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Epidemiology Survey of Antibiotics Use in Hospitals and Veterinarian Practices in Northern Regions of Cameroon

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ABSTRACT

Antibiotics are used in veterinary practice as growth promoter to improve animal production and to control animal diseases. Routine antimicrobials consumption led to resistant-strains selection an spread within animals, their environment, farmers and animal products consumer. As for animals, antibiotics are widely recommended for bacterial infections in human medicine. By the same process, antibiotic-resistance emergence in human is current event. This is why in our study the aim was to assess antibiotic use frequencies in human and veterinary practices without previous antibiogram or species identification. We focused on cocci gram prositif infections in Cameroon northern regions. Our results revealed high rate of ceftriaxone (24%), amoxicillin (29%) and cloxacillin (14%) prescription by health practitionner for cocci gram positif and Staphylococci infections. In livestock Penicillin-streptomycin (42%) and oxytetracyclin (38%) are the most use for mastitis, penicillin-diclofenac mix and penicillin-streptomycin were frequently indicated for dermatosis. Antibiotics are widely prescribed in northern regions either in human or in veterinary medicine and may lead to antibiotic-resistance.

Keywords-- Antibiotics, Human Medicine, Veterinarian Medicine, Resistance Emergence, Staphylococci

I. INTRODUCTION

Antimicrobials are currently use in animal production. They are used in animal as growth promoter to improve animal productivity[1]. They are also spent to treat and control animal infectious diseases [2]. Most antibiotics added in animal supply are also used in human health. Inspite of benefits related to antimicrobials use in animal, some risks are associated with this common practice. Misuse or overuse of antimicrobials in food-producing animal feed, for prophylactic and therapeutic led to selection and spread of antibiotic-resistant bacteria strains[1, 3, 4]. Resistant pathogens can be transmitted to human through direct contact with animals, animal products consumption, contaminate environment or genetic material transfer[3, 5-7]. Abusive use of antimicrobial and bacteria resistance has important health and socio-economic consequences both in human and animals. The impact of antimicrobial-resistance in human are treatment failure, long hospitalization, higher healthcare cost, prolonged infection and increase dead rate [8].

Antimicrobial resistance quicky rise with time and constitute major threat for human health. To standardize antibiotics usage, World Health Organisation (WHO) classify antimicobial depending of their relative importance and the prioritization criteria in human medicine. Different categories of antimicrobial classes were ranked as critically important, hightly important, important and highest-priority critically important for human treatments [9]. Actually, restriction utilization of medically important antimicrobial in foog-producing animal contribute to reduce antibiotic resistance (9 to 30%) in animal and human population [10].

To solve public health problem due to antimicrobial resistance, recently WHO established guidelines for antimicrobials use in food-producing animals. The guidelines recommended reduction use of medically important antimicrobials in food-producing animals for growth promotion, prevention or treatment of disease not clinically diagnosed. WHO also stipulate highest-priority critically important antimicrobial for human medicine should not be used for food-producing animals treatment or control of clinically diagnosed infectious diseases [11].

Despite recents recommendations, antimicrobial resistance rate still higher at some world area. Especially in some subsaharian African countries, the case of Cameroon. In North Cameroon regions, antimicrobial-resistance is not or less documented [12]. In this study we focus our investigation on the three northern regions of Cameroon to assess antibiotic frequencies use in contex of bacterial infection treatment in human medicine and veterinary practice in northern area. We targeted *Staphylococci* bacteria base only on gram staining method without culture for specific species identification and antibiogram for drugs succeptibility tests.

II. MATERIALS AND METHODS

Study Design, Area and Period

Cross sectional study was conducted in the three northern regions of Cameroon, from June to October 2016. The study it carried out in the health and veterinary services implanted in the three regions (Adamawa, North and Far north). Data were collected in health care medical centerswith no technical equipments to carry out bacterial specy identification and antibiogram assay. In theAdamawa region, health centers were : Regional hospital, Protestant hospital, Medical health center of Boumdjere and Sabongari in Ngaoundere Town. In the North region we had, the regional hospital, medical health center of Kolere and Foulbere, while in the Far north region regional hospital, Medico social center for Social national insurance fund (CNPS), and Medico Social Center of the Unversity of Marouawere concerned. Eleven (11) hospitals were visited and we interviewed 157 health workers for all occupation concern.

