classification.

Access	Illness/clinical condition (s)	Watch	Illness/clinical condition (s)	Reserve	Illness/clinical condition (s)
Amikacin	Meningitis	Azithromycin	Pneumonia, chest infection	Meropenem	Chest Infection
Ornidazole	Stomach infection	Ciprofloxacin	UTI		
Amoxicillin	Pneumonia, chest infection	Ofloxacin	Skin, bladder, and reproductive organ infections		
Ceftriaxone	Gonorrhea	Cefixime	UTI, STD		
Gentamicin	Infections	Levofloxacin	Pneumonia		
Penicillin	Growth of bacterial Infection	Cefpodoxime	Bronchitis		
		Meropenem	Abdominal Infection		
		Piperacillin	Pneumonia		

GPs=General physicians, WHO=World Health Organization, AWaRe=Access-Watch-Reserve, UTI=Urinary tract infection, STD=Sexually transmitted disease

Table-2: Antibiotics dispensed from the local medical stores are classified as per the WHO AWaRe framework.

Access	Illness/clinical condition (s)	Watch	Illness/clinical condition (s)
Doxycycline	Chest and dental infection	Cefpodoxime	Bronchitis, STDs, skin, nose, ear, sinus and throat infections.
Amikacin	Severe infection (blood, abdomen), lungs, skin, bones, joints, urinary tract	Cefixime	Skin, nose, ear, sinus and throat infections.
Amoxicillin	Bacterial infections, chest infections	Azithromycin	Chest infection (pneumonia), ear, nose and throat.
Benzathine	Respiratory tract infection		
Penicillin	Infections		

WHO=World Health Organization, AWaRe=Access-Watch-Reserve, STD=Sexually transmitted disease

Table-3: Antibiotics prescribed by veterinary practitioners are classified on the WHO AWaRe classification.

Access	Illness/clinical condition (s)	Watch	Illness/clinical condition (s)
Gentamicin	Infection	Ceftriaxone	STDs
Metronidazole	Mouth infection, pelvic, inflammatory disease	Oxytetracycline	Mycoplasma pneumonia
Nitrofurantoin	UTI	Tazobactam	Susceptible microorganism infection, intra-abdominal infection, UTI
Penicillin	Infection, injuries	Ofloxacin	Bacterial infections, skin infections, pneumonia,
Amoxicillin	Pneumonia, chest pain		
Sulbactam	Abdomen pain, female reproductive organ illness, bacterial infection, skin infection		

WHO=World Health Organization, AWaRe=Access-Watch-Reserve, UTI=Urinary tract infection, STD=Sexually transmitted disease

Table-4: Overlap in antibiotic use among humans and animals.

Access	Illness/clinical condition (s)	Watch	Illness/clinical condition (s)
Amoxicillin	Infections	Ofloxacin	Humans: Skin, bladder, and reproductive organ infections Animals: Bacterial infection, skin infection, pneumonia
Penicillin	Infections		

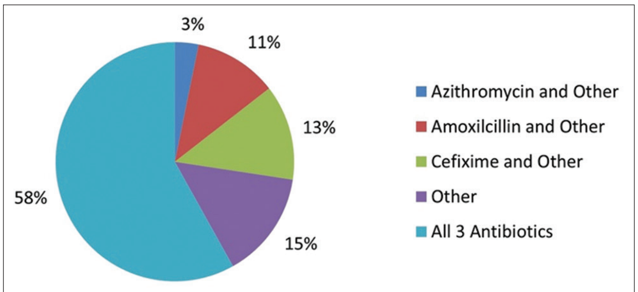

Figure-1: Top three antibiotics prescribed by general physicians.

