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Antimicrobial Resistance Profile of Bacteria Isolated from Canine and Feline Samples at the Preventive Veterinary Laboratory of the Federal University of Rio Grande do Sul (UFRGS) - Brazil

Karoline Zenatto, Tatiana Regina Vieira, Gustavo Enck Sambrano & Marisa Cardoso

ABSTRACT

***Background*:** Antimicrobial resistance (AMR) is a major global health threat. In small animals such as dogs and cats, antimicrobials are most commonly prescribed for skin and genitourinary diseases; therefore, the AMR of bacteria involved in these infections should be monitored. In addition, the results of antimicrobial susceptibility testing (AST) may be interpreted as a local epidemiological history of AMR. The Preventive Veterinary Medicine Laboratory (PVML) received clinical samples from dogs and cats for bacterial isolation and AST. Thus, this study aimed to assess the AMR of bacteria isolated from the samples of dogs and cats received at the Preventive Veterinary Medicine Laboratory (PVML).

***Materials, Methods & Results*:** Data from bacteriological examinations performed at the PVML of the Universidade Federal do Rio Grande do Sul (UFRGS) during 5 years were analyzed. Skin and ear canal samples were inoculated in 5% sheep blood agar, and urine samples were streaked on CHROMagar™ orientation. After incubation at 36±1°C for up to 72 h, identification and AST were performed according to routine protocols. Of 1,534 samples submitted to the PVML, 1,086 (70.8%) were collected from dogs and 29.2% from feline patients. Otological swabs (n = 533, 49.1%) were the most frequent samples from dogs, while cat urine samples (n = 384, 84.8%) predominated by far. Considering the canine samples, no bacterial growth (NBG) was observed in 443 (40.8%) samples, while only one colony type was noted in 516 (47.5%) samples. Gram-positive bacteria (n = 298) were more frequent than gram-negative bacteria (n = 77) in the skin. In urine samples, gram-negative bacteria (n = 94) were isolated more frequently than gram-positive bacteria (n = 47). In feline samples, a high number of NBG (n = 308, 68%) was observed. Gram-positive (n = 22) was predominant in comparison to gram-negative bacteria (n = 9) in cultures from the ear and skin swabs. *Enterococcus* spp. and *Escherichia coli* were the most frequently identified bacteria in urine samples. Among the *Staphylococcus* sp. strains of any origin, AMR frequency varied from 4.22% (amikacin) to 50.70% (sulfa/trimethoprim). *Enterococcus* spp. showed AMR frequencies from 12.5% (amoxicillin/clavulanic acid) to 62.06% (enrofloxacin). Among the gram-negative genera, *E. coli* presented AMR frequencies from 10.20% (gentamicin) to 60.0% (neomycin). The frequency of AMR was stable over time, and a profile of much higher resistance to fluoroquinolones in comparison to beta-lactams was observed.

***Discussion*:** The recurrence of skin and urinary infections implies the need for frequent treatment with antibiotics, which exerts selection pressure for resistance and multidrug resistance. In this study, the frequency of multidrug resistance was low, and the resistance to the tested antimicrobials showed high variation. However, a trend of high resistance to the fluoroquinolone group was observed in contrast to the low resistance to beta-lactams. This trend was consistent among the isolated bacteria, regardless of the type of sample or origin. The overprescription of fluoroquinolones in small animal practices has been widely documented in several countries. However, this class of antimicrobials, is highly prioritized for the treatment of infections in humans. Therefore, the selection of resistant strains has gained special emphasis, especially when considering the possibility of the transmission of resistant bacteria between pets and humans. In summary, the results of bacteriological tests conducted at the PVML-Universidade Federal do Rio Grande do Sul confirmed that ubiquitous bacteria predominate in clinical samples of dogs and cats. The high frequency of resistance to the fluoroquinolone group, while a predominance of susceptible strains in the first-choice drugs such as amoxicillin/clavulanic acid, may indicate excessive and empirical use of the second-choice drugs in clinical practice.