We worked in the veterinary clinics, feed mill, the head of association of breeders and veterinary pharmacies. In this part, we visited 23 services and 53 professionnals were interviewed.In order to compare antibiotic classes intook in human medicine and the related ones in veterinary medecine, we analysedin this study antibacterials prescribed specifically for presumed *Staphyloccus aureus* infections. In livestock we chosed to assess medicines used to cure mastitis, dermatosis and lameness which may be*Staphylococcus aureus*related infections. Cattle *Staphylococcus* infections are treated by just one, two or more chemicals. Monotherapy or multitherapy aim is to fight bacterial dissemination and related inflammation and pain.

Data Collection Method

Interviews were conducted by self administered questionnaire after obtained oral and written consent from all health professionals workers and veterinarian workers. The questionnaire was developped from different literature reviews[13, 14], and has three parts each. (1) Socio demographic variables namely age, sex, position for the first part ;(2) the second part constituted with information on the health institutions : type (public or private), level on the ministry classifiction, number of patient received and the (3) third part for health workers questionnairecomprise antibiotic used, if labortory produce result with antibiogram test, which antibiotic are used to treat infection related to *Staphylococcus* without antibiogram, for how long and what reason to choose this antibiotic. Same protocole was used for veterinarian excepted the third part here we asked questions related to the treatment administer fordermatosis and mammite, duration of treatment, antibiotic used in addition of animals food and if there is any proposition to share with us related to *Staphylococci*.

Data Quality Assurance

Before conducting the study, questionnaire was pretested in Ngaoundere. All participant health professionnals and veterinarians were briefly instructed to fill out the questionnaire. To the drug sellers who did not understand official languages, the questionnaire was explained in local language. Each questionnaire was checked daily during the data collection period to verify the completeness.

Data Analysis

Data were entered into Excel, cleaned and exported to Draft Part package for analysing. Descriptive statistic like means, frequencies and percentages were performed on different variables. The variables with a p value < 0.05 were considered statistically significant using One-way ANOVA and T-test analysing on GraphPad Prism 5.

III. RESULTS

Antibiotics Utilization for Cocci Gram Positif Human Infection in Northern Regions

Our results highlighted many antiobiotics used in case of cocci gram positif infections in human medicine(n=311, P value = 0.0011). In this study ceftriaxone (24%), amoxicillin (29%) and cloxacillin (14%) were widely indicated for gram positif cocci infection treatments unlike erythromycin (11%), ciprofloxacin (8%), oxacillin (7%), amoxicillin + clavulanique acid (6%), ampicillin (1%) and gentamycin (0,5%) which were less prescribed (figure 1A). Within 311 antibiotics presciptions for gram positif cocci, 156were (50%) suspected to be *Staphylococcus* species due to their pattern in microscopy after gram staining (gram positif cocci in clusters) without any specy's confirmation. Same antibiotics used for gram positif cocci infection treatments were indicated for *Staphylococci* infections (figure 1B). In our study antibiotics largely indicated for *Staphylococccus* genuselimination are the same recommended for gram positif cocci infections (same frequency's patterns) (figure 1A and 1B). As for gram positif cocci antibiotic prescriptions, more antibiotics were utilized for *Staphylococcus*specy's infections(P value = 0.0204). Inspite of significant antibiotics consumption in case of gram positif cocci and presumed *Staphylococcus* specy's infections, there was no difference in term of frequency of these antimicrobialsprescription in all three northern regions (P

value = 0.3512).These results obtained suggest that more antibiotics are given to patients suspected to be infected with gram positif cocci and specifiquely *Staphylococcus* species base only on gram staining pattern, without any previous antibiogram or species confirmation. We presumed that, This practice may have as consequences selection and propagation of antimicrobial-resistant strains within population.

