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Trends in the clinical use of antibiotics in a veterinary hospital in Nigeria, 2013 –2017

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Original Article

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Abstract

This study was a retrospective survey that evaluated the trend of clinical use and misuse of antibiotics on animals presented for veterinary care at the Veterinary Teaching Hospital, Nsukka, Enugu State, Nigeria, from January 2013 to December 2017. A total of 4851 case files were evaluated and, overall, antibiotics were used in 2316 cases (47.74%). The most frequently used antibiotics were a penicillin-streptomycin combination (36.53%), oxytetracycline (32.08%), gentamicin (19.78%) and sulphadimidine (5.35%); the frequency of use of other antibiotics was each less than 5%. The overall use of antibiotics increased significantly ($p<0.05$) across the study period, from 35.25% in 2013 to 52.38% in 2016. There was a significant ($p<0.05$) increase in the frequency of use of oxytetracycline (11.55% in 2013 to 40.31% in 2016) and sulphadimidine (0.8% in 2013 to 12.98% in 2017), but the frequency of penicillin-streptomycin use significantly ($p<0.01$) decreased from 74.5% in 2013 to 23.13% in 2017. The frequency of inappropriate use of antibiotics significantly ($p<0.01$) increased from 4.38% (2013) to 25.29% (2017), while that of non-compliance rose significantly ($p<0.01$) from 15.54% (2013) to 41.88% (2016). The frequency of use of antibiotics without definitive diagnosis/sensitivity testing was consistently high and did not significantly ($p>0.05$) vary across the study period (85.49% to 91.63%), but, that of the use of wrong antibiotic combinations significantly increased ($p<0.05$) from 5.58% (2013) to 23.63% (2017). It is concluded that the overall frequency of clinical use of antibiotics on animals, their inappropriate use, non-compliance and wrong combinations significantly increased across the study period.

Keywords: Antibiotics use, Animals, Veterinary Hospital, Nigeria, 2013-2017

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Introduction

Antibiotics have been in use since ancient times and their discovery, development and clinical use during the 20th century drastically reduced morbidity and mortality associated with microbial infections (Forrest, 1982; Waller and Sampson, 2018). More than 80% of the total antibiotics used in most nations are on animals (van den Bogaard and Stobberingh, 1999; FDA, 2010; Van Boeckel *et al*., 2015). Antibiotics are clinically used in animals for the prevention and treatment of bacterial diseases and the management of secondary bacterial infections associated with some viral diseases, and they are vital tools in the maintenance of health and productivity in these animals (Beyene and Tesega, 2014 ; Van Boeckel *et al*., 2015; Waller and Sampson, 2018). However, the misuse and/or irrational use of antibiotics has been reported to adversely reduce the quality of therapeutic outcomes, leading to increased morbidity and mortality, increased risk of adverse drug reactions and the emergence of antibiotic resistance (Gautam and Aditya, 2006; Bbosa and Mwebaza, 2013; Beyene and Tesega, 2014; Tanwar *et al*., 2014).

Antibiotic resistance is a globally recognized public health issue that threatens the effective prevention and treatment of microbial infections (WHO, 2014; Michael *et al*., 2014; FMAEH, 2017). Though most of the antibiotic resistance problems in human medicine stem from overuse or inadequate control of antibiotic use in humans, there are reports in available literature which show that the widespread use and misuse of antibiotics in animals contributes to the emergence of antibiotic-resistant microbes (ARM_S) of animal origin which can be transmitted to humans through the environment, food products and to agricultural workers and pet owners by direct contact (Van den Bogaard and Stobberingh, 1999; Barton, 2000; Guardabassi *et al*., 2004; Graham *et al*., 2009; Smith *et al*., 2013; Van Boeckel *et al*., 2015). Other studies show a close association between the prevalence of animal-associated ARM_S in humans and the levels of antibiotic use in animals (Prescott *et al*., 2002; Aarestrup, 2005; Vieira *et al*., 2011; Van Boeckel *et al*., 2015).

