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A recent update on the use of antimicrobials for animal health in Yogyakarta, Indonesia

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Abstract

Background and Aim: Animal antimicrobials must be studied to determine if they have the same types, norms of use, and resistance patterns as those used in humans. This study aimed to facilitate the analysis of data on the use of antimicrobials in veterinary medicine and to aid in developing a strategy to prevent the emergence of antimicrobial resistance (AMR) in humans and animals.

Materials and Methods: Data were obtained through a survey of 101 veterinarians working in animal clinics and independent practice in five regencies of Yogyakarta province.

Results: Both of the antibiotics, antiparasitic (78.6%) and, antiseptic and disinfectant (68.0%), and antifungal (31.1%) were the most frequently used types of antimicrobials, while antivirals were the least used (9.7%). The most often treated animals with antimicrobials are pets (37%), followed by large and small livestock (30%), poultry (15%), and exotic animals (14%). Of the respondents, 89% were aware of the factors contributing to AMR, but only 47% monitored developments and expanded their understanding of AMR. The most common antibiotic classes were penicillin (71), tetracyclines (50), sulfonamides (41), fluoroquinolones (31), and aminoglycosides (27).

Conclusion: All antimicrobials used in the animal health sector are also used in human medicine, which requires special consideration. This cross-use of antibiotics was a crucial factor in determining the cause of the spread of AMR between humans and animals.

Keywords: animal health, antimicrobial use, Yogyakarta.

Introduction

The Province of the Special Region of Yogyakarta consists of five regency communities located in the central-southern portion of Java Island: Yogyakarta, Sleman, Bantul, Kulonprogo, and Gunungkidul. Yogyakarta is one of the most prominent cities in Indonesia, and its population welfare is relatively high. In each district's animal clinics, independent practices, and animal health centers, veterinarians undertake animal health practices. Antimicrobials in animals are believed to be one of the causes of antimicrobial resistance (AMR); therefore, information is required regarding the amount, nature, pattern, and distribution of antimicrobial use in animals. Improved animal health services, especially for pets, have led to more and more use of antimicrobials, closer contact between animals and humans, and triggered easier transmission of microbes [1]. Animal antibiotics are empirically used for treatment, prevention, and growth-promoting compounds [2]. In general, antibiotic growth promoters are given in subtherapeutic amounts mixed in feed or drinking water. The mechanism of growth-promoting compounds is physiologically unclear. It has been proven that using sub-therapeutic doses cause a decrease in the diversity of microbial populations in the gut, thereby reducing competition in obtaining nutrients, reducing the number of bad microbes and the immune response, increasing the biosynthesis of vitamins in the intestine, and increasing metabolism [3–7]. Antibiotic residues in meat, dairy, and egg products also need to be considered as factors causing the spread of resistance in humans [8]. Resistant *Streptococcus* isolates were found in raw milk in the East Java area [9], resistant *Staphylococcus* in Etawah goats in Yogyakarta [10], and the other studies of resistance gene of broiler in Blitar by Witaningrum [11], resistance antimicrobial in broiler farms in some area of Indonesia [12], AMR cases in Yogyakarta and East Java [13], indicating that resistant microbes have spread widely especially in animals production in the Java Island area.

Additional provisions and regulations are required to restrict the use of antibiotics, particularly in animal-derived foods [14]. Food products of animal

origin are reservoirs of zoonotic disease agents resistant to antimicrobials [15]. Although there are more data on the use of antimicrobials and cases of resistance in livestock, it is important to analyze the use of antimicrobials in animal health practice as a contributor to AMR. According to Carvalho *et al.* [16] and Joosten *et al.* [17], the use of antimicrobials in pets is increasing so that contact between humans and pets becomes a source of transfer of resistant microbes. The relationship between animals and pets is a source of the spread of AMR that needs to be studied continuously.