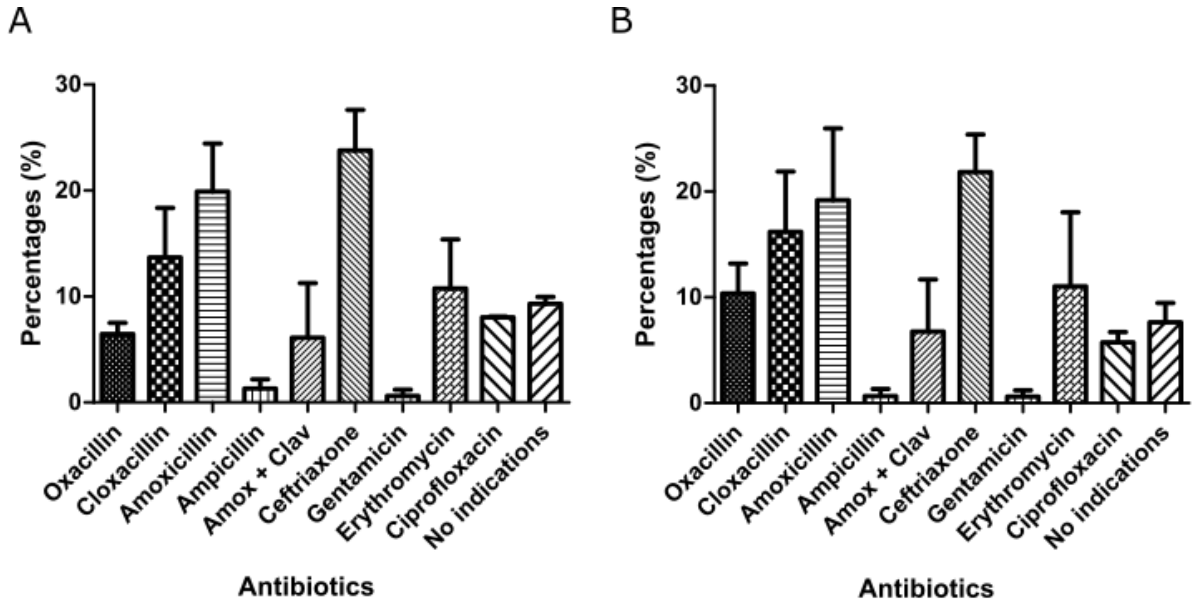

Figure 1: Antibiotic frequencies use for cocci gram positifs bacteria (A) and Staphylococci human infections (B). Amox + Clav=amoxicillin+clavulanate.

Determination of Medical Practitioners Implication in Potential Drugs-Resistant Bacteria Emergence

Our investigations show high number of antibiotics were managed by care providers for different grades (P value < 0.0001). Large number of medical staff who provided a lot of antibiotics to infected persons without any preliminary antibiotic succeptibility test are assistant nurses (25/159) followed by nurses (14/159), unlike senior nurses (5/159), medical doctors (5/159) and specialists in medicine (1/159) (figure 2A). Aside of personnel's degree, duration of professional experiences mattered substantially in our study. Our results revealed that antibiotics prescription by medical staff lessen with years of experiences. More the personnel is skilled (many years of professional experiences) least they recommended antibiotics without antibiogram, in ages of experiences depending manner (P value < 0.0001). personnel who lasted less than five year in the field (medical practice) (22/158) are more likely to give antibiotics in case of bacterial infection suspicion than those who lasted longer ([20 and +[years, 3/158) (figure 2B). Furthermore more practitioners wereseniors ([50 to 60[and [60 and +[years, 4 and 1 staffs out of 157 respectively) less they used antibiotics to treat assumed gram positif cocci and *Staphylococcus* species sick patients in ages-depending manner (P value < 0.0001). On the contrary younger staff ([20 to 30[and [30 to 40[years, 19 and 18 medical health-cares out of 157 respectively) are more apt to considerably prescribe antibiotics (figure 2C). Moreover beside personnel grades, ages, experience duration, gender analysis showed high rate of females staff rather than male ones according to antibiotic recommendations propencity (P value 0.0346) (figure 2D). Our results emphasised social and demographic data influences on abusive of antibiotics by medical staff which may lead to antimicrobial-resistance. This suppose the important role played by health staff on selectionand dissemination of antibiotic-resistant bacteria strains in northern Cameroon regions.