There is a paucity of information in available literature on the trends of use and misuse of antibiotics in animals globally and specifically in West Africa. A recent report by the World Organization for Animal Health (OIE, 2016) re-stated this paucity of data on use of antimicrobials in animals all over the world and showed from their last survey spanning 2010 – 2015, that only reports for the year 2015 were available from most continents, including Africa. Other researchers also made a case for increased research in the area of trends of antibiotics use in animals (Bbosa and Mwebaza, 2013; Beyene and Tesega, 2014). There is thus a need for documentation of the trends of the use of antibiotics in animals, especially, when we consider the role that antibiotic use in animals plays in the overall antibiotic resistance crises. This present study evaluated the trend of use and misuse of antibiotics in a veterinary hospital in Nigeria, for a five-year period, January 2013 to December, 2017.

Materials and Methods

The study was a retrospective survey of hospital records at the Veterinary Teaching Hospital (VTH), Nsukka, Enugu State, Nigeria. The VTH Nsukka is located within the Nsukka campus of the University of Nigeria and renders veterinary clinical services to animal owners in Enugu State and adjoining communities in Kogi and Benue States of Nigeria, in addition to serving as a veterinary referral centre for other states in the eastern part of Nigeria. The VTH is also a training/teaching hospital for clinical students of the Doctor of Veterinary Medicine (DVM) programme of the Faculty of Veterinary Medicine, University of Nigeria Nsukka, and Fellowship Diploma students of the College of Veterinary Surgeons of Nigeria, Nsukka Study Centre. The coordinates of Nsukka, where the VTH is located, are: latitude – 6°51'28.19" N and longitude – 7°23'44.77" E.

The period of study was five years, spanning from January 01, 2013 to December 31, 2017, and all cases presented in the hospital during this period were evaluated. A total of 4851 documented cases were studied, comprising case presentations on 54 cats, 11 cattle herds, 4074 dogs, 395 goats, 12 horses, 56 pigs, 67 poultry, 52 rabbits, 118 sheep and 12 zoo primates. Approval for the use of hospital records for the study was sought by the investigators and obtained from the Director, VTH Nsukka. By default, all clients that presented animals for treatment at the hospital consented to their records being used for studies/research that would benefit animal health and humanity. The confidentiality of patients and client personal information/data was maintained using number codes for the individual cases.

For each case presentation, basic biodata (species, sex and age) of the animal presented was obtained. The primary complaint of the client/case presentation and the diagnosis (tentative or definitive) was noted and, if further laboratory tests such as antibiotic sensitivity tests were conducted, this was also noted. The antibiotics administered to each patient (where antibiotics were used) and the patient's compliance to treatment were recorded. Cases of misuse and/or irrational use of antibiotics in the categories of inappropriate use, wrong combination (Gautam and Aditya, 2006) and use without definitive diagnosis or antibiotic sensitivity tests, where appropriate, were noted.

Data obtained was collated year by year for the antibiotics in general and the specific antibiotics, one by one. The data was subjected to descriptive statistics and expressed in percentage frequencies. The frequencies across the years were compared using Chi square and Fisher's exact test as appropriate. The statistical package for social sciences (SPSS) version 16.0 for Windows was used for the analyses. Summaries of the results were presented in form of tables and bar charts.

Results

Out of the 4851 case files studied, 2316 (47.74%) were treated with antibiotics (Table 1). The overall percentage of cases treated with antibiotics significantly ($p < 0.05$) increased progressively across

the study period (2013 – 2017), ranging from 32.25% in 2013 to its highest value of 52.38% recorded in 2016 (Table 1).

The most frequently used antibiotics across the study period were the penicillin-streptomycin combination (36.53%), followed closely by oxytetracycline (32.08%), then gentamicin (19.78%) and sulphadimidine (5.35%) (Figure 1). Ceftriaxone (3.50%), doxycycline (2.46%), ciprofloxacin (1.94%) and an amoxicillin-clavulanate combination (1.04%) followed (Figure 1). The frequency of use of enrofloxacin was 0.82%, while that of ampicillin was 0.47%; those of amoxicillin and neomycin were each 0.43%, and the least used antibiotic was tylosine (0.39%) (Figure 1). Across the five-year study period, the frequency of use of ceftriaxone, oxytetracycline and sulphadimidine increased significantly ($p < 0.05$), while that of the penicillin-streptomycin combination significantly ($p < 0.01$) decreased (Table 2). The frequency of use of ciprofloxacin significantly ($p < 0.05$) rose in 2014 and 2015 and dropped in 2016 and 2017 (Table 2). There were no significant variations ($p > 0.05$) in the frequency of use of the amoxicillin-clavulanate combination, amoxicillin, ampicillin, doxycycline, enrofloxacin, gentamicin and neomycin across the study period (Table 2).