This study aims to obtain data on the use of antimicrobials in the Yogyakarta province by practicing veterinarians. The survey results represented the AMR condition in Indonesia because Yogyakarta had the most veterinary practitioners compared to other regions in Indonesia. The lack of data correlated to AMR issues in Indonesia [12] than other countries in South East Asia would be a problem in initiating the strategy to combat the resistance problem. The research results are expected to help understand the distribution, type, and pattern of use of antimicrobials in animals and can help build a strategy to prevent AMR for public health.

Materials and Methods

Ethical approval

All research activities have been formally approved by the Yogyakarta Provincial Animal Husbandry Service and the Special Region of Yogyakarta branch of the Association of Veterinarians (Perhimpunan Dokter Hewan Indonesia cabang Daerah Istimewa Yogyakarta).

Study period and location

The questions asked for responses to characterize the status of antimicrobial use from January to November 2021. The study gathered information from 101 veterinarians working in the field of animal health. The participants had to meet certain predetermined criteria, including practitioners, having a license from the Government Animal Husbandry Service for each district, and being officially registered as members of the Indonesian Veterinary Association of Special Region of Yogyakarta. Respondents were dispersed throughout five districts, specifically the cities of Yogyakarta (15), Sleman (39), Bantul (28), Kulonprogo (6), and Gunungkidul (13).

Data collection

The number of respondents varied in each city due to the large number of animal centers, hospitals, and independent practices that were located in each city. The purview of the survey includes collecting data on the degree to which veterinarians pay attention to and know AMR, the type of animal and the antimicrobial used, as well as the antimicrobial that is most frequently used. The survey was conducted by sending a Google Form containing a list of questions that the analysis consultant team had verified to each respondent in person or online. All question lists are of the type of free-choice answers so that respondents may choose more than one answer. Surveyors visited several practice locations to assist in filling in and explaining the questions on the form. Many veterinary clinics and independent veterinary practices are still implementing restrictions on direct visits to practice locations due to the COVID-19 pandemic.

Statistical analysis

Most of the answers were presented descriptively based on the sum of all the respondents' answers that then processed and calculated using Microsoft Excel Software (Microsoft Office LTSC Professional Plus 2021).

Results

The use of antimicrobials and the type of animals treated

Types of the practice of the veterinary profession as respondents came from independent practice (51%), joint practice (25%), animal clinics (23%), and animal hospitals (1%). The results of studies on the use of antimicrobials show rational veterinary considerations and understanding of the reasons for selecting drugs based on 48.25% and 34.32% of diagnosis and laboratory results and as much as 17.41% based on professional experience during practice (Tables-1 and 2). Separate questions about the types of antimicrobials that are most often used (very often and often) resulted in antibiotic and antiparasitic (both 78.6%) being the most frequently used, followed by antiseptic and disinfectant (68.9%), then antifungals (31.1%), and antivirals were the least used, namely, 9.7%. Table-3 descriptively shows how the distribution responses of the most frequently used antimicrobials compare to the occasionally used ones (antiviral and antifungal). The veterinarians occasionally (sometimes, seldom, or never) use antifungal or antiviral, indicating low fungal and viral infections in animals in the Yogyakarta region.

The types of animals treated with antimicrobials are shown in Figure-1. The figure depicts that veterinarians treated most animal pets (37%, primarily cats

Table-1: Type of veterinarian practices.

Type of practice	Percentage
Independent practice	51
Join practice	25
Animal clinics	23
Animal hospitals	1

Table-2: The use of antimicrobials based on veterinarian consideration.

Consider using antimicrobials	Percentage
Diagnostic approach	48.25
Laboratory results	34.32
Experience	17.41

and dogs) with antimicrobials, following the large and small animals (16% of cattle and 14% of goat and sheep), poultry (15%, mostly chicken), and exotic animals (16%). Treating antimicrobials in fish is complicated, and veterinarians seem to avoid the antimicrobials used in fish to manage their health.

Antibiotic use and veterinarian's understanding of AMR

Figure-2 shows the 14 classes of antibiotics used by veterinary practitioners in the Yogyakarta province. All these types of antibiotics are also used in humans. Some types are even included in the category of critically and highly important antibiotics used in human health (the WHO 2019). Based on the criteria of very often and often answers (Figure-3), penicillin is the most widely used in veterinary medicine (71 responses), followed by tetracyclines (50), sulfonamides (41), fluoroquinolones (31), aminoglycosides (27), cephalosporins (22), and other groups (1–5 responses).