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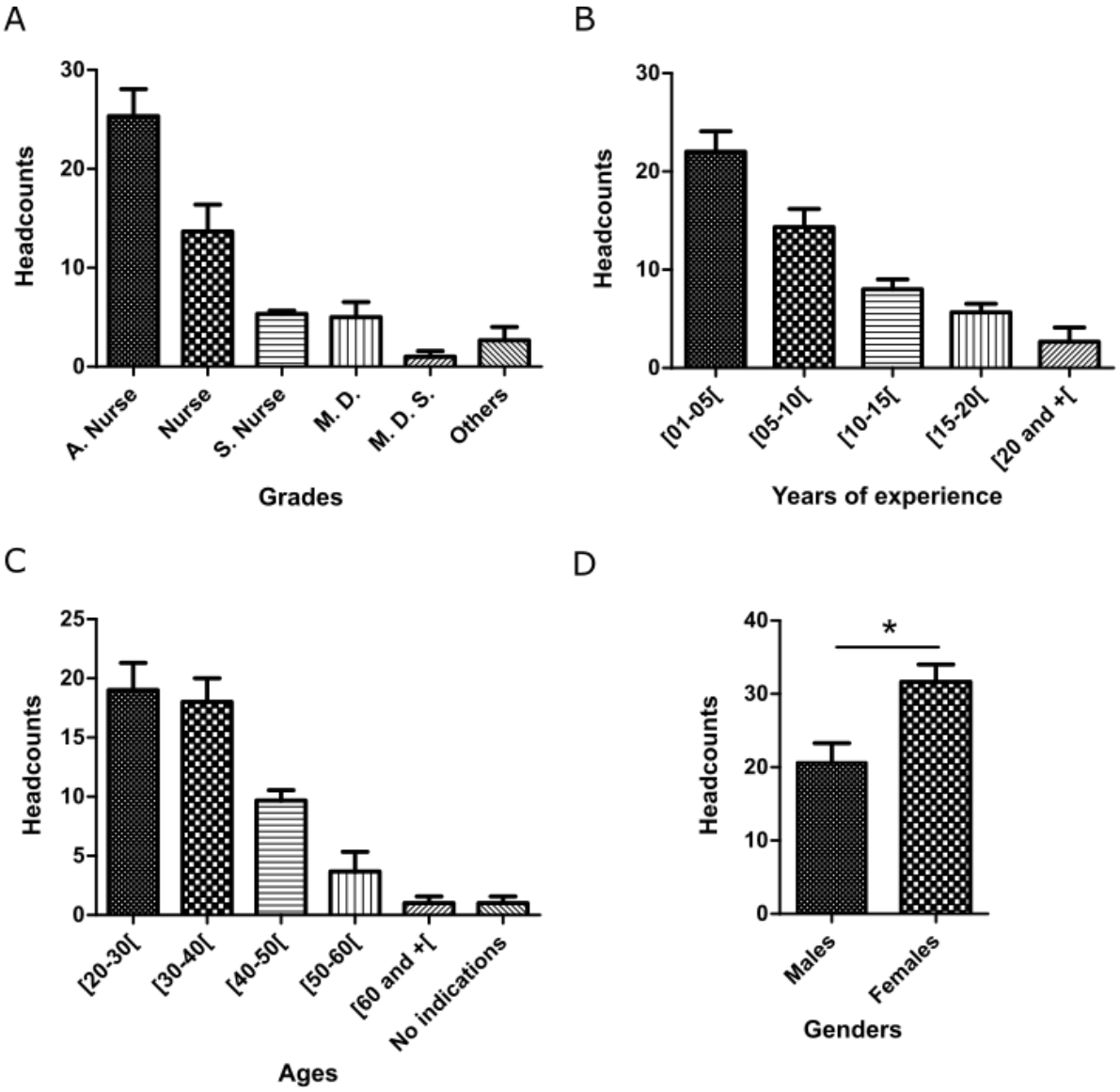

Figure 2: Social and demographic impact on antibiotic recommendation trend by grades (A), years of experiences (B), ages (C) and genders (D). A. Nurse=assistant nurse; S. Nurse=senior nurse; M D=medical doctor; M D S=medical doctor specialist.

