Advances in Social Science, Education and Humanities Research (ASSEHR), volume 98
1st International Conference Postgraduate School Universitas Airlangga:
Implementation of Climate Change Agreement to Meet Sustainable Development Goals (ICPSUAS 2017)

Antimicrobial usage surveillance of cattle in Indonesia to address Antimicrobial resistance

Havan Yusuf[1], Theera Rukkwamsuk[1], Syafrison Idris[2], Mathilde Paul[3]
[1]InterRisk Program, Faculty of Veterinary Medicine, Kasetsart University, Chatuchak, Bangkok, 10903 THAILAND
E-mail : havanyusuf@yahoo.com
[2]Directorat General of Livestock and Animal Health Services, Ministry of Agriculture, Jakarta, 12550 INDONESIA
[3]National Polytechnic Institute of Toulouse, Toulouse, 31029 FRANCE

***Abstract*-- Antibiotics for animals are used for treating infections, preventions, and growth promoters. However, these practice resulting the emergence of resistant bacteria and the widespread of AMR strains. The objective of this study is to create a baseline information of AMU for cattle in Indonesia by using iSIKHNAS. Materials for this study consist of antibiotic treatment data in iSIKHNAS from 2014 to 2016, animal health officer data, and Index of animal drugs 2016. Data analysis consists of description of AMU in cattle, syndromes associated with AMU, identification of the actors, and VCIA's analysis. There are 70498 treatments for cattle. They are increased from 2014 to 2016. Monthly treatment patterns are increased from September to December. Oxytetracyclin is the most common active molecule used in the treatment with 60.99%. Bacterial disease are treated by antibiotic only on 9.39% of the treatments and most of antibiotics are used for non bacterial disease such as viral and parasitic disease. 30.49% of antibiotic treatment are provided by veterinarians with 699 persons and 67.57% by paravets with 1497 persons. Animal health officer shows good result for defining diagnosis from clinical signs. The problem occurs when the antibiotic is chosen for non-therapeutic applications. Tetracycline was the most common class of antibiotic . At around 61.96% to 99.56% of antibiotics that used for cattle is classified as VCIA. AMU has been commonly used to treat non bacterial disease. It is because the lack of knowledge and limited number of veterinarian.**

Keywords : AMU, surveillance, cattle

I. INTRODUCTION

Antimicrobials have been widely used in livestock sector for treatment, prevention, growth promoters, and to increase the feed efficiency. However, recently antimicrobial usage (AMU) practice in animal resulting the emergence of resistant bacteria and the widespread of antimicrobial resistance (AMR) strains [1–3]. The efficacy of antibiotic treatment is on the wane as a result of the emergence and dissemination of AMR. Despite the need to combat AMR, the discovery of new antibacterial drugs has waned in recent years [4,5]. As a result, OIE developed Veterinary Critically Important Antibiotics (VCIA), the antibiotic class that identified as essential against specific infections and there is a lack of sufficient therapeutic alternative [6].

II. OBJECTIVES

Following this situation, surveillance of AMU has been widely recommended internationally in recent decades and data collection promoted in all sectors (human medicine, veterinary medicine and agriculture) [7–9]. iSIKHNAS (Indonesia's new integrated animal health information system) is a surveillance based on farmer reporting system that support reporting of disease, animal population, treatment of animals etc [10]. By analyzing the data treatment in the iSIKHNAS, the objectives of this study is to create a baseline information about antimicrobial usage of cattle in Indonesia.

III. METHODS

A. Data Extraction

Materials for this study consist of the date treatment for cattle, the officer data in the iSIKHNAS, and Index of animal drugs in Indonesia on 2016. Data from the treatment sub compartment was extracted by all year, all location, and all differential diagnoses. Data was filtered for year 2014 to 2016 and for cattle species only. The AMU data has several columns, it consists of (i) Case ID, (ii) Date, (iii) Province, city, district, village, (iv) Antibiotics (commercial), (v) Dosages (vi) number of animals treated, (vii) Signs, (viii) Diagnosis, and (ix) Officer. Several columns have been added to AMU data: (x) Active molecule, (xi) Number of active molecule, (xii) Class of antibiotics, (xiii) number of antibitotic class (xiv) Disease category (bacterial, viral, parasitical, or others) and (xv) Background of the actors (vet, paravet, others).

B. Data Anaysis

1) Description of the antimicrobial usage in cattle

Data was analysed to determine the distribution by year, month, and the location by province to get the spatio-temporal pattern. The most commonly used antimicrobials by the commercial name and the active molecule were analyzed with the dosages used in the treatment.