Keywords: otitis, dermatitis, urinary infection, dogs, cats, antibiotic resistance, AMR.

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Laboratório de Medicina Veterinária Preventiva (LMVP), Departamento de Medicina Veterinária Preventiva, Faculdade de Veterinária (FaVet), Universidade Federal do Rio Grande do Sul (UFRGS), Porto Alegre, RS, Brazil. CORRESPONDENCE: T.R. Vieira [tatianareginavieira@gmail.com]. Laboratório de Medicina Veterinária Preventiva - FaVet - UFRGS. Av. Bento Gonçalves n. 9090. CEP 91540-000 Porto Alegre, RS, Brazil.

INTRODUCTION

Antimicrobial resistance (AMR) is a major global health threat [20], and the relationship between AMR and antibiotic use is well established [2]. Any use of antimicrobials can select for AMR; however, selective pressure is amplified by overuse, sub-inhibitory dosage, or inappropriate treatment duration [8].

In companion animal veterinary medicine, antimicrobial stewardship has been interpreted as a scheme to encourage the responsible use of antimicrobials by decreasing prescription rates without increasing negative patient outcomes [8]. The efficacy of any treatment among other factors is based on pathogenic agent identification, antibiogram performance, and local epidemiological history, particularly in relation to the AMR profiles of the pathogenic agents that circulate in each region [21]. In small animals such as dogs and cats, antimicrobials are most commonly prescribed for skin (52%) and genitourinary (11%) diseases; therefore, the monitoring of AMR of bacteria involved in these infections should be prioritized [5,6].

The Preventive Veterinary Medicine Laboratory (PVML) received clinical samples from dogs and cats to perform bacterial isolation and antimicrobial susceptibility testing (AST). The AST results may be interpreted as the local epidemiological history of AMR and a guide for initiating antibiotic treatment before definitive pathogen identification and AST. Thus, this work aimed to study bacteria isolated from dogs and cats for monitoring the development of AMR involved in these infections

MATERIALS AND METHODS

Study design

This descriptive retrospective study investigated data from bacteriological examinations performed at the PVML during the period of 2016-2020. Bacteriological examinations requested by veterinarians for the clinical diagnosis of urinary disease, pyoderma, or otitis in dogs or cats were included in the study. All clinical samples were collected by veterinarians during clinical consultation at the Veterinary Medical Teaching Hospital (HCV) of the Federal University of Rio Grande do Sul (UFRGS), Porto Alegre, RS, Brazil. A requisition form with patient information, previous use of antimicrobials, and the drugs that were asked to be tested accompanied all samples. Urine was collected by cystocentesis or bladder catheterization performed by veterinarians, whereas swabs from the skin or external ear canal were collected in cases of pyoderma and otitis. All other types of samples analyzed during this period at PVML were not included in this study.

Bacterial isolation and identification

Bacterial isolation was performed according to the literature [16]. Skin and ear canal samples (commonly received in swabs) were inoculated in 5% sheep blood agar, incubated under aerobic conditions at 36 ± 1°C for up to 72 h, and checked every 24 h. Blood agar plates with no bacterial colonies after 72 h were considered to have no bacterial growth (NBG). Blood agar plates showing significant bacterial growth (at least 5 isolated colonies or mixed colonies of up to 3 morphological types) were subjected to phenotypic identification and AST.

Urine samples were processed according to the collection procedure (cystocentesis or catheterization). For urine collected by cystocentesis, 10 µL of the sample was streaked on plates containing the differential culture medium CHROMagar™ Orientation[1], and the plates were incubated under aerobic conditions at 36 ± 1°C for up to 72 h. Agar plates without bacterial colonies after 72 h were considered to have NBG, and colonies from samples with growth were subjected to phenotypic identification and AST. Urine samples collected via catheterization were subjected to colony counting. After homogenizing the sample, 100 µL was spread on the surface of differential CHROMagar™ Orientation1 agar plates and incubated under aerobic conditions at 36 ± 1°C for up to 72 h. The number of colonies (colony forming units [CFU]) obtained was then multiplied by a correction factor (10x) to 1 mL. Samples with counts between 10^4 and 10^5 CFU/mL were suggestive of bacterial infection, whereas counts higher than 10^5 CFU/mL were indicative of clinical bacteriuria [16]. Bacterial identification and AST were performed in these cases. Phenotypic identification of bacteria was performed by gram staining and biochemical tests, as previously described [16].