Watch group; chloramphenicol was most commonly used in Uganda, amoxicillin in Tanzania, and metronidazole in India [23]. In another cross-sectional study conducted in Uganda on the use of antibiotics to treat humans and animals, oxytetracycline hydrochloride was found to be the most commonly used antibiotic for veterinary purposes [24]. Another cross-sectional survey carried out in Kenya on antibiotic practices and knowledge of antibiotic retailers showed that there was a significant overlap between 10 and 15 classes of antibiotics sold for human and animal use. According to the study findings, penicillin, metronidazole, fluoroquinolones, and first- and second-generation cephalosporins are the most commonly used antibiotics in humans. Tetracyclines, sulphonamides, penicillin, and macrolides are used for veterinary purposes [7]. In a study conducted in France on the use of antimicrobials, there has been considerable overlap between antimicrobial usage in human and animal medicine [25]. The Center for Disease Dynamics Economics and Policy Report on Antibiotic Use and Resistance in Food Animals reviewed antibiotic use across India's poultry, dairy, and fishery sectors. Tetracyclines, gentamycin, ampicillin, amoxicillin, cloxacillin, and penicillin were used to treat dairy animals and ampicillin, erythromycin, oxytetracycline, and enrofloxacin were used for fisheries [6]. A study conducted in Zambia in a hospital setting, examining antibiotic prescribing patterns according to the WHO AWaRe classification reported ceftriaxone (26.6%), metronidazole (22.6%), amoxicillin (10.4%), amoxicillin/clavulanic acid (5.6%), and azithromycin (5%) as the most frequently prescribed antibiotics; prescribing of the watch group of antibiotics was higher (42.1%) than the WHO recommended threshold [3].

While the WHO aims to allocate at least 60% of total antibiotic consumption globally to the access group, our study findings suggest that it is difficult to achieve this goal. Indiscriminate prescribing and inappropriate dispensing of antibiotics in both human and animal medicine have led to the development of bacterial AMR. From a "one health" perspective, using human antibiotics on animals can lead to decreased efficacy of antibiotics and the emergence of AMR species, thereby jeopardizing the health and well-being of all human-animal-environment components. The strength of our study is that we triangulated the information from interviews with GPs, pharmacists, and veterinary practitioners and obtained overlapping results. Our study provides evidence that the use of antibiotics in human and animal medicine overlaps in the rural blocks of Pune. We were able to classify the results according to the WHO AWaRe classification and understand the extent of inappropriate antibiotic use, thus paving the way for effective antibiotic stewardship. This exploratory pilot study was conducted in only two blocks of Pune District. Due to the small sample size, the findings of this study cannot be generalized to rural India. Another limitation of this study is the small sample size of veterinary practitioners. These findings highlight the need for an intervention emphasizing health education regarding antibiotic stewardship and changing the behaviors and practices of healthcare professionals, pharmacists, farmers, and livestock producers. We argued that systemic development is essential to make veterinary antibiotic formulations available, accessible, and affordable for small-scale livestock providers, farmers, and poultry owners to avoid continued use of human antibiotics for animal health purposes. Improving the accessibility of veterinary formulations and increasing public awareness of antimicrobial stewardship practices will contribute to the provision of quality care, thus reducing the global burden of AMR.

Conclusion

Our study only confirmed the overlap in antibiotic use across the human and animal health sectors, which poses a grave challenge for materializing the "one health" approach interventions and threatens the health and well-being of the human-animal–environment trio. It is recommended that further research be carried out to highlight the reasons and practices for the use of human antibiotics for animal health purposes. Furthermore, we recommend further research on why watch group antibiotics are used more often than other antibiotics while demonstrating the importance of adhering to the WHO AWaRe classification.

Authors' Contributions

AMK: Conceptualized the study, participated in the design, coordination, data collection and analysis of the study, and critically drafted, revised, and reviewed the manuscript. SSH: Analyzed the data and drafted the manuscript. PAS, YPH, NRF, PPW, APR, and MSP: Participated in data collection and data analysis and revised the manuscript. PP and PM: Coordination of the study, data collection, analysis, and critically revised the manuscript. All authors have read, reviewed, and approved the final manuscript.

Acknowledgments

We gratefully acknowledge our institutes, the Department of Health Sciences under the School of Health Sciences at Savitribai Phule Pune University and the KNP College of Veterinary Science under the Maharashtra Animal and Fishery Sciences University, Nagpur, for allowing us to conduct this study. We are grateful to the GPs, veterinary practitioners, and pharmacists from Junnar and Mulshi blocks of Pune district who participated in this study. We gratefully acknowledge the funding support received from the Indian Council of Medical Research, Division of Epidemiology and Communicable Diseases, New Delhi, India, for the *ad hoc* research project (AMR/Adhoc/240/2020-ECD-II).

Competing Interests

The authors declare that they have no competing interests.

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