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Awareness of Antimicrobial Resistance and Antimicrobial Drugs Prescription Pattern in Small Animal Clinical Practice in Ogun State, Nigeria

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ABSTRACT

Antimicrobial resistance (AMR) is a global health challenge in veterinary and human health, leading to monitoring of resistance and promotion of responsible antimicrobial use. This survey assessed the use of antimicrobials among government veterinarians in Ogun state, Nigeria. Clinicians were requested to fill questionnaires designed to extract information on the frequency of antibiotics use, antibiotic prescription patterns and evaluation of perception on AMR and use of antibiotics with compromised efficacy in veterinary practice in the last three years. Fifty-two (52) questionnaires were administered and duly completed upon return. Data analysis showed 100% awareness of AMR with 80.8% (42/52) agreeing to have encountered AMR in the course of managing small animal cases. The tetracycline class of antibiotics 49(94.2%) was the most prescribed, followed by aminoglycosides 40(76.9%) and fluoroquinolones 35(67.3%). Empirical therapy (34/52) 65.4% is the most common treatment option among clinicians while 18 (34.6%) out of 52 clinicians performed antibiotic susceptibility testing along with laboratory diagnosis as treatment guide. Furthermore, 75.0% of the respondents affirmed administering antibiotics formulated for human use in small animal treatment. Thirty-three (63.5%) respondents administered human antimicrobials in animals according to the recommended dosage in humans. This survey identified that AMR was common in small animals in the state studied and this may be due to the irrational use of antibiotics. Promoting antimicrobial stewardship in small animal medicine therefore is paramount to mitigating antimicrobial resistance and data obtained from this study will contribute to developing evidence-based policy on the rational use of antibiotics in small animal practice in Nigeria.

Key words: Antimicrobial resistance, Veterinarians, Antibiotic sensitivity test, small animal medicine, Prescription

INTRODUCTION

Antibiotics are an essential part of veterinary practice as they are used routinely to prevent and treat bacterial diseases (Buckland et al. 2016). The efficacy of antibiotics is rapidly declining due to resistance resulting from widespread appropriate or even inappropriate use (Wayne et al., 2011). According to the Center for Disease Control and Prevention (CDC) report, in one veterinary teaching hospital study, 40% of canine antibiotics were prescribed for patients with no evidence of infection. (Wayne et al., 2011). Bacterial resistance to antibiotics is increasingly becoming a problem worldwide. Selective antibiotic pressure is a major determinant of emergence and dissemination of antibiotic resistance. Resistance among bacterial colonies occur through several mechanisms, including introduction of resistant bacteria into a formerly susceptible colony, mutation that confers resistance, transfer of mutation from resistant strain, selection of resistant strains through antibiotic pressure, or dissemination of resistant bacteria caused by poor infection control (Gould, 1999). Although the use of antimicrobial agents selects for and promotes transfer of resistance, data on antimicrobial agent prescription in small animals is scarce (Cantón and Bryan, 2012). Laboratory diagnosis of pathogens enables identification and antibiotic resistance profiles. However, reports have established that many veterinarians do not carry out culture and sensitivity testing (CDC, 2016). Twenty-six percent (26%) of the veterinarians in Nigeria are in the public sector and this has necessitated a preliminary survey among veterinarians in government employment. Globally, most of the available data on antimicrobial use and resistance are from Europe and North America, while the situation in other continents especially Africa is poorly documented. The paucity of data on the level and pattern of use of antimicrobials in veterinary practice in Nigeria is the justification for this preliminary survey

MATERIALS AND METHODS

Study design

This is a cross-sectional study on the pattern of antimicrobial use among clinicians in small animal practice in Ogun State Nigeria from 2016 to 2019. The study covered eight veterinary clinics (Figure 1) operated by the Veterinary Department of the Ministry of Agriculture, Ogun State (primary veterinary care provider) and the Veterinary Teaching Hospital (VTH) of the Federal University of Agriculture, Abeokuta (FUNAAB) (tertiary veterinary care provider). Out of 42 veterinary officers in the State Veterinary Department, 39 participated in the survey while 13 small animal clinicians participated in the survey at the VTH FUNAAB. The average annual small animal case load in all the Veterinary clinics under the purview of the Vet. Department of the state is about 3,500 animal patients while the VTH FUNAAB has an average annual small animal case enrolment of about 1,200.