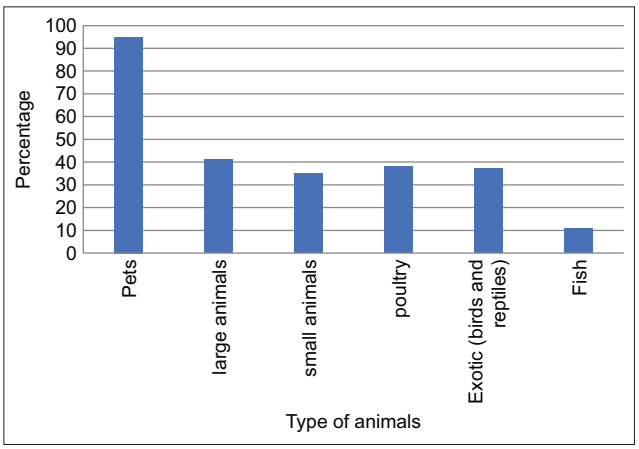
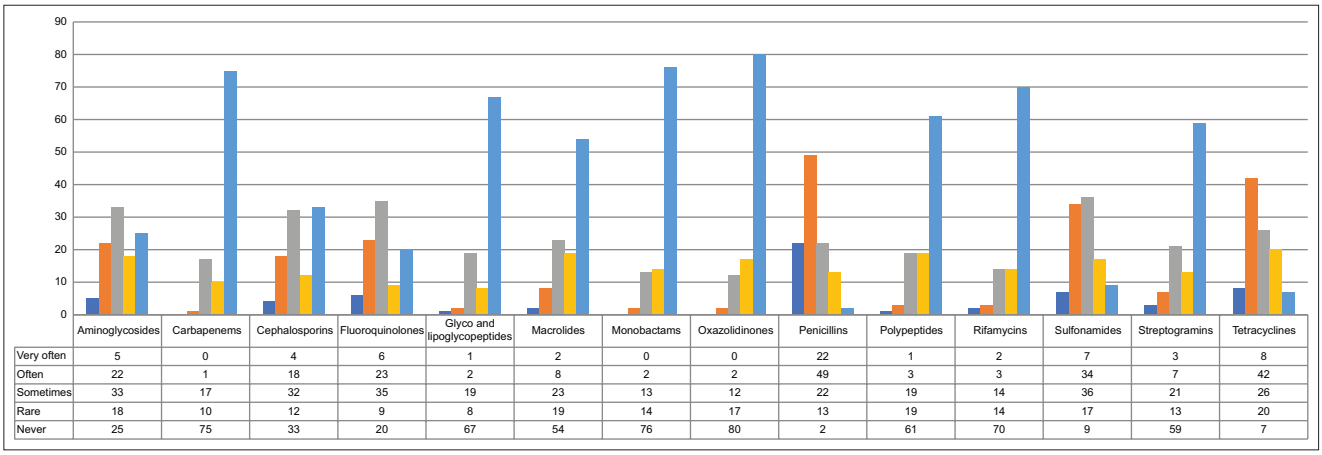


Figure-1: The type of animals treated with antimicrobials.

The veterinarian practitioners understanding of AMR was 89% based on their well explanations about the factors causing AMR. Unfortunately, only 47% of veterinarians actively follow the issue related to AMR. Figure-4 describes the considerations of veterinarians that 50% and 37% prefer to decide the dosing of antimicrobials based on the reference and drug leaflets, followed by experience (10%) and other considerations (3%), respectively. Figure-5 shows how far the veterinarian's knowledge of the factors that cause AMR and his insight into the latest developments in AMR.