2) Syndromes associated with antimicrobial usage

Analysis was done by listed each differential diagnosis from each treatment. One diagnosis has one

to several signs, thus every sign appeared from one treatment were listed to find out the most common diagnosis and signs. The correctness of treatment was analyzed by the diagnosis categories. The parameter diagnosis was categorized into single diagnosis and multiple diagnosis. The single diagnosis categorized as bacterial, viral, parasitic, several (caused by bacteria and other causes) and others (non bacterial). Multiple diagnosis was categorized as bacteria and without bacteria.

3) Identifying the actors

The analyses aim to determine which actors conducted the most antibiotic treatment and to count the personnel of animal health officer in Indonesia. Actors knowledge and correctness of the treatment was analyzed by disease category distribution.

4) VCIA analysis

The antibiotics that categorized as a Veterinary Critically Important Antimicrobial Agents (VCIA) by OIE are Aminoglycosides, Amphenicols, the 3rd and 4th Cephalosporins generations, Macrolides, Penicilins, Floroquinolones, Sulfonamides, and Tetracyclines. The VCIA analysis was to determine the precentage of the VCIA antibitotic used in the treatment. We also analyzed the actors distribution by VCIA.

IV. RESULT

The total number of antibiotic treatment data for cattle was 70498. The total data by year increased from 2014 to 2016. There are 2937, 22856, and 44705 treatments, respectively. Monthly antibiotic treatments distribution fluctuate over the months, however the pattern increases from September to December. There are 333 antibiotics by commercial name, most of the antibiotics compose of single active molecule (236). It is followed by a combination of two active molecule (95) and three active molecules (2). There are 75 different formulas by active molecule composition, single molecule is the most common with 43 formulas. It is followed by combination of two molecules with 31 formulas and three molecules with 2 formulas. Most of the treatments use single molecule on 49327 (69.97%). It is followed with two molecules on 17801 (25.25%) and three molecules on 3370 (4.78%) treatments, respectively.

Vet-Oxy LA and Vet-Oxy SB is the most commonly used antibiotic by commercial name for 11991 (17.01%) and 10476 (15.40%) of the treatment, followed by Colibact Inj. for 6061 (8.6%), Medoxy L for 4238 (6.01%), Colibact bolus for 3479 (4.93%), and Sulfa strong for 3216 (4.56%) of treatments. These five antibiotics out of 333 commercial antibiotic represent 55.97% of the treatment. Oxytetracyclin is the most common active molecule used in the treatment with 60.99% (Table 1). East Java has the highest number of treatment with 20567 (29.17%) and higest number of cattle population (28,87% of national population (Table 2). Antibiotic treatments are mostly administered by injection on 63211 (89.66%) treatments. It is followed by bolus on 3782 (5.36%), gram on 2915 (4.13%), and other dosages on 590 (0.84%) of the treatments.

TABLE 1. Active molecule distribution

Active molecule	Total	%
Oxytetracycline	42994	60.99
Sulfadiazine and trimethoprim	11149	15.81
Penicillin and streptomycin	4875	6.92
Sulfadiazinesodium. sulfadimidinesodium and sulfamerazinesodium	3216	4.56
Enrofloxacin	1353	1.92
Amoxycillin	1132	1.61
Sulfadoxine and trimethoprim	1057	1.50
Others	4722	6.7

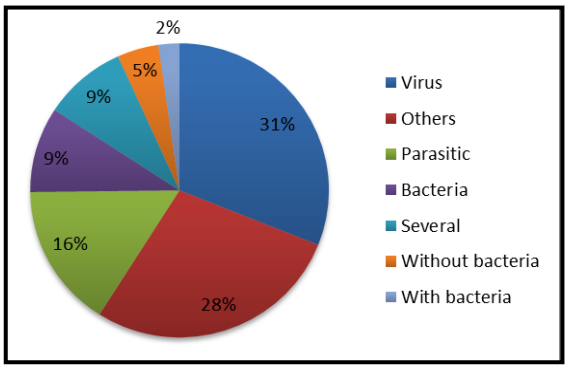
The syndromic analysis result for diagnosis shows that 178 diagnosis with bovine ephemeral fever is the most common disease appear on 19156 (27.17%). It is followed by helminthiasis on 6285 (8.92%), retained placenta on 4796 (6.8%), enteritis on 3963 (5.62%) and miasis on 3849 (5.46%) treatments, respectively. Signs analysis shows there are 179 signs with fever as the most common sign appear on 18198 (13.89%) treatments. It is followed by anorexia on 15076 (11.51%), diarrhea on 12646 (9.65%), lameness on 9110 (6.95%), emaciation on 5746 (4.39%), and weakness on 5373 (4.1%) treatments, respectively. The result of disease category distribution shows that most of the antibiotic treatment is used for viral disease on 21893 (31.05%) while bacterial disease is only for 6622 (9.39%) of the treatments (Fig 1).