Table 1 The overall trend and distribution of the clinical use of antibiotics on animals presented for veterinary care at the veterinary hospital across the five year study period (2013 – 2017)

Study period	*Number of cases in which antibiotics were used in the year*	*Total number of cases presented in the hospital in the year*	*Percentage frequency of use of antibiotics in the year*
2013	251	712	35.25% [a]
2014	379	834	45.44% [b]
2015	512	1033	49.56% [b]
2016	573	1094	52.38% [b]
2017	601	1178	51.02% [b]
Totals for the five-year study period.	**2316**	**4851**	**47.74%**

[a, b,] Different superscripts on the percentage frequencies column indicate significant ($p < 0.05$) variations in the frequency of antibiotic use across the study period, 2013 – 2017.

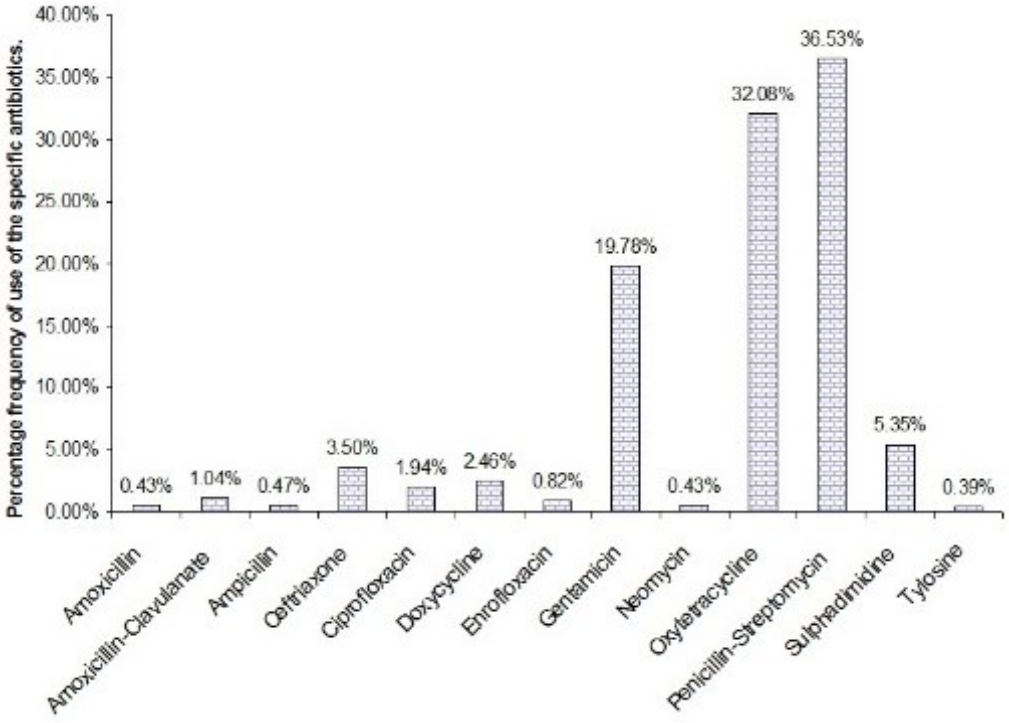

Figure 1 The percentage frequency of use of the specific antibiotics in the 2316 cases in which antibiotics were used in animals presented at the veterinary hospital, 2013 – 2017