Antimicrobial Susceptibility Testing - AST

Three to 5 isolated colonies from Tryptic Soy Agar[2] were suspended in NaCl 0.85% until achieving the turbidity equivalent to McFarland 0.5. The suspension was spread on Müller Hinton Agar[2] following the recommendations of the literature [4]. Discs impregnated with antimicrobials were then deposited on the surface of the inoculated agar and incubated at 37°C overnight. Inhibition zones were measured and

compared to the diameters corresponding to susceptibility or resistance according to the Supplement of the Performance Standards for AST [4] and Performance Standards for Antimicrobial Disks and Dilution Susceptibility Tests for bacteria isolated from animals [3].

Data analysis

The following information was extracted from the PVML data bank: sample type (urine, skin swab, otological swab); animal species (dog or cat); antimicrobials requested to be tested by the veterinarian; bacterial identification; and resistance or susceptibility to the tested antimicrobials. The identified bacteria were grouped as follows: coagulase-negative staphylococci (CNS), coagulase-positive staphylococci (CPS), *Enterococcus* spp., *Escherichia* coli, *Proteus* spp., and *Pseudomonas* spp. The frequencies of each bacterial group according to animal species and sample type were expressed as percentages. The percentage of resistance to each antimicrobial tested was determined for each bacterial group isolated from the sample type in cats and dogs.

RESULTS

During the period of this study, 1,534 examinations were submitted to PVML for bacteriological culture analysis. Of these, 1,086 (70.8%) were collected from dogs, and 29.2% from feline patients. Otological swabs (533 = 49.1%) were the most frequent samples subjected to bacteriological testing in dogs, while cat urine samples (384 = 84.8%) predominated by far.

Among the canine samples, NBG was observed in 443 (40.8%) samples, only 1 colony type was observed in 516 (47.5%), and a mixed culture was found in 108 (9.9%) samples (Table 1). Gram-positive bacteria (298) were more frequent in single cultures originating from the ear and skin swabs than gram-negative bacteria (77). In turn, urine samples originated more frequently from gram-negative bacteria (94) than from gram-positive bacteria (47) in single cultures. Mixed cultures were represented by several combinations; however, CNS/*Proteus* spp. and *Enterococcus*/*Proteus* spp. predominated in the ear swabs and urine samples, respectively.

Table 1. Results of canine samples processed at the Preventive Veterinary Medicine Laboratory (PVML) - UFRGS between 2016 and 2020.

Culture	Ear swab	Skin swab	Urine	TOTAL
NBG	198	32	213	443
CPS	79	47	3	129
CNS	102	63	24	189
Enterococcus spp.	3	3	18	24
Streptococcus spp.	0	1	2	3
Subtotal	184	114	47	345
E. coli	12	-	69	81
Proteus spp.	20	1	21	42
Pseudomonas spp.	43	1	4	48
Subtotal	75	2	94	171
CPS/CNS	6	1	-	7
CPS/*Enterococcus* spp.	1	-	-	1
CPS/*Streptococcus* spp.	0	1	1	2
CPS/*E. coli*	3	-	-	3
CPS/*Proteus* spp.	5	3	-	8
CPS/*Pseudomonas* spp.	1	-	-	1
CNS/*Enterococcus* spp.	6	-	1	7
CNS/*Streptococcus* spp.	0	1	-	1
CNS/*E. coli*	4	-	-	4
CNS/*Proteus* spp.	10	2	-	12
CNS/*Pseudomonas* spp.	9	-	-	9
Enterococcus spp./*E. coli*	0	-	17	17
Enterococcus spp./*Proteus* spp.	3	-	8	11
Enterococcus spp./*Pseudomonas* spp.	6	-	-	6
E. coli/*Proteus* spp.	0	2	4	6
E. coli/*Pseudomonas* spp.	9	-	-	9
Proteus spp./*Pseudomonas* spp.	4	-	-	4
Subtotal	67	10	31	108
Other	9	1	9	19
TOTAL	533	159	394	1,086

NBG: no bacterial growth; CPS: coagulase-positive staphylococci; CNS: coagulase-negative staphylococci.

