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Antimicrobials use pattern under organized and unorganized dairy production conditions in southern India

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ABSTRACT

The aim of this study was to estimate the antimicrobial use pattern against various clinical conditions under organized and unorganized dairy production conditions in selected areas of Tamil Nadu and Karnataka. Four organized dairy farms and one veterinary teaching hospital were surveyed covering Krishnagiri and Kolar districts of Tamil Nadu and Karnataka (India), respectively. The data were collected from practicing veterinarians (104) through questionnaires and in farms through treatment records. Milk samples (100) were also qualitatively screened for antibiotic residues in these farms. Mastitis and other udder health related problems were the most common (34%) followed by gastro intestinal tract (GIT) (20%) and postpartum uterine infections (PUI: 20%) in organized dairy farms. Overall, penicillins and its combinations (40%) and tetracyclines (33%) group of antibiotics were mostly used for treatment of above clinical conditions. About 13% of the milk samples were qualitatively positive for antibiotic residues in organized farms. Veterinarians rated mastitis (22%) followed by PUI (15%), respiratory disorders (14%) and GIT problems (12%) as the most common reasons for administrating antibiotics in field conditions, based on Garrett's ranking method. Penicillins, cephalosporins and tetracycline (36%) group of antibiotics were the most commonly prescribed for all clinical conditions. In the case of clinical mastitis, 20% veterinarians preferred cephalosporins group followed by penicillins and its combination (18%). It is concluded that mastitis is the most common reason for antibiotic usage in dairy animals and thus, an effective mastitis management programs are required to reduce the antimicrobial consumption.

Keywords: Antimicrobials, Dairy India, Mastitis, Milk antibiotic residues, Veterinarians

Antimicrobials usage in domestic animals has potential impact on public and environmental health issues through development of antimicrobials resistant (AMR) bacteria. Besides, antimicrobial residues also affect milk processing industries through interference with cultures. The association between increased antibiotic use and AMR development has been documented in human and veterinary medicines (Grave *et al*. 1999). A strong correlation between consumption of eight classes of antibiotics and prevalence of AMR *E. coli* in cattle is also reported by Van Boeckel *et al.* (2015). Antibiotics consumption data at regional or national levels in dairy animals are an important prerequisite for an understanding of AMR problems (European Commission, 2011). The existing surveillance programs on veterinary antimicrobials consumption in European Union (European Surveillance of Veterinary Antimicrobial Consumption: ESVAC, 2016) and in USA (The US Food and Drug Administration: FDA, 2016) are some of the examples for such implementation. The EU report revealed that tetracyclines and penicillins group of antibiotics were the most commonly sold antibiotics for food animals during 2013 (EMA, 2015). However, in majority of the low- or middle-income countries including India, systematic and reliable data on veterinary antimicrobial consumption or use pattern are not available and no regulatory framework available for the use of antimicrobials in livestock reared for domestic consumption. Van Boeckel *et al.* (2015) reported that India is the fourth largest consumer of antimicrobials in food animal's production after China, United States, and Brazil during 2010, based on indirect estimation through animal census and thus this study has many limitations.

Various methods have been explored in veterinary medicines to collect antimicrobials use data including through mailed questionnaires, surveillance of on-farm treatment records, sales records from pharmaceuticals and pharmacies, residues levels in food of animal's origin and collection of discarded drug packets in dairy farms (Redding 2014) and many of these methods are not practiced in developing countries including India. Understanding the present antibiotics use pattern is essential for promoting the judicious use of veterinary antibiotics, a key strategy to

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reduce AMR. Antibiotic consumption data will also provide status of drug use or misuse, public health risks associated with dairy industry, magnitude of disease problems and needful control strategies to improve farming practices (Sawant *et al*. 2005). Accordingly, the aim of this study was to estimate the antibiotic use pattern against various clinical conditions in dairy animals maintained under organized and unorganized production conditions in southern India.