Data collection

Hard copies of questionnaires were administered to veterinarians in small animal clinics at the VTH FUNAAB and to all veterinary officers in the Ogun state Department of Vet. Services with the exception of two chief veterinary officers (CVO) and one assistant chief veterinary officer (ACVO) who are principally policy makers and core administrative officers.

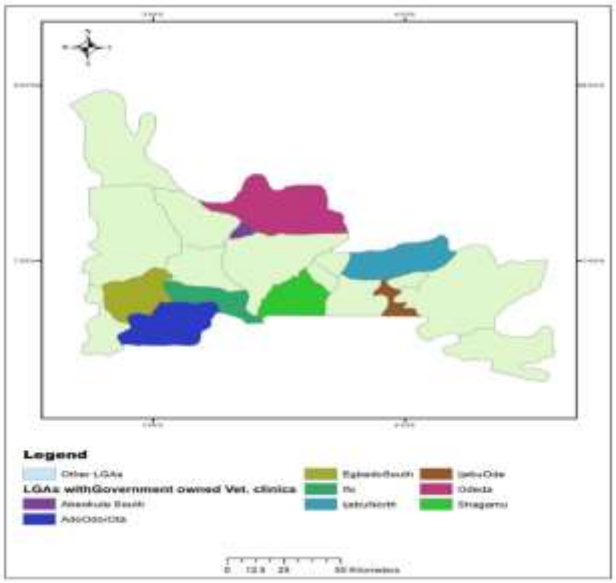

Figure 1: Map of Ogun state showing the location of government clinics

Data and Statistical Analysis:

Data obtained from the questionnaire were entered into excel (Redmond, Washington, US), coded and analyzed using the Statistical Package for Social Sciences (SPSS version 20). Data were presented as frequencies and percentages and analyzed using Pearson Chi-square and Linear-by-Linear Association.

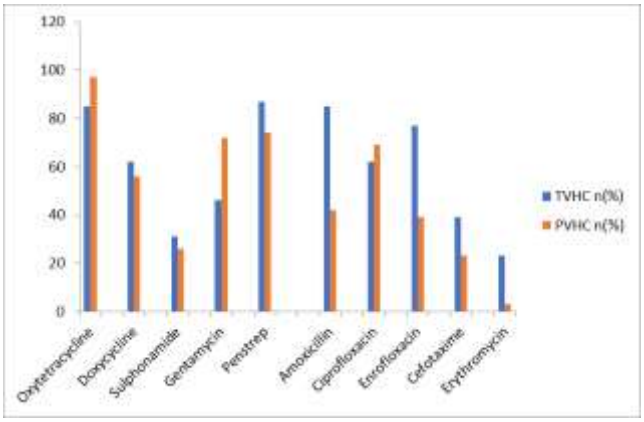

Figure 2: Antibiotics prescription pattern in primary and tertiary veterinary health facilities

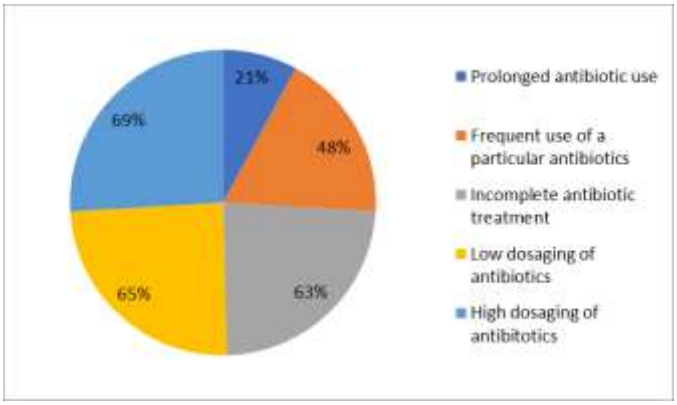

Figure 3: Factors contributing to antimicrobial resistance in small animal medicine