The categories and instances of misuse/irrational use of antibiotics are listed in Table 3. The use of antibiotics without a definitive diagnosis or antibiotic sensitivity test had the highest frequency (88.13%), followed by non-compliance (31.91%), then wrong combinations (17.88%) and, lastly, inappropriate use (13.99%) (Figure 2). The inappropriate use of antibiotics significantly ($p < 0.05$) rose from 4.38% in 2013 to its highest value of 25.29% in 2017, while non-compliance also significantly ($p < 0.05$) rose from 15.54% in 2013 to 41.88% (its highest) in 2016 (Table 4). The use of wrong combinations of antibiotics also rose significantly ($p < 0.05$) from 5.58% in 2013 to 23.63% in 2017 but there were no significant ($p > 0.05$) variations in the frequency of use of antibiotics without definitive diagnosis/antibiotic sensitivity testing (85.49% to 91.63%) (Table 4).

Table 2 The trend of use of specific antibiotics on animals presented at the veterinary hospital across the five year study period (2013 – 2017)

	Number of cases in which specific antibiotics were used across the years, with percentages in brackets.					
	2013	***2014***	***2015***	***2016***	***2017***	***Totals***
Amoxicillin	0 (0%)	0 (0%)	0 (0%)	1 (0.17%)	9 (1.50%)	10
Amoxicillin-Clavulanate	0 (0%)	0 (0%)	0 (0%)	14 (2.44%)	10 (1.66%)	24
Ampicillin	0 (0%)	0 (0%)	0 (0%)	0 (0%)	11 (1.83%)	11
Ceftriaxone*	0 (0%)	0 (0%)	21 (4.10%)	19 (3.32%)	41 (6.82%)	81
Ciprofloxacin*	0 (0%)	19 (5.01%)	24 (4.69%)	2 (0.35%)	0 (0%)	45
Doxycycline	6 (2.39%)	11 (2.90%)	14 (2.73%)	12 (2.09%)	14 (2.33%)	57
Enrofloxacin	0 (0%)	0 (0%)	0 (0%)	3 (0.52%)	16 (2.66%)	19
Gentamicin	51 (20.32%)	74 (19.53%)	89 (17.38%)	96 (16.75%)	148 (24.63%)	458
Neomycin	0 (0%)	0 (0%)	0 (0%)	2 (0.35%)	8 (1.33%)	10
Oxytetracycline*	29 (11.55%)	108 (28.50%)	152 (29.69%)	231 (40.31%)	223 (37.10%)	743
Penicillin-Streptomycin*	187 (74.50%)	174 (45.91%)	185 (36.13%)	161 (28.10%)	139 (23.13%)	846
Sulphadimidine*	2 (0.80%)	9 (2.37%)	11 (2.15%)	24 (4.19%)	78 (12.98%)	124
Tylosine	0 (0%)	0 (0%)	0 (0%)	4 (0.70%)	5 (0.83%)	9
Total number of cases in which antibiotics were used	***251***	***379***	***512***	***573***	***601***	***2316***

*Asterisk on a specific antibiotic indicates significant variations ($p < 0.05$) in the frequency of its use across the five-year study period (2013 – 2017).

Table 3 Categories and specific instances of misuse/irrational use of antibiotics on the animals presented at the veterinary hospital during the study period, 2013 - 2017

Category A. Inappropriate use:

i. Administration of oxytetracycline injection to an animal that came for routine de-worming.
ii. Administration of penicillin-streptomycin combination or oxytetracycline injection to animals diagnosed of helminthosis.
iii. Administration of antibiotics (oxytetracycline, gentamicin or penicillin-streptomycin combination) to animals diagnosed of organophosphate poisoning.
iv. Giving antibiotics (ampicillin or penicillin-streptomycin combination) to dogs that were presented for routine vaccination.
v. Administration of oxytetracycline or gentamicin to animals diagnosed of tick infestation.
vi. Administration of gentamicin to dogs diagnosed of hookworm infestation.

Category B. Wrong Combinations:

a. Co-administration of oxytetracycline, gentamicin and sulphadimidine to dogs in the management of parvovirus enteritis.
b. Co-administration of gentamicin plus penicillin-streptomycin combination with vincristine in the treatment of transmissible venereal tumour.
c. Co-administration of penicillin-streptomycin combination plus oxytetracycline and gentamicin to dogs in the management of canine distemper.