In feline samples, a high number of NBG (308 = 68%) was observed; and this result accounted for 74.2% of the urine samples analyzed (Table 2). Among the samples with bacterial growth, 24.7% presented only one type of bacteria and 3.3% were mixed cultures. In addition, in feline samples, gram-positive bacteria (22) predominated in comparison to gram-negative bacteria (9) in cultures from the ear and skin swabs. However, in the urine samples, gram-positive (38) and gram-negative (43) bacterial isolation was similar. Among them, *Enterococcus* spp., *E. coli*, and mixed cultures of these 2 species were the most frequently identified.

Table 2. Results of feline samples processed at the Preventive Veterinary Medicine Laboratory (PVML) - UFRGS between 2016 and 2020.

Culture	Otological swab	Skin swab	Urine	TOTAL
NBG	18	5	285	308
CPS	4	4	6	14
CNS	10	3	8	21
Enterococcus spp.	1	-	24	25
Subtotal	15	7	38	60
E. coli	-	1	24	25
Proteus spp.	-	2	15	17
Pseudomonas spp.	5	1	4	10
Subtotal	5	4	43	52
CPS/*E. coli*	1	-	-	1
CPS/*Pseudomonas* spp.	1	-	-	1
CNS/*Enterococcus* spp.	-	1	2	3
Enterococcus spp./*E. coli*	-	1	4	5
Enterococcus spp./*Proteus* spp.	-	-	2	2
Enterococcus spp./*Pseudomonas* spp.	-	-	2	2
E. coli/*Proteus* spp.	-	-	1	1
Subtotal	2	2	11	15
Other	6	4	8	18
TOTAL	45	20	384	453

NBG: no bacterial growth; CPS: coagulase-positive staphylococci; CNS: coagulase-negative staphylococci.

The frequencies of AMR among the isolated bacterial species, regardless of the sample and animal of origin, are depicted in Table 3. In several cases, a given antimicrobial was not tested because the bacterial species presented intrinsic resistance towards this antimicrobial or because the veterinarian did not include this drug among those to be tested in the requisition form. Among the *Staphylococcus* sp. strains, the resistance frequency varied from 4.22% (amikacin) to 50.70% (sulfa/trimethoprim). The other gram-positive genus (*Enterococcus* spp.), in turn, presented higher resistance frequencies, which varied from 12.5% (amoxicillin/clavulanic acid) to 62.06% (enrofloxacin). Among the gram-negative genera, the resistance frequencies were distributed as follows: from 10.20% (gentamicin) to 60.0% (neomycin) for *E. coli*, from 16.0% (amoxicillin/clavulanic acid) to 43.75% (sulfa/trimethoprim) for *Proteus* spp., and from 0% (ceftazidime) to 76.12% (enrofloxacin) for *Pseudomonas* spp. Fluoroquinolones and beta-lactams were the antimicrobial classes most frequently asked to be tested by veterinarians. In this regard, enrofloxacin, which belongs to the fluoroquinolone class, was among the top 2 antimicrobials with a higher resistance frequency in all bacteria tested. The resistance frequency for this antimicrobial varied from 41.30% (in *E. coli*) to 76.12% (in *Pseudomonas* spp.). In contrast, the resistance frequencies observed among beta-lactams were much lower. Considering amoxicillin/clavulanic acid, which was the most frequently tested in this class, the resistance frequencies varied from 9.26% (in *Staphylococcus* spp.) to 20.14% (in *E. coli*). *Pseudomonas* spp. are intrinsically resistant to most antimicrobials from the beta-lactam class; therefore, only a few strains were tested against ceftazidime, and none were resistant.