RESULTS

All 52 veterinarians enrolled into the study completed and responded to questions appropriately (Table 1). There were more male clinicians (59.6%) in small animal practice in public service than females (40.4%). Most respondents were 6-10 years in practice (40.4%) followed by clinicians with over two decades practice experience (21.2%). In addition to the Doctor of Veterinary Medicine (DVM) degree, most clinicians (73%) had postgraduate degrees. Besides being small animal practitioners, the respondents were also involved in large (42%), food animal practice (43%) and wildlife (2%). The variation in prescription pattern and practice was compared between veterinarians that work as primary veterinary health care (PVHC) providers in the Veterinary Department of the Ministry of Agriculture and those that work as tertiary veterinary health care (TVHC) providers at the VTH FUNAAB (Table 2). The tertiary veterinary care facility had higher frequency of daily antibiotic use (38.4%) with over 90% of them performing laboratory diagnosis with antibiotic testing prior to instituting treatment.

A slight variation was observed in the duration of antibiotics administration between respondents in PVHC (41%) and those in TVHC (53.8%). However, there were differences in the preference for injectable antimicrobials in PVHC (82.1%) and TVHC (53.8%). Also, more than 70% of clinicians administered antibiotics formulated for human to treat small animals by ensuring the body weight was considered for antibiotic dosing. The disparity in the class of antibiotics frequently prescribed was compared for the primary and tertiary veterinary health care providers (Table 3). The same classes of antibiotics were commonly prescribed by both categories of veterinary health care providers although the TVHC providers frequently prescribed a broad range of antibiotics. Tetracyclines (97%), beta lactams/aminoglycosides (74%), aminoglycosides (72%), fluoroquinolones (69%) and beta lactams (41%) were considered the most commonly used antimicrobials by PVHC providers while beta lactams/aminoglycosides and beta lactams/beta lactam inhibitors (84.62%) respectively, tetracyclines (73.08%), fluoroquinolones (69.23%), aminoglycosides (46.15%), beta lactams (38.46%) and folic acid inhibitors (30.78%) were mostly prescribed at the TVHC. Macrolides were the least prescribed class of antibiotics with less than 10% frequency of prescription for PVHC and 23.1% for TVHC providers (Figure 2).

Regarding efficacy of antibiotics, over 80% of the respondents agree that Teteracycline (especially oxytetracycline) is the most compromised antimicrobials, none opined that doxycycline has been compromised (Table 4). Infections in small animals are difficult to manage using Aminoglycosides and Beta lactam/Aminoglycosides class of antibiotics with 23.1% and 19.2% responding in the affirmative respectively. Beta lactams and macrolides were reported to be effective.

All respondents are aware of AMR in small animal practice and over 80% have experienced AMR in small animal antimicrobial therapeutics in the last three years (Table 5). Majority (96.2%) of the respondents believe that misuse of antibiotics results in loss or reduced efficacy of antibiotics against specific pathogens. Respondents in the PVHC treat recurrent and persistent infections by increasing duration of chemotherapy (5.8%), changing the antibiotics without recourse to culture and sensitivity test (57.7%) or changing the antibiotics after carrying out culture and sensitivity test (15.4%) while all (100%) respondents in the TVHC carry out culture and sensitivity test when treating recurrent or persistent infection.

Majority of the respondents (69%) believe that high dosing of antibiotics contributes to the development of AMR in small animals; while 65% believe that the use of sub-optimal dose precipitates AMR. A good proportion (63%) of the respondents agree that incomplete antibiotic treatment contributes to AMR and 48% are of the opinion that frequent use of a specific antibiotic was responsible for AMR. Only 28% of the respondents indicated that prolonged use of antibiotics could lead to the development of AMR (Figure 3). Although all veterinarians that participated in the study opine that performing culture and sensitivity test will go a long way to limit the burden of antimicrobial resistance, most PVHC providers do not perform culture and sensitivity tests prior to antibiotic prescription.