Antibiotics and Other Drugs for Assumed staphylococci Cattle Infections

Our results indicated that many antibiotics are indicated for mastitis treatment (P value < 0.0001). Penicillin-streptomycin (procainepenicillin and dihydrostreptomycin) combination (42%) and oxytetracyclin (38%) are largely used to cure mastitis. Combikel (Procaine benzylpenicillin, Dihydrostreptomycin sulphate, Dihydrostreptomycin procaine hydrochloride) (11%) and anti-inflammatory drugs (2%) are less appropriated. Lastly penicillin-diclofenac(procainepenicillin anddiclofenac) mixture, procain (benzatyl benzylpenicillin procain) and ampicillin-dexamethason combinationsdid not corresponded for mastitis therapy (figure 3A). Antibiotics consumption pattern was the same in the three differents northern regions (Adamawa, North and Far North) (figure 3B). Dermatosis (P value = 0.2036) and lameness (P value = 0.1848) were also handled by antibiotics, however they were less suitable. Nevertheless few of antibiotics given for dermatosis were mostly penicillin-diclofenac mix in Adamawa region and penicillin-streptomycin in North and Far North. About Lambing ampicillin-dexamethason and penicillin-diclofenac were highly utilized in Adamawa and North respectively (data not shown). Procaine and ampicillin-dexamathason were not useful for bacterial skin issues in our investigations. About limb concerns penicillin-streptomycin and anti-inflammatories were inappropriated (figure 3C). More but not only antibiotics are meant to cure *Staphylococcus*

aureus infection in livestock. Inspite of risk of antimicrobial-resistance assosiate with antibiotic use in veterinary medicine, in our study few number of antibioticswere concerned. Antibiotics used were penicillins (penicillins and ampicillin), aminosides (streptomycin) and cyclines (oxytetracyclin) for mono and multitherapy. Our results suppose that antibiotics used in livestock for bacterial infection treatment may not be key factor for antimicrobial-resistant strain in northern regions.