MATERIALS AND METHODS

Estimation of antimicrobial use under organized dairy production conditions: The incidence of various clinical conditions and antibiotic usage patterns were estimated using treatment records (5 to 10 years data) maintained at 4 selected organized dairy farms and in a teaching veterinary hospital (1-year data from large animal clinic). Farm one maintained both indigenous and crossbred cows, while other farms maintained only Holstein Friesian (HF) and Jersey crossbred cows. The animal identification number, date of treatment, type of clinical conditions and major class of antibiotics used were collected from records. We observed about 2,916 treatments against 3,072 clinical conditions across the farms and hospital. Of which about 2,392 clinical conditions were considered for evaluation of treatments pattern. Animals diagnosed with other minor clinical conditions and not treated with antibiotics were not considered for evaluation of treatment pattern. During the study period, we also collected individual animal milk samples (farm 1:34, farm 2: 23; farm 3: 14 and farm 4: 23 samples; total: 94) and pooled samples from milk cans (two each from farm 2, 3 and 4) of these farms and screened (qualitatively) for antibiotic residues using commercially available microbial drug residues analysis kits (M/s Neugen Diagnostics India Pvt. Ltd., Hyderabad). The principle of this kit is spore germination-based assay using *B. stearothermophilus* 953 as indicator organism against b-lactams, sulphonamides, aminoglycosides, tetracyclines, macrolides and miscellaneous group of antibiotics.

Estimation of antimicrobial use under unorganized dairy production conditions by practicing veterinarians: Veterinarians from Krishnagiri and Kolar districts of Tamil Nadu and Karnataka states (India), respectively were participated in this study (n=104). The questionnaire developed for this study was adapted from previous studies (McEwen *et al.* 1991, Zwald *et al*. 2004, Sawant *et al*. 2005, Cattaneo *et al*. 2009, Redding *et al*. 2014) with suitable modification. The questionnaires contained 46 questions, about incidence and antibiotics usage pattern against various clinical conditions in dairy animals with particular emphasis on mastitis management, knowledge of antibiotic and its public health consequences. The questionnaire was pre-tested with veterinarians working outside the study area, having similar characteristic that of study population. The pre-tested questionnaire was self-administered to the respondents during monthly meeting of veterinarians.

Statistical analysis: The data were analyzed by simple descriptive statistical methods using Microsoft excel software and results were expressed in frequencies and percentages. The veterinarians were asked to rank the various clinical conditions and group of antibiotics usage and Garrett's ranking technique was used to analyze these ranking based questions. These orders of merit were transformed into units of scores by using the following formula.

$$\text{Per cent position} = \frac{100\,(R_{ij} - 0.5)}{N_j}$$

where R_{ij} = Rank given for the ith drug by jth respondent
N_j = Number of drugs ranked by jth respondent.

The percent position is converted into scores by referring to the table given by Garrett and Woodworth (1969). Then for each factor the scores of the individual respondents were added together and divided by the total number of respondents for whom scores were added. These mean scores for all the clinical conditions and drugs were arranged in descending order and the most common clinical conditions and drugs were identified through the ranks assigned.

RESULTS AND DISCUSSION

Antimicrobial use under organized dairy production conditions: The data collected from treatment records across the farms and hospital revealed that mastitis and other udder health related problems followed by GIT problems and postpartum uterine infections (PUI) are the common clinical conditions for antimicrobials use in dairy animals (Table 1). However, the occurrence of various health disorders varied across the farms. For example, PUI in farm 1, GIT problems in farm 2, mastitis and other udder health related disorders in farm 3 and 4 and fever of unknown origin in veterinary teaching hospital were the most commonly recorded indication for antimicrobial use. The results of overall antibiotic usage pattern revealed that penicillins and its combination and tetracyclines group of antibiotics were mostly used for treatment of all clinical conditions (Table 2). Similar to the trend of various health disorders occurrence, the antibiotic usage pattern, even for particular clinical condition was also found be different among the farms. It indicated that the prescribing pattern of the antibiotics varied among the farms and hospital. The differential prescription behavior among the veterinarians were reported in EU countries due to animal production system, availability of drugs, price of drugs and general situation regards to various clinical conditions (ESVAC, 2013). In addition, maintenance of different breeds, herd size and management practices in these farms could also be a reason for different prescription behavior among the veterinarians (Sawant *et al*. 2005; Redding *et al*. 2014). Overall about 86% of total antibiotic use was against mastitis, GIT, PUI and foot problems. Of which, mastitis and GIT problems were most frequently treated with antibiotics, while foot problem and PUI were less frequently treated with antibiotics (Table 3). Penicillin and its combinations were the most commonly

Table 1. Incidence of various clinical conditions in dairy animals maintained in organized farms