Discussion

According to a survey report on AMR conditions in several Southeast Asian countries [18], antibiotics in primary health facilities in this region still had not to have standard policies and rules, making them vulnerable to antibiotic abuse. The use of antibiotics as growth promoters, especially the sub-therapeutic use in cattle and poultry, is significantly believed to cause AMR because the body mass of an animal allows microbes to mutate more easily and will contaminate food of animal origin [19–23]. Antibiotics have been used for over 40 years in livestock, resulting in the direct spread of antibiotic-resistant bacteria to humans. Many studies have been published in peer-reviewed scientific literature, providing additional evidence of the spread of antibiotic-resistant microbes from livestock animals into human food [24–26]. Table-1 describes the types of animal health services in Yogyakarta, and



	Aminoglycosides	Carbapenems	Cephalosporins	Fluoroquinolones	Glyco and lipoglycopeptides	Macrolides	Monobactams	Oxazolidinones	Penicillins	Polypeptides	Rifamycins	Sulfonamides	Streptogramins	Tetracyclines
Very often	5	0	4	6	1	2	0	0	22	1	2	7	3	8
Often	22	1	18	23	2	8	2	2	49	3	3	34	7	42
Sometimes	33	17	32	35	19	23	13	12	22	19	14	36	21	26
Rare	18	10	12	9	8	19	14	17	13	19	14	17	13	20
Never	25	75	33	20	67	54	76	80	2	61	70	9	59	7

Figure-2: The antibiotic used by veterinarians.

Table-3: The most frequently used type of antimicrobial.

The frequency of use	Antibiotic (%)	Antiviral (%)	Antifungal (%)	Antiparasitic (%)	Antiseptic or disinfectant (%)
Very often	18 (17.5)	2 (1.9)	7 (6.8)	16 (15.5)	31 (30.1)
Often	63 (61.1)	8 (7.8)	25 (24.2)	65 (63.1)	40 (38.8)
Sometimes	22 (21.3)	40 (38.8)	46 (44.6)	20 (19.4)	30 (29.1)
Seldom	0 (0)	32 (31.1)	19 (18.4)	2 (1.9)	2 (1.9)
Never	0 (0)	21 (20.4)	6 (5.8)	0 (0)	0 (0)

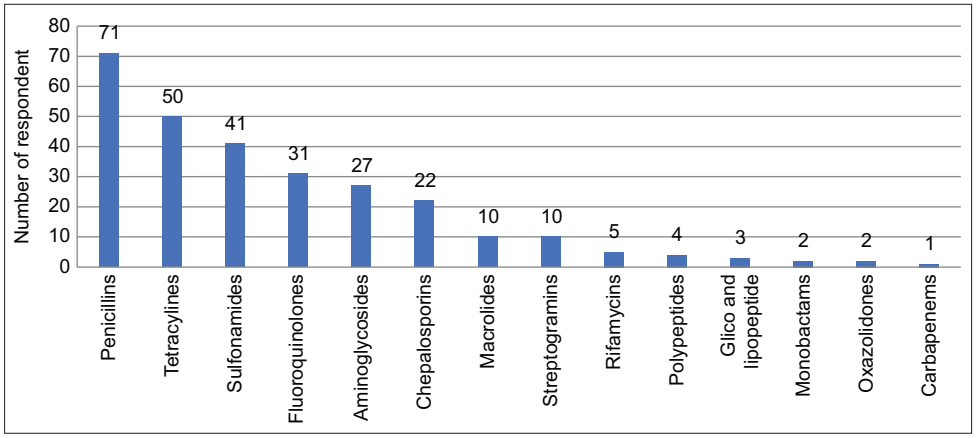


Figure-3: The frequency use of antibiotics.