Table 1: Demographic details of small-animal clinicians (n= 52)

VARIABLE	FREQUENCY (%) OF RESPONDENTS
Gender	
Male	31(59.6)
Female	21(40.4)
Years of practice	
0-5 years	8(15.4)
6-10 years	21((40.4))
11-15 years	7(13.5)
16-20 years	5(9.6)
Above 20 years	11(21.2)
Workplace	
Veterinary Department, Ministry of Agriculture	39(75)
VTH COLVET, FUNAAB	13(25)
Possession of additional degree post DVM	
Yes	38(73.1)
No	14(26.9)
Secondary patient load	
Large animal	42(80.8)
Food animal	43(82.7)
Wildlife	1(1.9)

VTH COLVET, FUNAAB (Veterinary Teaching Hospital, College of Vet-Medicine, Fed. Univ. of Agric., Abeokuta)

Table 2: Antimicrobial prescription considerations and pattern of use

VARIABLES	PVHC	TVHC	P value
Frequency of antibiotic use			
Daily	9(23.1%)	5(38.4%)	
Every other day	5(12.8%)	1(7.8%)	
At least once a week	13(33.3%)	4(30.8%)	0.730
Every other week	1(2.6%)	1(7.8%)	
Once a month	11(28.2%)	2(15.4%)	_____
Laboratory diagnosis before prescription			
Yes			
No	6(15.4%)	12(92.3%)	0.534
	33(84.6%)	1(7.7%)	
Antibiotic sensitivity test before prescription			
Yes	6(15.4%)	12(92.3%)	0.534
No	33(84.6%)	1(7.7%)	

Duration of antibiotics administration			
Minimum of 3 days	18(46.2%)	2(15.4%)	
Minimum of 5 days	16(41.0%)	7(53.8%)	
Mandatory 7 days	0(0%)	0(0%)	
Follow manufacturers instruction	5(12.8%)	6(46.2%)	
Discontinue when symptoms abate	1(2.6%)	0(0%)	
Preferred antibiotics formulation			
Oral	4(10.3%)	4(30.8%)	
Injectable	32(82.1%)	7(53.8%)	
Both (Oral & Injectable)	3(7.7%)	2(15.4%)	0.841
Indecisive	0(0%)	0(0%)	
Adapts human formulation for veterinary use			
Yes	29(74.4%)	10(76.9%)	1.00
No	10(25.6%)	3(23.1%)	
Adapts recommended human dose for small animals			
Yes	14(35.9%)	1(7.7%)	0.256
No	25(64.1%)	9(69.2%)	
Indecisive	0(0%)	3(23.1%)	
Uses body weight as index for small animal dosaging			
Yes	25(64.1%)	9(69.2%)	0.340
No	0(0%)	1(7.7%)	
Undecided	14 (35.9%)	3(23.1%)	

PVHC – Primary veterinary health care (Ministry of Agriculture)

TVHC – Tertiary veterinary health care (College of Veterinary Medicine, FUNAAB)

Table 3: Antibiotics frequently prescribed in small animal treatment

ANTIBIOTIC CLASS	ANTIBIOTIC NAME	PVHC	TVHC	TOTAL
Tetracycline	Oxytetracycline	38 (97.4)	11(84.62)	49(94.2)
	Doxycycline	23 (59.0)	8 (61.54)	30(57.7)
Folic acid inhibitor	Sulphonamide	10 (25.6)	4 (30.78)	14(26.9)
Aminoglycosides	Gentamicin	28 (71.8)	6 (46.15)	34(65.4)
Beta lactam/ Aminoglycoside	Penicillin- Streptomycin	29 (74.4)	11 (84.62)	40(76.9)
Beta lactam	Amoxicillin	16 (41.0)	11 (84.62)	27(51.9)
Fluoroquinolone	Ciprofloxacin	27 (69.2)	8 (61.54)	35(67.3)
	Enrofloxacin	15 (38.7)	10 (76.92)	25(48.1)
Cephalosporin	Cefotaxime	9 (23.7)	5 (38.46)	14(26.9)
Macrolides	Erythromycin	1 (2.56)	3 (23.08)	4(7.7)