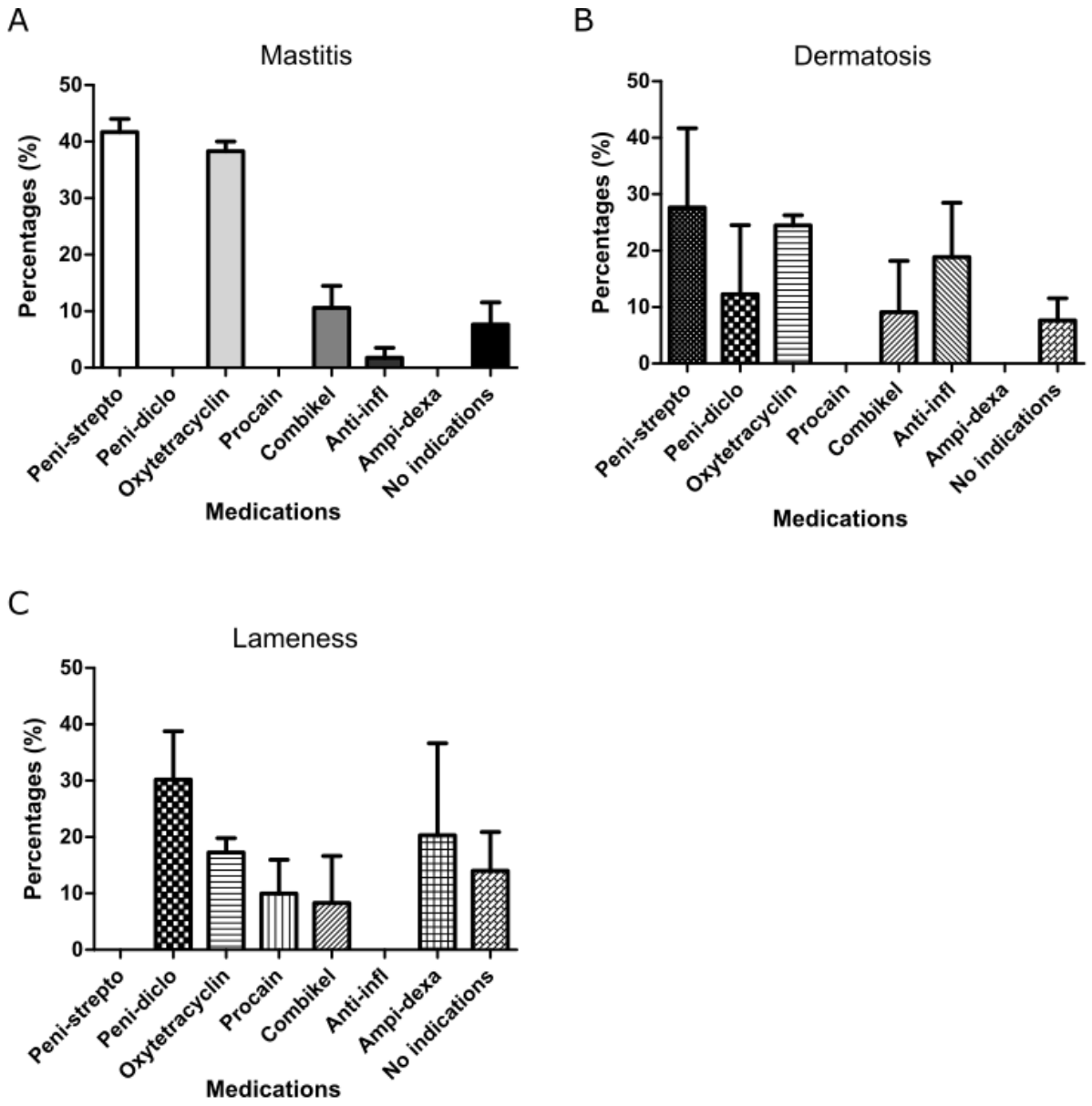

Figure 3: Frequencies of drugs utilized formastitis and dermatosis infection treatments in northern regions. A) mastitis, B) dermatosis and C) lameness. Peni-strepto=penicillin+streptomycin; Peni-diclo=penicillin+diclofenanc; Anti-infl=anti-inflammatory; Ampi-dexa=ampicillin+dexamethasone.

Oxytetracyclin and Vitamin Supplements Usage as Growth Factor in Livestock

Antibiotics are also used in veterinary medicine not only for bacterial infections but also to promote growth and enhance animal productivity [1]. For this last purpose antibiotics like oxytetracyclin were added into livestock foodstuffs. Likewise vitamins are by the same way supplemented animal diet in different northern regions. Both vitamins and oxytetracyclin food addition were made in quite similar level. Vitamin supplements level was slighlty high (40%) with no significant difference as compared to oxyetracyclin (25%) (P value = 0.6149)(figure 4A). Apart from Adamawa and Far North, North was the only region where oxytetracyclin

antibiotic was most frequently utilized (46 %) (figure 4B). Our results suggest less use of antibiotics as growth promoter in northern regions. Only one antibiotic were used as growth factor regardless of it frequency which was hight, but remain least than vitamins supplementation practice.