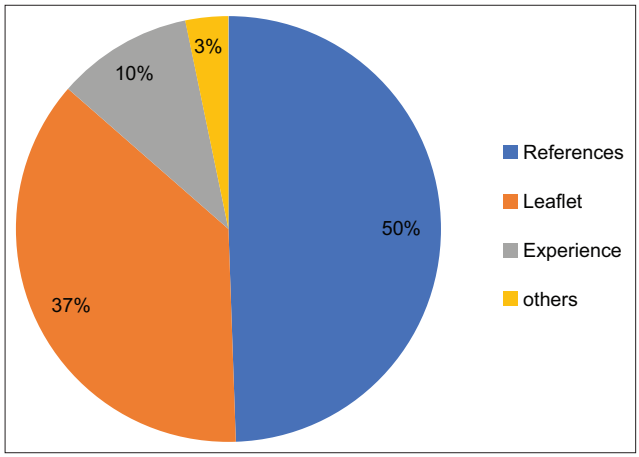


Figure-4: Consideration of antimicrobial dosing.

independent practice dominates in providing services in this region (51%), illustrating the growing number of pet owners, so easily accessible health facilities are needed. Most types of antimicrobials are classified as potent drugs (especially antibiotics) and should only be given on the advice of a veterinarian. Table-2 shows the reasons for giving these drugs, and in general, it seems that antimicrobials are given after going through a physical and laboratory examination. However, about 17% of respondents answered based on their experience. Based on the results of an animal type treated with antimicrobials (Figure-1), pets (cat and dog) were the most species treated with antimicrobials; meanwhile, the small and large cattle, poultry, and exotic animals ranged from 14% to 16%, and fish has the smallest percentage (4%). Yogyakarta region is the center of education and culture in the southern part of Central Java, where the agricultural sector is more dominant than livestock or fisheries. Antibiotics, antiparasitics, antiseptics, and disinfectants seemed to be in balance (68.9%–78.6%). Meanwhile, the antifungal and antiviral effects were less (Table-3). Reflecting on the study results (Figure-1) that pets, especially dogs and cats, are the species that receive the most treatment with antimicrobials, it is necessary to conduct a further study about the transmission of resistant microbes through contact between humans and pets. So far, it is still challenging to find references about the incidence of AMR in pets in the Southeast Asia region. However, research on isolates resistant to *Staphylococcus aureus* in cats from several clinics and veterinary hospitals has also found multidrug-resistant strains [27]. As a comparison, studies of AMR in dogs and cats have been carried out in several European countries [17]. The result was the discovery of 27% of *Escherichia coli* isolates that were resistant to at least 1 type of antibiotic used. The highest resistance was recorded to amoxicillin (18%), whereas the 13% as multidrug-resistant isolates.

Special attention must be given to the type of antibiotics used for animal health in the Yogyakarta region, because as many as 14 classes of antibiotics have been found that are also used in humans (Figure-2). Moreover, most of these antibiotics are critically important (aminoglycosides, carbapenems, fluoroquinolones, glycopeptide and lipoglycopeptide, macrolides, monobactams, oxazolidinones, penicillin, polypeptides, and rifampicin) and highly important antimicrobial (cephalosporins, sulfonamides, streptogramins, and tetracyclines), and penicillin class were the most used antibiotics in this region (Figure-3). Research conducted by Joosten *et al.* [17] found that 83% of the antimicrobials used in dogs and cats were broad-spectrum, and 71% were critically important. According to Myers *et al.* [28], the crossover use of antimicrobials between animals and humans will be very detrimental because it causes adverse reactions and accelerates the spread of AMR. This study also mentions that in several African and East Asian countries, there is still a lot of crossover use of antimicrobials, and access to antimicrobials at animal health service centers is relatively easy, whereas a similar condition also occurs in Yogyakarta. The fact that some generations of antibiotics were still a drug of choice in veterinary medicine indicates that their level of effectiveness is still good. In contrast, these antibiotics may have resistance to some pathogenic bacteria

in humans, such as tetracyclines and sulfonamides. Carbapenems, a new generation of beta-lactam antibiotics used to treat multidrug-resistant diseases in humans, have been shown to be no longer effective against *Acinetobacter baumannii*, *Klebsiella pneumoniae*, *E. coli*, and *Lysinibacillus fusiformis* bacteria [29]. The results of studies (Figures-2 and 3) show that carbapenems are starting to be used to treat animal diseases, indicating that these drugs may be quite effective. The use of one type of antibiotic in animals and humans, or vice versa, is likely to cause an increase in the level of resistance to that type of antibiotic. To prevent the wide spread of AMR due to the widespread use of antibiotics, it is necessary to have rules that separate the use of antimicrobials between humans and animals.