Clinical condition	Farm 1	Farm 2	Farm 3	Farm 4	Hospital	Total
Mastitis and other udder related problems	263 (23%)	133 (18%)	264 (55%)	273 (43%)	31 (28%)	964 (31%)
Foot problems	188 (17%)	72 (10%)	28 (6%)	–	–	288 (9%)
Postpartum uterine infections	305 (27%)	108 (15%)	44 (9%)	106 (17%)	7 (6%)	570 (19%)
Wound	109 (10%)	72 (10%)	72 (15%)	46 (7%)	17 (15%)	316 (10%)
GIT problems	123 (11%)	299 (42%)	27 (6%)	105 (17%)	16 (14%)	570 (19%)
Fever of unknown origin	133 (12%)	13 (2%)	45 (9%)	99 (16%)	36 (33%)	326 (11%)
*Other conditions	10 (1%)	22 (3%)	2	–	4 (4%)	38 (1%)
Total No. of treatment	1131	719	482	629	111	3072

Values are number of treatments against each clinical condition and its percentages. *Other clinical condition includes dullness, tail operation, swelling near neck, recumbency, hard cervix, calving difficulties, abscess, abortion, etc. GIT, gastro-intestinal tract.

Table 2. Antibiotic use pattern against various clinical conditions in organized dairy farms

Antibiotic class	Farm 1	Farm 2	Farm 3	Farm 4	Hospital	Overall
Penicillins and its combinations	368 (38%)	250 (35%)	264 (55%)	237 (38%)	53 (48%)	1172 (40%)
Aminoglycosides	42 (4%)	78 (11%)	77 (16%)	75 (12%)	6 (6%)	279 (10%)
Tetracyclines	419 (43%)	117 (16%)	82 (17%)	310 (49%)	40 (36%)	968 (33%)
Fluroquinolones	0	137 (19%)	44 (9%)	2	1	185 (7%)
Sulfonamides and its combinations	146 (15%)	105 (15%)	14 (3%)	5 (1%)	2 (2%)	272 (9%)
*Other antibiotics	–	32 (4%)	–	–	8 (8%)	40 (1%)
Total No. of treatment	975	719	482	629	111	2916

Values are frequency of treatments by using various classes of antibiotics against all clinical conditions and its percentages. *Other antibiotics include cephalosporins, chloramphenicol, clindamycin, etc.

used drug for mastitis and foot problems, sulfonamide for the treatment of GIT and tetracycline for PUI. Several researchers reported that the mastitis is the most common reasons for antibiotic usage as also observed in our study (Bartlett *et al*. 2001; Pol and Ruegg 2007). Mastitis is the most common indication and treatment with benzyl penicillin is the most common practice in Sweden (Sverige 2014). Other studies also reported that β-lactams antibiotics are the most commonly used drug for treatment of mastitis (Sato *et al*. 2005; Sawant *et al*. 2005). In USA, mastitis was found to be most commonly treated disease followed by lameness, reproductive and GIT problems (USDA 2008) as also observed in our study. We also reported that penicillins and their combinations was the most commonly used antibiotic for clinical mastitis in Indian dairy animals (Manimaran *et al*. 2014). We found that supportive therapy such as non-steroidal anti-inflammatory drugs, vitamins preparations, antiseptic solutions, haemocoagulase preparations, etc. were frequently used for foot problem, PUI and mastitis management. Non-antibiotic preparations for mastitis affected animals are reported by several researchers (Zwald *et al.* 2004; Pol and Ruegg 2007) and indeed, the efficacy of vitamins and anti-inflammatory drugs in mastitis affected cows was also reported by Pol and Ruegg (2007).

Presence of antibiotic residues in 13% of individual and

Table 3. Treatment pattern against major clinical conditions in organized dairy farms and veterinary hospital

Antibiotic class	Mastitis	GIT	Foot problems	PUI	Total
Penicillins and its combinations	631 (65%)	1	149 (52%)	70 (13%)	851 (37%)
Aminoglycosides	112 (11%)	64 (11%)	1	14 (2%)	191 (8%)
Tetracyclines	87 (9%)	163 (29%)	37 (13%)	294 (52%)	581 (24%)
Fluroquinolones	42 (4%)	60 (11%)	9 (3%)	19 (3%)	130 (5%)
Sulfonamides and its combinations	–	271 (48%)	–	–	271 (11%)
Other antibiotics*	20 (2%)	–	8 (3%)	–	28 (1%)
Total antibiotic use	892 (92%)	559 (99%)	204 (71%)	397 (70%)	2052 (86%)
Other drugs**	75 (8%)	11 (1%)	82 (29%)	172 (30%)	340 (14%)
Total No. of treatment	967	570	286	569	2392

GIT, gastro-intestinal tract problems; PUI, postpartum uterine infections. *Other antibiotics include cephalosporins, chloramphenicol, clindamycin etc. **Other drugs includes Non-Steroidal Anti-Inflammatory Drugs (NSAIDs: Meloxicam), Antiparasitic drugs (Dectomax, Ivermectin), Vitamins preparations (Tribivet), Antiseptic solutions (Wokadine), Haemocoagulase preparations (Batropase and Stardrim), etc.

pooled milk samples further confirms the antibiotic usage in these organized farms. Several researchers reported that mastitis is one of the most important risk factors for violation of antibiotics residues in milk as also observed in our study (McEwen *et al*. 1991; Mellenburger 1998).