TABLE 2. Cattle population and AB treatment in cattle

Class	Total	%
Tetracyclines	43684	61,96
Sulfonamides	16176	22,95
Penicillin aminoglycosides	5039	7,15
Penicillin	2474	3,51
Fluoroquinolones	1746	2,48
Others	455	0,65

**Pop : Population, T : Treatment*

Fig 1. Disease category distribution



The actors analysis shows that 30.49% of treatments are provided by veterinarians. Paravets has the higher precentage with 67.57%. There are 2277 persons conduct antibiotic treatments, most of them are paravets (1497) and veterinarians (699) (table 3). Disease category analysis for actors shows that from 21498 diagnosis made by the veterinarian consists of 33.64% viral disease, while bacteria is diagnosed for 11.31%. Similiar to the diagnosis made by paravets, from 47636 diagnosis out of of 33.64% are viral disease and bacteria is diagnosed for 8.6% (Table 4).

TABLE 3. Background of actors

Actors	T	T (%)	P	P (%)
Paravet	47636	67.57	1497	65.74
Veterinarian	21498	30.49	699	30.70
Inseminator	913	1.30	35	1.54
Others	451	0.64	46	2.02
Total	***70498***		***2277***	

**T : Treatment, P : Personnel*

TABLE 4. Disease category distribution by actors

Disease Category	P %	V %
Virus	30.17	33.64
Others	29.77	23.50
Parasitic	17.74	11.02
Bacteria	8.60	11.31
Several	8.23	10.80
Without bacteria	3.58	6.63
With bacteria	1.91	3.10

**P: Paravet, V: Veterinarian*

Antibiotic class analysis shows that most of the antibiotic consist of single class with 15 different class used for 65114 (92.36%) of treatments. There are 12 formula that compose of combination of two class and used for 5384 (7.64%) of the treatments. Tetracycline is the most common class used on 43684 (61.69%) followed by sulfonamides on 16176 (22.95%) of the treatments (Table 5). 99.56% of antibiotic used for cattle in Indonesia composed of antibiotic class classified as VCIA. The non VCIA antibiotics consist of lincosamides, polypeptides, quionolones, and 1st generation of chepalosporins.

Table 5. Antibitiotic class distribution

Province	Pop	Pop (%)	T	T (%)
Jawa Timur	4799365	28.87	20567	29.17
Nusa Tenggara Barat	1100743	6.62	7654	10.86
Jawa Tengah	1819883	10.95	6714	9.52
Sulawesi Selatan	1355467	8.15	5482	7.78
Jambi	149157	0.90	5310	7.53
Sumatera Utara	684495	4.12	2986	4.24
Lampung	661208	3.98	2502	3.55
Jawa Barat	556132	3.34	2450	3.48
Aceh	600818	3.61	2304	3.27
Gorontalo	202953	1.22	2227	3.16
Riau	238965	1.44	2188	3.10
Others (22 provinces)	4457217	26.81	10114	14.35
Total	**16626403**		**70498**	

V. DISCUSSION

Treatment data from 2014 to 2016 considered to be sufficient for valid analysis with modifications on data acquisition in order to develop more information. Data from 2013 was removed because the number was too low and data from 2017 was removed as it was incomplete. Indonesia has 33 provinces across thousands island, the introduction of iSIKHNAS requires a lot of times, on the contrary trainers are limited. As the development of iSIKHNAS requires numeruous and continuous training, total treatment data were low in the begining but it showed a progress as data keep increasing by year.

Monthly antibiotic treatment shows that during rainy seasons the disease pattern increased. Recent studies suggest that immune systems are weakened during winter (rainy in Indonesia) and by harsh weather conditions in ways that could affect their ability to defend against infectious disease [11]. As antibiotics are used not only for bacterial disease, the increase of disease infections will be followed by the increase of AMU. It is a controversial practice involves antimicrobials used in non-therapeutic applications such as prophylaxis, metaphylaxis, and growth promotion [12]. Out of 333 commercial antibiotics and several antibiotic can not be found in Index of animal drugs 2016 developed by DGLAHS. It means that the antibiotic is not registered. This situation supposed to be an important issue that need to be solved in the near future. Supportive data such as antibiotic formula, active molecule, composition, antibiotic production is important to be analysed, especially relates to the usage of antimicrobial.