The health problem in animals must be treated with proper antimicrobials to decrease the spread of AMR. The veterinarian play an important role in controlling the problem of AMR toward conditions of better management of antimicrobial use for animal health. Veterinary practitioners must know the proper use of antimicrobials and their role in inhibiting microbial resistance has to improve. According to Palma *et al*. [1], multisectoral coordination in preventing AMR is urgently needed because it will facilitate the treatment and selection of the right antimicrobials by veterinarians. The result in Figure-5 shows how the level of knowledge about causative factors, especially the role and prevention of microbial resistance, still needs to be improved (<50% of respondents). "Antibiotic dosing" is one of the important considerations to ensure the level of drugs that enter the body can actually kill pathogenic antimicrobials. Ali *et al.* [30] stated that antibiotics dosage requires a special strategy to obtain maximum therapeutic results due to changing and improving microbial resistance mechanisms. Figure-4 shows the results of the veterinary practitioner's considerations in selecting doses. Although most of them refer to references to drug use, it does not guarantee that the choice has considered the problem of developing AMR. The "antibiotic dosing" strategy is not only about calculating the dose and duration

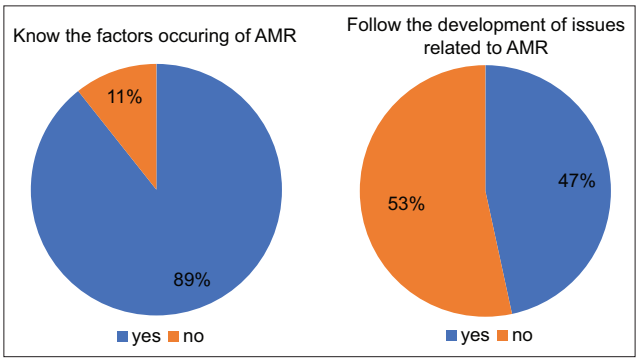


Figure-5: The opinion of veterinary practitioners regarding the causal factors and development of antimicrobial resistance.

of administration but also considering the pattern or mechanism of resistance developed by microbes [31]. Rational use of antimicrobials and restrictions on the production of antibiotics have been carried out by the Indonesian government by establishing several regulations from the agricultural and livestock sector. A sustainable national action plan to combat AMR has been established, covering several sectors such as agricultural, environmental, aquaculture, human, and animal health. National Action Plan for Health Security Indonesia 2020–2024 has responded comprehensively to improved capacity in preventing, detecting, and responding to disease outbreaks, pandemics, and nuclear, biological, and chemical emergencies which have the strategy as One Health program such as AMR or zoonotic diseases [32]. The action plan collaborated with many bodies and institutions as a multisectoral area to build the One Health approach. It is hoped that the results of this study can be a useful representative input to see the condition of antimicrobial use in animal health, especially in the Yogyakarta region, which is then considered in developing strategies to prevent the spread of AMR for wider area coverage.

Conclusion

Antimicrobial resistance is a global problem that must be solved cross-sectorally. In animal health, the use of antimicrobials in domestic animals must be regulated and possible to avoid the spread of AMR, especially to humans. One of the problems in starting this arrangement is the availability of data on antimicrobial use in animals, which so far has been difficult to find because not many integrated surveys and analyses of antimicrobial use have been conducted. Data on antimicrobials in animals will be very useful for developing a strategy to combat AMR globally.

Authors' Contributions

ADW and AWR: Conceptualization, design of the study, and project administration. AWR, DCBS, and AIS: Investigation and collected data. AMP, AIS, and IF: Formal analysis, interpreted the data, and visualization. ADW and IF: Writing-original draft preparation. ADW and DCBS: Edited the manuscript. All authors have read, reviewed, and approved the final manuscript.

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Competing Interests

The authors declare that they have no competing interests.

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