The analysis of the resistance profile according to the sample type is presented in Table 4. For most of the antimicrobials tested, skin and ear samples from dogs presented a higher frequency of resistance in AST compared with samples from cats. In contrast, the bacteria isolated from urine samples from cats presented resistance more frequently than those isolated from canine samples in AST. Concomitant resistance to 3 or more classes of antimicrobials (multidrug resistance [MDR]) was not common, and only 56 strains isolated from dogs and 9 from cats were considered MDR.

The frequency of AMR was stable over time (2016-2020), considering the 3 most tested antimicrobial classes (aminoglycosides, beta-lactams, and fluoroquinolones) (Figure 1). Here, the resistance frequency represents the results of AST performed on the most frequently isolated bacteria (*Staphylococcus* spp., *Enterococcus* spp., *E. coli*, and *Proteus* spp.) from urine, skin, and ear samples from dogs and cats. The profile of much higher resistance to fluoroquinolones in comparison to beta-lactams was also evidenced in this case.

Table 3. Antimicrobial resistance of selected bacteria isolated from urine, skin or ear swabs of dogs and cats processed at the Preventive Veterinary Medicine Laboratory (PVML) - UFRGS during the period of 2016 and 2020.

Class/Antimicrobial	*Staphylococcus* spp. (n = 407)		*Enterococcus* spp. (n = 93)		*Escherichia coli* (n = 157)		*Proteus* spp. (n = 108)	
	Tested (n)	Resistance (%)	Tested (n)	Resistance (%)	Tested (n)	Resistance (%)	Tested (n)	Resistance (%)
Beta-lactams								
Amoxicillin/ Clavulanic acid	324	9.26	64	12.5	144	20.14	100	16.0
Cephalexin	260	9.23	RI	-	88	13.63	55	27.27
Ceftazidime	NT	-	NT	-	NT	-	NT	-
Fluoroquinolones								
Ciprofloxacin	181	35.91	63	41.26	90	38.88	62	20.96
Enrofloxacin	335	42.68	87	62.06	138	41.30	88	43.18
Marbofloxacin	105	40.0	48	39.58	61	32.78	45	37.77
Norfloxacin	123	39.83	59	38.98	72	43.05	43	41.86
Aminoglycosides								
Amikacin	71	4.22	RI	-	NT	-	NT	-
Gentamicin	256	34.37	RI	-	49	10.20	53	18.86
Neomycin	176	30.68	RI	-	20	60.0	34	38.23
Tobramycin	193	27.98	RI	-	30	16.66	33	24.24
Others								
Clindamycin	53	58.50	RI	-	-	RI	RI	-
Doxycycline	154	12.33	37	35.13	36	44.44	RI	-
Sulpha/Trimethoprim	71	50.70	RI	-	59	33.89	32	43.75

*Strains isolated from urine samples and skin or ear swabs were included in the analysis.

Table 4. Antimicrobial resistance frequencies of bacteria* isolated from urine and swab samples from cats and dogs processed at the Preventive Veterinary Medicine Laboratory (PVML) - UFRGS during the period of 2016 and 2020.

Class/Antimicrobial	Skin and ear swabs				Urine samples			
	Dogs		Cats		Dogs		Cats	
	Tested (n)	Resistance (%)	Tested (n)	Resistance (%)	Tested (n)	Resistance (%)	Tested (n)	Resistance (%)
BETA-LACTAMS								
Amoxicillin/ Clavulanic acid	344	11.91	24	0	186	15.59	97	16.50
Cephalexin	286	13.28	11	18.18	110	8.18	22	18.18
FLUOROQUINOLONES								
Ciprofloxacin	266	30.83	8	12.50	103	39.45	48	37.50
Enrofloxacin	276	67.75	40	30.0	165	43.64	95	54.74
Marbofloxacin	126	40.47	9	22.22	78	34.61	61	47.54
Norfloxacin	-	-	-	-	91	35.16	74	48.65
AMINOGLYCOSIDES								
Amikacin	119	10.92	2	0	-	-	-	-
Gentamicin	335	35.52	25	80.0	57	14.03	17	35.29
Neomycin	237	39.66	20	25.0	-	-	-	-
Tobramycin	294	23.13	20	15.0	-	-	-	-
OTHERS								
Doxycycline	143	16.78	12	33.33	59	30.51	45	26.66
Sulpha/Trimethoprim	58	58.62	4	25.0	57	29.82	26	57.69

*Only strains of *Staphylococcus* spp., *Enterococcus* spp., *E. coli* and *Proteus* spp.