East Java is the province with the highest cattle population and antibiotic treatment. East Java located in Java Island, the most developed island with the highly supported infrastructure for animal health. It has 84 animal health centre with 110 veterinarians and 74 paravets [13]. Nusa Tenggara Barat is the second largest province with the highest antibiotic treatment (10.86%). Even though it has only 6.62% of cattle population [14]. Nusa Tenggara has been a source of cattle for another province in recent year. In the last five years Nusa Tenggara Barat has 10.02% of population growth, 8% of cows growth, and 5% decrease of calf death and the good economic value of cattle farm [15].

According to Act No. 18/2009 on Livestock and Animal Health, veterinary and paravet are the only officer who has the permission to conduct antibiotic treatment [16]. Most of antibiotic treatment is conducted by paravet (63.47%) and followed by veterinarian (32.52%). Paravets in Indonesia come from various educational background such as veterinary vocational program, livestock sceince, livestock vocational high school, or people from others background (regular high school, inseminator, or vaccinator) who received a training to be a paravets.

The syndromic analysis result shows that BEF was the most common diagnosis appear with the most clinical sign appear, such as, fever, anorexia, lameness, emaciation, and weakness. BEF infection occurs in mild to severe clinical signs, such as, a fever, salivation, ocular and nasal discharge, recumbency, muscle stiffness, lameness and anorexia [17]. Animal health officer in Indonesia shows a good correlation to define the diagnoisis based on the clinical sign. However, the disease category analysis for actors shows that antibiotic commonly used for virus, parasitic, and other non bacterial disease. In addition, the bacterial disease has diagnosed in low precentage. Disease diagnosis relies on a combination of farmers' knowledge and the availability of diagnostic tools. In treating animal, the empirical-based knowledge is more often being implemented rather than the concurrent epidemiological and clinical factors. The treatment also rarely involves laboratory testing confirming the presence of bacterial infection. The availability of the service and the cost of the tests for the animals limit the usage. [18, 19].

Oxytetracyclin is the most common active molecule that has been used with tetracycline--as the most commonly class used. Tetracycline is critically important in the treatment of many bacterial and chlamydial diseases in a wide range of animal species and commonly used due to their low cost [1]. In Indonesia, drugs are stocked from beginning of the year. As tetracycline is cheap, easy to find, and a long acting antibiotic, the veterinary services prefer to stock tetracycline with limited number of alternative antibiotic. The resistance rates of tetracyclines are very high, as it is observed from pigs and poultry in China and Taiwan. Thus, Indonesia are in critical moment to change the policy of the use of tetracycline.

99.56% of antibiotic that used for cattle in Indonesia is contained of antibiotic that classified as VCIA. According to the OIE, VCIA is meant for serious animal disease. When it compounds within the class, it is identified as essential against specific infections and used as the last option [6]. Increasing the number of alternative antibiotic can be one of the solution, however the creation of new antibiotics are limited in recent years. In a recent article, the IDSA reports that only a single new antibiotic has been approved by FDA since 2010, and few new drugs are in the pipeline. The resistance for approving new antibiotics because of the incidence of MDR pathogens is increasing, as well as the low returns on investments [20]. This result indicates that Indonesia requires a better government control and regulation towards the use of antibiotic especially for antibiotic with high number of usage in recent years that classified as VCIA.

Important findings from iSIKHNAS antibiotic treatment data analysis are: 1. the AMU is commonly used to treat non bacterial disease; 2. Most of the treatment is done by paravets, it refers to the problem of knowledge and limited number of veterinarian; 3. The 90.93% of antibiotic is classified as VCIA. However this study also has several limitations, first this study only covers the Java Island as the most developed island in this country, so it does not represent the circumstances of the remote islands. Second, consistency of the report also limited our study to go further on the frequency of treatments. Third, information on the exact population is missing as the number of animals sometimes do not consistent with the quantity of antibiotic distribution (i.e. thousands of bolus and 4L antibiotics is not only for one herd). Thus, we can recommend the policy maker to create a regulation and law enforcement for AMU in cattle and to improve the coverage and consistency of iSIKHNAS report.

Acknowledgements

This study is supported by InterRisk Master Program, Faculty of Veternary Medicine, Kasetsart University. Many thanks are goes to Directorate General of Livestock and Animal Health Services, Ministry of Agriculture, Republic of Indonesia for provided the internship and iSIKHNAS data.

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