Category C. Non-Compliance:

1. Not completing the routine specified period (commonly 3 – 5 days) of antibiotic administration.
2. Not returning for a repeat dose of long acting oxytetracycline (normally 3 days after the administration of the first dose).

Category D. Use of antibiotics without definitive diagnosis and/or antibiotic sensitivity testing.

i. Use of antibiotics without culture and identification of the bacterial organism responsible for the disease/infection.
ii. Use of antibiotics without antibiotic sensitivity testing that will show the specific antibiotics which the organism responsible is sensitive to.

Table 4 The trend and distribution of the various categories of misuse/irrational use of antibiotics in the 2316 cases treated with antibiotics at the veterinary hospital, 2013 – 2017

Categories of misuse of antibiotics.	***No. of cases in which specified category of misuse was recorded across the years, with percentages in brackets.***						
	2013	***2014***	***2015***	***2016***	***2017***	***Totals***	***Sig. level***
Inappropriate use.*	11 (4.38%)	24 (6.33%)	46 (8.98%)	91 (15.88%)	152 (25.29%)	324	$p < 0.01$
Non- Compliance.*	39 (15.54%)	66 (17.41%)	185 (36.13%)	240 (41.88%)	209 (34.78%)	739	$p < 0.01$
Use of antibiotics without definitive diagnosis and/or sensitivity testing.	230 (91.63%)	324 (85.49%)	452 (88.28%)	504 (87.96%)	531 (88.35%)	2041	$p > 0.05$
Wrong combinations.*	14 (5.58%)	36 (9.50%)	118 (23.05%)	104 (18.15%)	142 (23.63%)	414	$p < 0.05$
Total number of cases in which antibiotics were used.	***251***	***379***	***512***	***573***	***601***	***2316***	

*Asterisks on a category of misuse indicates significant variations in its frequency across the five-year study period (2013 – 2017); * = $p < 0.05$, ** = $p < 0.01$

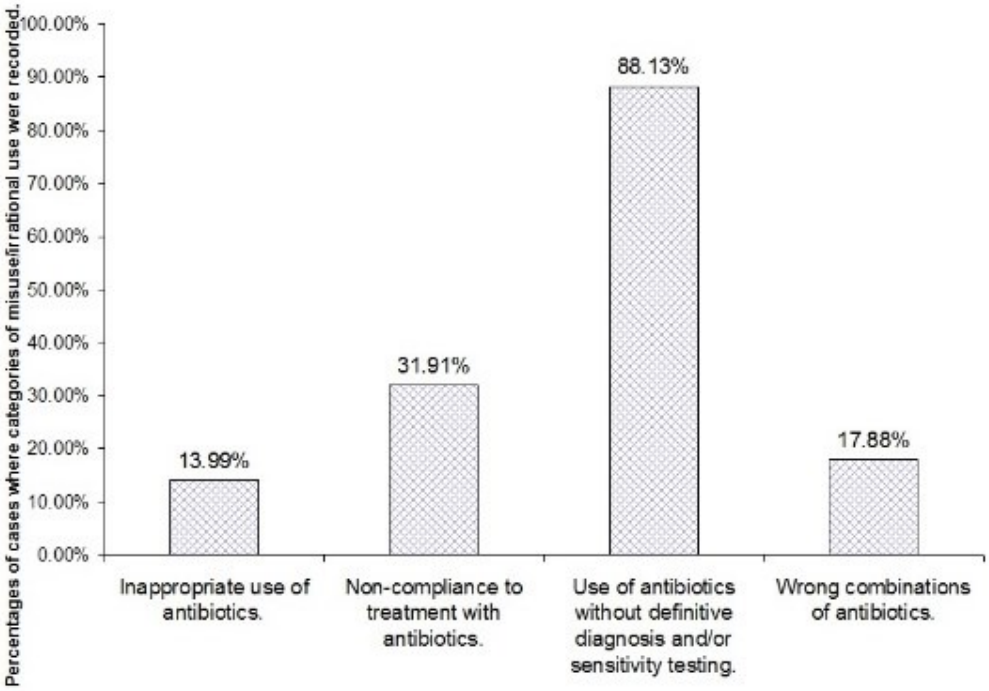

Figure 2 The percentage frequency of the various categories of misuse/irrational use of antibiotics in 2316 cases documented in the veterinary hospital, 2013 – 2017