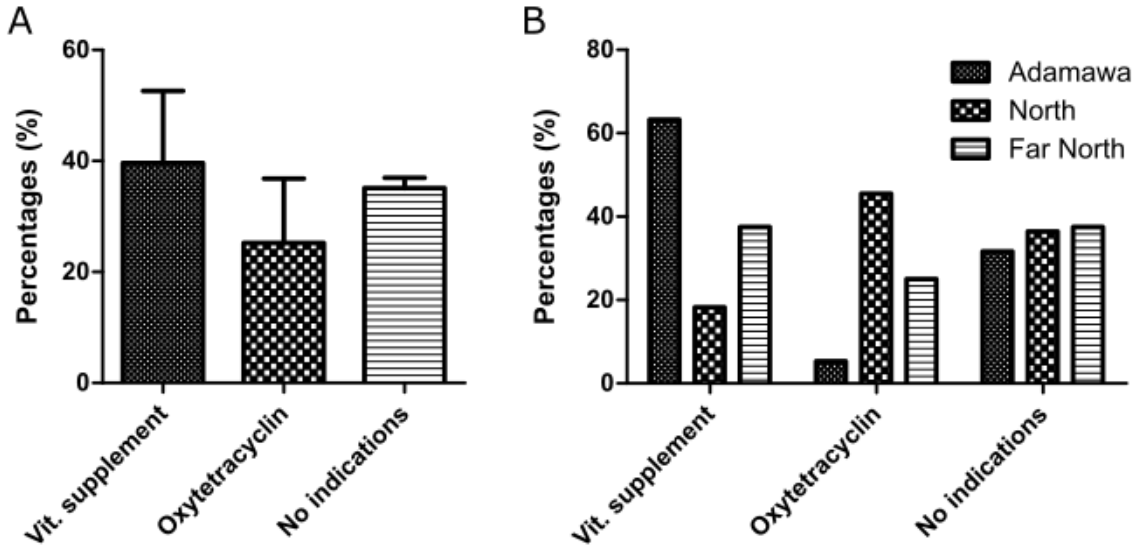

Figure 4: Vitamin and oxytetracyclin supplements livestock frequencies in northern regions (A) and in separately Adamawa, North and Far North regions (B).

IV. DISCUSSION

In the Northem regions of Cameroon, many laboratories lack materials to achieve antibiogram before treatment of patients. In this case β-lactamin family drugs were highly recommended for assumed cocci Gram positif bacteria and specifically *Staphylococci*the third generation of cephalosporin in particular. Other antimicrobials such as aminoglycosides, macrolides and quinolones were also prescribed for the same purpose. Among these antibiotics only few of them are used in our study to challenge *Staphylococcus aureus* infections without previous antibiogram and specy's identification. This practice is one of many others to contribute to resistant-strains emergence and dissemination within community and in hospital environment. This may have as consequences therapeutic failure due to potential resistant-strains penicillinase producer, extended hospitalization and substantial cost of treatment[15]. A part from penicillin first-line drugs used against *Staphylococcus* infections, health practitioners shifted towards broad spectrum antibiotics (cephalosporins) to minimize treatment failure in case of facing resistant-strains. Both first and second antibiotic prescription habits may contribute to antibacterial resistant-strains occurrence. These hypothesis are strengthened by the observation of hight prevalence of *Staphyloccus aureus*resistant strains in northern regions. 52% and 42% of *S. aureus* strains isolated from several samples were oxacillin- and cefoxitin-resistants respectively in this area. Amongst all the resistant-strains 84.5% antimicrobial strategy was beta-lactamase production (GAKE Bouba, unpublished data) in these three regions. In northern regions medical care-givers could be important actors of the most important public health issue of antibiotic resistance.

Many antibiotics are use for prevention and control of animal health conditions. The case of mastitis which is the most common infection associated with milk reduction production quality and it is treated by antibiotics for United-Statesdairy cow production. Mastitis is primary reason for antibiotic use in dairy cattle. Cephalosporin (53.2%) were often use for this purpose, followed by lincosamide (19.4%) and penicillins G/dihydroxystreptomycin [16]. In our study Penicillin-streptomycin combination (42%) and oxytetracyclin (38%) were highly recommended for mastitis. Investigation make in Sweden on subclinical mastitis dairy cow highlighted *Staphylococcus aureus* (19%), coagulase negative Staphylococcus (CNS, 16%), *Streptococcus dysgalactiae* (9%), *Streptococcus uberis* (8%), *Escherichia coli* (2.9%) and *Streptococcus* spp. (1.9%) identified pathogens. Same study showed 4% of *S. aureus* and 35% of CNS displayed resistance to penicillin G as observe in French study [17, 18]. Another study carried out in Rhône-Alpes France region identified mastitis bacterial species from cow milk. The firt four pathogens were *Streptococcus uberis*, *Escherichia coli*, coagulase-positive staphylococci (CPS) and CNS were the most frequently isolated species, with proportions of 22.1%, 16.0%, 15.8% and 9.5% respectively [18]. Other experiments performed on *Staphylococcus aureus*