Table 4: Compromised antibiotics in small animal treatment

ANTIBIOTIC CLASS	ANTIBIOTIC NAME	TVHC n(%)	PVHC n(%)	TOTAL n(%)
Tetracycline	Oxytetracycline	9(69.2)	33(84.6)	49(80.8)
	Doxycycline	0(0)	0(0)	0(0)
Folic acid inhibitor	Sulphonamide	0(0)	0(0)	0(0)
Aminoglycosides	Gentamicin	4(30.8)	8(20.5)	12(23.1)
Beta lactam/ Aminoglycoside	Penicillin- Streptomycin	3(23.1)	7(17.9)	10(19.2)
Beta lactam	Amoxicillin	0(0)	0(0)	0(0)
Fluoroquinolone	Ciprofloxacin	0(0)	0(0)	0(0)
	Enrofloxacin	2(15.4)	5(12.8)	7(13.7)
Cephalosporin	Cephalosporin	0(0)	0(0)	0(0)
Macrolides	Macrolides	0(0)	0(0)	0(0)

Table 5: Awareness and experience of antimicrobial resistance

VARIABLES	NUMBER (%) OF RESPONDENTS		
	PVHC	TVHC	P value
Have you ever heard of antibiotic resistance			
Yes	39 (100)	13(100)	*
No	0(0)	0(0)	---------
Have you experienced antibiotic resistance in small animal treatment			
Yes	30(81.1)	12(93.3)	0.267
No	7(18.9)	1(6.7)	
Do you think misuse of antibiotics can lead to loss of sensitivity of pathogen to an antibiotic			
Yes	37(94.9)	13(100)	0.539
No	2(3.8)	0(0)	
How do you treat recurrent and persistent infections			
Increase duration of treatment using same drug	3(5.8)	0(0)	0.539
Change drug without carrying out culture and sensitivity test	30(57.7)	0(0)	
Carry out culture and sensitivity test	6(15.4)	13(100)	

*** -** No statistics are computed because awareness of antibiotic resistance was constant

DISCUSSION

Findings from this study suggest that all veterinarians who participated in the survey are aware of AMR and an appreciable number have experienced resistance to antibiotics in managing cases in small animal practice at one time or the other in the last three years (Table 5). A small proportion of the study participants from the State

Veterinary Department perform laboratory diagnosis and antibiotic sensitivity tests before prescription, while a higher proportion of clinicians at the University VTH carry out laboratory diagnosis and antibiotic sensitivity testing prior to prescription of antibiotics (Table 2). This variation may be attributed to the inadequacy of laboratory facilities and clinical microbiologists in various veterinary clinics in Ogun State and the difficulties associated with sample preservation and shipping to and from the various veterinary clinics in the suburban areas to the referral Veterinary laboratory. On the other hand, in the VTH, there are standard laboratory facilities, clinical microbiologists, who are trained and ready to deploy this equipment for laboratory investigation. The VTH handles a lot of referrals in which laboratory diagnosis is key to confirming diagnosis and instituting appropriate treatment measures. Researchers in the University who utilize clinical data perform laboratory testing, culture and sensitivity tests prior to instituting treatment. Also, the VTH has more elitist clients who understand the importance of laboratory diagnosis to veterinary practice and can afford to pay for such services compared to the low income of the indigenes requiring veterinary services in sub-urban areas (DeHaan *et al.,* 1991; Faramade *et al.,* 2016). Both groups show similar preference for injectable antibiotics (table 2) probably because of the ease of administration as opposed to what is obtained elsewhere with reported preference to oral routes of antimicrobial administration ((Johnston, 1998; Rantala *et al*., 2004; Escher *et al*., 2011; Buckland *et al.,* 2016; Singleton *et al.,* 2017). This preference is seen more in the parenteral administration of long acting tetracyclines which have broad spectrum activity and are convenient for a one-off use (Eagar *et al*., 2012). Clinicians at the State Department had higher preference for injectable drugs compared to those at the VTH (table 2). Clinicians at the VTH administered antimicrobials through the oral route (30.8%) compared to those at the State clinics (10.3%). This variation may be influenced by the presence of functional boarding facilities and paravets for in-patient animals in the VTH. This action enhances drug administration and monitoring of pharmacological effects of oral dosing as opposed to what is obtainable in the State veterinary clinics where boarding facilities are few and restricted only to the metropolis. In both groups of clinicians in this study, drugs formulated for humans were used for veterinary purpose with respondents employing body weight as an index for drug dosing (table 2). Reports have suggested however, that, veterinary-specific antimicrobials are the best for the treatment of infection in small animals considering that xylitol – (a sugar substitute) present in some human-grade drug formulations is potentially toxic to some species such as dogs (Kramer, 2019).