Discussion

A high frequency of use of antibiotics was recorded in this study (47.74%) and it is believed that this may not be as a result of high levels of occurrence of bacterial disease; rather it may reflect a combination of bacterial and viral diseases burden and also surgical cases because antibiotics are commonly used in clinical management of viral diseases, in surgery to prevent infection of surgical wounds and in several other disorders, as treatment for possible 'secondary bacterial infections' (Beading and Slifka, 2004; Hendaus *et al*., 2015). Such high frequency of antibiotic use may also be partly blamed on the 'loosely enforced drug use regulations' with regards to prescription only medicines (POMs), as detailed in the recent national report on antimicrobial use and resistance in Nigeria (FMAEH, 2017). This high frequency of use of antibiotics is thus in agreement with reports in the available literature of the combined frequency of occurrence of bacterial and viral diseases, surgical cases, wounds and other disorders in which antibiotics are commonly used in veterinary hospitals in Nigeria (Ebbo *et al*., 2003; Garba *et al*., 2011; Shima *et al*., 2015) and some other tropical countries (Sarker *et al*., 2015; Islam *et al*., 2019). The overall 47.74% frequency of use of antibiotics recorded in the present study is slightly higher than the 46.4% reported in a 2012 – 2013 survey of antimicrobial use on livestock in Adama District Veterinary Clinic, Central Ethiopia (Beyene *et al*., 2016) but was lower than the 54.4% (2009 – 2013 study) and 60.41% (2012 – 2017 study) reported by Beyene *et al*., (2015) and Mojo *et al*. (2019), respectively, in studies in veterinary hospitals in Ethiopia. The significantly progressive increase in the frequency of use of antibiotics from 35.25% in 2013 to its peak of 52.38% in 2016 as recorded in the present study is worthy of note. It is thought that this is an indication that progressively more antibiotics were being used to manage diseases and disorders presented in the hospital; it may not be a reflection of a high occurrence of bacterial diseases as earlier stated. This is a cause for concern, as this increasingly higher frequency of use, which is commonly associated with misuse/irrational use (as recorded in the study) may be responsible for the escalating level of antibiotic resistance (Bbosa and Mwebaza, 2013; Michael *et al*., 2014; WHO, 2014), as the results of systematic reviews of the Nigerian literature revealed that resistant bacteria are commonly recovered from domestic animals and foods of animal origin (Kabir *et al*, 2004; FMAEH, 2017).

The finding in this study that the overall most commonly used antibiotic during the study period was the penicillin-streptomycin combination, is believed to be due to the earlier perception by clinicians that a penicillin-streptomycin combination delivers a broad spectrum (gram-positive and gram-negative) anti-bacterial protection (Ullah and Ali, 2017), and the sharp fall in the frequency of its use across the study period from 74.50% to 23.13% also reflects a loss of trust in its efficacy across time (WHO, 2014, Munita and Arias, 2016), which is mainly attributable to the near total (100%) resistance of most pathogens in most parts of Nigeria to penicillin (Fashae *et al*, 2010; Nsofor and Iroegbu, 2013; FMAEH, 2017). The frequency of use of a penicillin-streptomycin combination in animals was not reported to be the highest in earlier reports in the available literature (Roderick *et al*., 2000; Beyene *et al*., 2015; OIE, 2016; FMAEH, 2017; Mojo *et al*., 2019), rather, the frequency of use of oxytetracycline which was recorded as the second highest in this present study was reported in the literature to be the antibiotic with the highest usage frequency globally (OIE, 2016) and also in veterinary hospitals in Ethiopia, East Africa (Beyene *et al*., 2015; Mojo *et al*., 2019). It should be noted, however, that the World Organization for Animal Health (OIE) stated in their report that the data