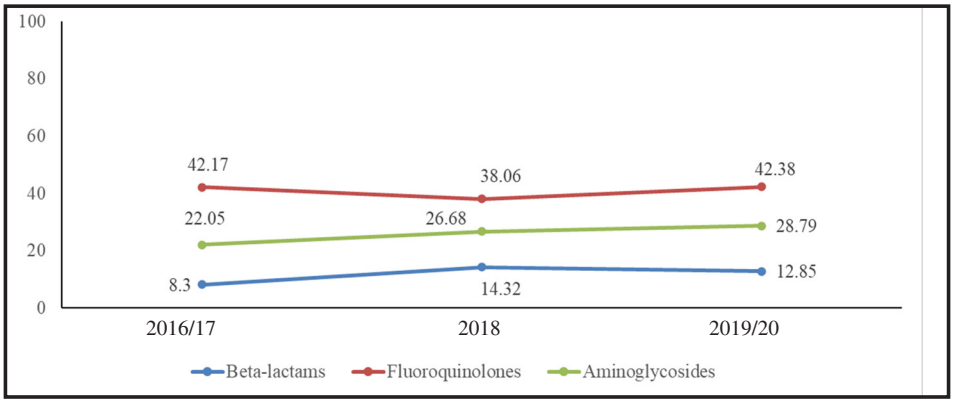

Figure 1. Percentage of resistance over time to the most tested antimicrobial classes in canine and feline samples analyzed at the Laboratory of Preventive Veterinary Medicine Laboratory (PVML) - UFRGS.

DISCUSSION

This retrospective study evaluated the most frequently isolated bacteria and their AMR in clinical samples from dogs and cats processed at the PVML-UFRGS. In dogs, ear and skin swabs together constituted more than half (63.72%) of the samples processed in the period, in agreement with the estimate that tegumentary diseases contribute to up to 70% of appointments of dogs in small animal practices [17]. Despite the low threat to the patient's life, itching and pain associated with the lesions and the inflammatory response contribute to intense discomfort for the patient and can lead to more serious complications. In most cases, a bacterial infection is associated with an underlying disease, recurrence of the infection, and frequent repetition of treatments, adding another factor of concern in these cases [8]. The predominance of coagulase-positive and coagulase-negative *Staphylococcus* in skin disease is widely recognized [9,1] and was also evidenced in the present

study, in which almost half of the isolates belonged to these groups in both simple and mixed infections.

In contrast, in cats, the predominance of urine samples was evident. Although urinary tract infections (UTIs) occur much less frequently in cats than in dogs [7], their occurrence is closely associated with chronic kidney and metabolic diseases, which are frequent in felines [7,12]. In the present study, *E. coli* and *Enterococcus* spp. were the most commonly isolated bacteria, in agreement with previous studies [7,18]. Often, the origin of the bacteria causing UTI is the patient's intestinal tract [10], and the bacteria ascend upward to the bladder. Similar to skin disorders in dogs, the risk of recurrence of UTI represents a challenge in veterinary clinical practice and requires repeated antibiotic therapy.

The characteristic of recurrent infection implies the need for frequent treatment with antibiotics, which is considered to exert selection pressure for AMR and MDR. In the analyzed records, the frequency of MDR was low, and resistance to the tested antimicrobials showed high variation. However, it was possible to observe a trend of high resistance to the fluoroquinolone group in contrast to the low resistance to beta-lactams. This trend was consistent among the isolated bacteria, regardless of the type of sample of their origin. Likewise, the concomitant resistance between different antimicrobials of the quinolone group (results not shown) indicates that the mere change of antibiotics among this group does not appear to be a reasonable therapeutic option.