isolated from bovine mastitis milk reported 19% resistance to tetracyclin and 14% resistance to penicillin, only one strain were multiresistant [19]. Canadian antimicrobial resistance test on mastitis dairy cattle *S. aureus* strains exhibited penicillin (35.4%), ampicillin (15.4%) and tetracyclin (8.8%) resistance [20].

Beside mastitis, lameness is one of the mostly cattle foot-related health issue handled by antibiotics. In our study antibiotics were not widely used for lambing treatment. Though ampicillin-dexamethason and penicillin-diclofenac mix were mainly use in Adamawa and North regions. In addition of beta-lactam family, other antibiotics were recommended for lameness problems and skin issues like dermatitis; tertacyclines, macrolides, sulfonamides and aminoglycosides in North-East Benin region [21]. These drugs are expected to target lameness related pathogens which are in majority as *Dichelobacter nodosus*, *Fusobacterium necrophorum*, *Treponema* spp., and *Actinomyces pyogenes* [22]. Apart from previous mentioned antibiotics, dairy cattle dermatitis could also be manage by salicylic acid which is also used for hyperkeratotic skin diseases in livestock [23]. Dermatisis pathogens associated are spirochetes like *Treponema phylotypes* then *Campylobacter jejuni*, actinomycetes, *Porphyromonas* spp., *Prevotella bivia*, alpha hemolytic *Streptococcus* spp., *E. coli*, and *Staphylococcus* spp [23, 24].

Mastitis, lameness and dermatitis, three differents cattle diseases are cured mostly by antibiotics. In our inquiry antibiotics were also used for these same purposes but this practice show minor interest due to small amount of antibiotic use in northern region compare to other studies in high-income countries[25, 26].

In our study antibiotics were less used as growth promoter for livestock. The only one antibiotic added in northern livestock food beside vitamins was oxytetracyclin in tiny proportion unless antibiotics recommended for some animal health issues. Antimicrobials misuse either for growth promotion or for controlling animal diseases may lead to emergence of antibiotic-resistant strains. It is important to avoid abusive consumption by limiting or eliminating antimicrobial from veterinary practice. Antibiotic ban in animal industry has no significant consequence on production. In absence of antibiotic food supply, poultry and Pork yield dicrease just for 2% in africa, america and asian/pacific developping countries [4]. Antibiotics restriction in livestock subsequently led to lessen cow milk production by 0.4% within 4 years in developping country as US, which represent 356 million kilograms [27]. This has negative economic impact on dairy production annual cost[27, 28].

Antimicrobials use in livestock both for food supplement or for infectious diseases treatment is promising in northern region of Cameroon. Nevertheless, it is important to establish monitoring program in this region and all over the country to restrict abusive antibiotic use. Antibiotic alternatives like vaccine, hygiene improvement, endolysins, hydrolases, bacteriophages and immune modulators for disease prevention may also be introduce in farming. Probiotics, prebiotics, phytochemicals and organic acids may be use as antibiotics alternative for growth promotion [29].

V. CONCLUSION

We carried out cross sectional study in northern regions to evaluate antibiotics comsumption frequencies in human an veterinary medicines. Antibacterials were widely use in human for cocci gram positif and *Staphylococci* in this area. In our study animal mastitis, dermatitis and lameness were handle by antimicrobials in livestock. Like for human diseases, in this study animal health problems previously mentioned were mostly cured by large amount of antimicrobials. This practice may have as consequence antimicrobial-resistance and specifically antibiotic-resistance which is important public health issue worldwide. It is thus important to roll out supervision program in Adamawa, North and Far North northern Cameroon regions to avoid antibiotic-resistant strains emergence.

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