The most commonly prescribed class of antibiotics in this study are tetracyclines, beta-lactams/aminoglycosides and fluoroquinolones (table 3). These findings agree with a previous study by Adesokan *et al*. (2015) who reported that tetracyclines (33.6%), fluoroquinolones (26.5%) and beta-lactams/aminoglycosides (20.4%) constitute the majority of the antibiotics used over three years in the treatment of livestock diseases in southwestern, Nigeria. Similarly, Aminoglycoside (Gentamycin) was cited as the highest ranked prescription antibiotics for treatment of secondary bacterial infection in parvoviral enteritis in dogs in some veterinary clinics in Nigeria (Gberindyer *et al.,* 2017). In contrast, a study in the United States reported

Amoxicillin-clavulanate as the most frequently prescribed antibiotic, followed by cefazolin/cephalexin, enrofloxacin, ampicillin/amoxicillin and doxycycline (Shea *et al.*, 2011).

Findings from this present study suggests that resistance is driven by the frequency of the usage of these antibiotics (figure 3). This is in line with previous report that a significant decline in the proportion of bacterial isolates resistant to penicillin G and ampicillin following decrease in the hospital usage of these drugs (Prescott *et al.*, 2002). A major finding from this study is the non-availability of laboratory diagnosis and antimicrobial susceptibility testing as guide to antimicrobial prescription. For responsible antimicrobial stewardship and judicious antimicrobial use, laboratory services in disease diagnosis are very important. In this study, clinicians at the state veterinary clinics are more likely to misuse antimicrobials than those from the VTH. They probably will be using antimicrobials for cases that do not require them due to lack of laboratory diagnosis thereby more likely to use the wrong antimicrobials due to lack of antimicrobial sensitivity testing. They may not even commence treatment with the cheap and readily available first line antimicrobials because of their desire to achieve maximum result in the absence of AST. However, those at the VTH will be more careful in the use of antimicrobial. Therefore, the VTH clinicians will be more judicious in the use of these drugs. Also, most clinicians at the state clinics change antimicrobials or increase the dosage when AMR is observed while those at the VTH will rely on laboratory testing to guide their prescription. The clinicians at the State clinics manage more animals and are located at various suburban areas across the state compared to those at the VTH that is in only one location with less case load. Thus, the actions and inactions of clinicians at the state clinics will have greater impact on AMR than their counterparts in the teaching hospital.

Veterinary clinicians in the VTH are more versatile in the use of a wider range of antimicrobials other than tetracyclines, beta lactams and aminoglycosides when compared to their counterparts in the state veterinary clinics (figure 2). This preference might have been influenced by different factors such as utilization of diagnostic resources and influence of other veterinary specialists while prescribing, it may be suggested that stringent antibiotic stewardship is necessary in Ogun State. Most participants reported administering of antibiotics in dosages above and below the recommended therapeutic level as the key drivers of AMR (table 5). It is inferred that there is a consensus that AMR development in small animal practice is associated with abuse, misuse and overuse. In this study, resistance observed may not be attributed to exclusively resistant bacterial strains but wrong diagnosis. When antimicrobials are used in situations that do not require antimicrobials, there will be no response/cure.

The limitation of this study is that convenience sampling was used, resulting in a small number of government-employed small animal clinicians. Another limitation is that there was no quantification of the amount of antimicrobial used in the various clinics over the three-year period and data was not collated on the reasons/clinical diagnosis for which antimicrobials were prescribed. In spite of the limitations, this study achieved a good response rate with participants

providing detailed information to assigned questions.

CONCLUSION

Despite the awareness of AMR among small animal clinicians in government employ, majority (86%) adopt empirical treatment. There is therefore a need for attitudinal change and prohibition of arbitrary use and indiscriminate dosing of antimicrobials rather small animal clinicians should resort to laboratory services to guide their prescription. The government should implement policies that will encourage mandatory clinician's prescription for last-option antibiotics for veterinary use.

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