The high frequency of resistance to fluoroquinolones leads to the assumption that these drugs have been used frequently and possibly empirically in clinical practice; that is, without performing AST. The overprescription of fluoroquinolones in small animal practices has been widely documented in several countries [8,19]. Moreover, resistance levels to fluoroquinolones in bacteria isolated from dogs and cats reported in Brazil are also high [13]. In turn, this class of antimicrobials is considered a high priority for the treatment of human infections. Therefore, the selection of resistant strains has gained special emphasis, especially considering that there may be the transmission of resistant bacteria between pets and humans [8,15].

Although not observed in our study, colonization of dogs and cats by methicillin-resistant *Staphylococcus* or vancomycin-resistant *Enterococcus* has been demonstrated and appears to occur more frequently than previously believed [15]. Moreover, the repeated use of antimicrobials can be the driver for the selection of bacteria resistant to any antimicrobial among the resident microbiota of dogs and cats, which can later be transferred to humans or exchange resistance genes with bacteria that colonize humans. Close contact between pets and owners facilitates transmission through direct contact or the environment [1].

The need for the prudent use of antimicrobials in dogs and cats is not only related to the need to preserve the efficacy of drugs, especially the second and third-choice drugs such as quinolones and cephalosporins, for the treatment of patients. This issue also affects public health. The Ministry of Agriculture, Livestock, and Supply recently released a manual on the prudent use of antimicrobials in pets as part of the actions within the National Action Plan for the Prevention and Control of Antimicrobial Resistance [14]. This initiative focuses on the management of hospital use of antimicrobials and recommendations to guide their clinical prescription. Among the main recommendations is the ongoing evaluation of antimicrobial therapy outcomes as well as prescribing behavior in hospitals or clinics. Additionally, the prevention of health conditions that lead to the need for antibiotic therapy and the development of a diagnostic database on clinical microbiology and AMR is also recommended.

Experiences in other countries have shown that the introduction of antimicrobial use policies in small animal practice had a positive impact on reducing antimicrobial use, especially those of the second choice. However, this is a long and ongoing process that must be constantly reviewed and depends on the continuing education of veterinarians. Thus, the results of the present study demonstrate that the second-choice drugs, such as fluoroquinolones, which have shown a high and constant level of resistance over time, are more often prescribed than the first-choice drugs, such as amoxicillin/clavulanic acid, which have much lower frequencies of resistance. This illustrates the importance of using diagnostic tests to identify the pathogen involved in clinical conditions and assess its AMR profile, thus avoiding the empirical use of the second-choice antimicrobials, especially those critically important to human health. Additionally, there is a need to optimize antimicrobial administration regimens by following the recommendations on the label

in terms of dose, regular administration intervals, and the minimum time interval required [8]. These measures are often challenging to implement in veterinary clinics; however, one should seek to achieve the 5Rs (responsibility, reduction, refinement, reallocation, and review) in the prescription of antimicrobials, as proposed by the WHO-OIE and included in the MAPA document [14, 21]. In particular, the need for prudent use of antimicrobials in small animal practice should gain attention from veterinarians as part of tackling bacterial resistance using a One Health approach.

CONCLUSIONS

In summary, the results of bacteriological tests conducted at PVML-UFRGS confirmed that ubiquitous bacteria, such as *Staphylococcus*, *Enterococcus*, and *E. coli*, frequently predominate in most clinical samples of dogs and cats. The resistance profiles of these bacteria demonstrated a high frequency of resistance to the fluoroquinolone group throughout the evaluated period. In contrast, the first-choice drugs such as amoxicillin/clavulanic acid presented a predominance of susceptible strains, which might indicate excessive and empirical use of the second-choice drugs in clinical practice.

MANUFACTURERS

[1]CHROmagar. Paris, France.

[2]MilliporeSigma. Burlington, MA, USA.

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