used for their compilation was mainly records obtained in 2015, though the reports should have covered 2010 to 2015 (OIE, 2016). The finding in the present study of a progressive and significant increase in the use of oxytetracycline across the study period (2013 - 2017), with its peak in 2016, concurs with this OIE report (OIE, 2016), because as the recorded frequency of the use of penicillin-streptomycin waned across the study period, the frequency of use of oxytetracycline rose. The waning of the frequency of the use of penicillin-streptomycin was also additionally associated in this study with a rise in the frequency of use of sulphadimidine and ceftriaxone – antibiotics commonly used in the treatment of resistant organisms (Katzung et al, 2012; Waller and Sampson, 2018).

The categories and instances of misuse/irrational use of antibiotics recorded in the present study can form a basis for the recommendation of reforms in clinicians' attitude of suspecting and anticipating secondary bacterial infections in practically all case presentations and treating them thus. The findings of these specified categories and instances of antibiotic misuse in the present study is in agreement with the reports of FMAEH (2017) which highlighted that there is poor prescription monitoring and loosely enforced regulation of guidelines on the use of prescription only medicines (POMs) in Nigeria and which further recommended a strict implementation of drug regulation guidelines and engagement of clinicians, pharmacists and proprietary medicine vendors on the importance of rational use of antibiotics. The conscious engagement of all health workers with the fact that their irrational use/misuse of antibiotics may possibly be fuelling antibiotic resistance in the population and its public health significance is needed to stem the tide of misuse and the increasing levels of antibiotic resistance in the country.

The very high frequency of antibiotic treatments without definitive diagnosis recorded in this study (88.13%) is believed to be partly accounted for by this mentality of suspecting possible secondary bacterial involvement at all times and also, partly, by the fact that bacterial culture and identification takes a comparatively longer time (several days in most cases when compared with instances of the diagnosis of parasitic and metabolic diseases that can be done on the instant with results delivered within 10 – 15 minutes), and clinicians and animals owners may not patiently wait for this number of days before instituting treatments. Though high, the frequency of the use of antibiotics without definitive diagnosis as recorded in this study is relatively lower than the 96.6% and 98.2% reported by Beyene *et al*., (2015) and Mojo *et al*. (2019), respectively, in veterinary hospitals in Ethiopia. The tendency to prescribe and start administration of antibiotics before definitive diagnosis is one of those areas where the enlightenment of all health workers may help to curtail irrational use, because the national report on antimicrobial use and resistance in Nigeria (FMAEH, 2017) reported a low level of awareness of antimicrobial resistance among health professionals in the country.

The high frequency of non-compliance to antibiotic treatment recorded in this study may be attributed to lack of knowledge on the part of the owners of such animals and inefficiency on the part of animal health workers in their ability to inform animal owners of the value of completing their treatment regimens even if their animals seem to have recovered. The irrational use of wrong combinations recorded in this study concurs with earlier reports on this by Gautam and Aditya (2006) and should form a basis for sensitization and enlightenment of clinicians and clinical students on the possible adverse reactions that may follow such combinations, plus the higher cost that may not produce requisite improvement in the therapeutic outcome. The instances of inappropriate use of antibiotics recorded in this study is commonly based on the earlier stated misconception among clinicians of suspecting and treating for possible secondary bacterial infections at almost every case presentation (Beading and Slifka, 2004; Hendaus *et al*., 2015); this should be discouraged.

Based on the results of the study, it is summarized and concluded that, across the study period (2013 – 2017), there was an increased frequency in the use of antibiotics, and also an increase in the frequency of misuse/irrational use, in the form of inappropriate use, non-compliance and use of wrong combinations. The use of antibiotics without definitive diagnosis was consistently high all through the study period. Continual sensitization and enlightenment of clinicians, clinical students and animal owners on the possible adverse consequences of misuse/irrational use of antibiotics is recommended.

Statement of Animal Rights: Only hospital records were used for the study. This use of the hospital records was duly approved by the Director of the Hospital. Animals were not directly used for the study.

Conflict of Interest: The authors declare no conflict of interest.

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