Antimicrobial use under unorganized dairy production conditions by practicing veterinarians: The analysis of data collected from practicing veterinarians using Garrett's ranking method revealed that the mastitis and other udder health problems and PUI were the common reasons for antibiotic usage in lactating dairy animals under unorganized field conditions. Veterinarian revealed that penicillin and its combinations, cephalosporins and tetracycline were the most commonly used antibiotic for treatment of all clinical conditions in dairy animals. Veterinarian prescribed mostly cephalosporins and penicillin group of antibiotics for clinical mastitis, cephalosporins for PUI and fluroquinolones for respiratory tract diseases. De Briyne *et al.* (2014) reported that mastitis, respiratory disease, diarrhea and locomotor problems as the most important reasons for antibiotics use in EU dairy cattle. They also reported that penicillins, cephalosporins and tetracyclines were commonly used drugs for mastitis and PUI as observed in our study. Obritzhauser *et al.* (2016) also reported that udder diseases, respiratory tract diseases and foot diseases were most common indications for antimicrobial use in Australian dairy cattle. Saini *et al*. (2012) reported that cephalosporins, penicillins and tetracyclines were the most commonly used drugs in Canadian dairy farms. In contrast to organized dairy farms, more usage of cephalosporins under unorganized dairy production conditions is cause for concern as most of the countries are reducing or avoiding the usage of higher generation and human importance cephalosporins in dairy animals (Kuipers *et al.* 2016). Therefore, further studies on the kind of cephalosporins used under field conditions are required.

Mastitis management practices by practicing field veterinarians: About 95% of the field veterinarians used clinical signs as major criteria for diagnosis and for evaluation of treatment response in mastitis affected animals and 72% of the veterinarian perceived satisfaction over treatment response. About 85% of the veterinarians preferred the combined routes of drugs administration (i.e. both intramammary (IMM) and parental), rather than IMM (2%) or parenteral routes alone (13%) for the treatment of mastitis while, majority (61%) of them treated mastitis cases for 2–3 days of duration. For IMM therapy, veterinarians were mostly preferred penicillins (70%) than cephalosporins (25%), while the reverse was true for the parenteral route of therapy. In USA, cephapirin is the most commonly used drug followed by penicillins group against mastitis (USDA, 2008).

In the present study, about 58% veterinarians changed the antibiotics during treatment of single episode of clinical mastitis due to lack of immediate response to administered drug (66%) rather than cost (12%) and other reasons (22%). Pol and Ruegg (2007) also reported frequent changes of IMM antibiotics due to treatment failure and cost of the drugs. About 50% of the veterinarians felt that antibiotics are inevitable for mastitis management and 80% of the veterinarians increased the dose or duration in severe cases of mastitis indicated the extra-lable use of antibiotics for mastitis. Although 60% of the veterinarians used ethno veterinary medicines (EVM) for treatment of mastitis, about 51% veterinarians perceived that EVM alone had little efficacy in mastitis affected animals and 19% felt that EVM can replace the antibiotics requirements for mastitis management (data not presented).

Veterinarian's belief, drug selection, communication needs and their awareness about antimicrobials: About 64% of the veterinarians believed that there was a misuse of antibiotics due to the quacks or farmers themselves and only 30% farmer follows withdrawal period under field conditions. However, about 82% of the veterinarians advised farmers to follow the withdrawal period or discard the milk of antibiotic treated animals. About 75% of the veterinarians believed that they called by farmers for treatment, at end stage of diseases rather than immediately after diagnosis (25%). About 91% veterinarians believed that AMR problems were being present under field conditions, at least in few cases. Irrespective of clinical conditions, veterinarians reported that they selected the antibiotics on the basis of personal experience (82%) rather than laboratory diagnosis. They also revealed that clinical conditions (48%) followed by cost (33%) and availability (12%) were the major criteria for antibiotic selection under field conditions (data not presented) as also reported by Postma *et al.* (2016) and De Briyne *et al.* (2013) in EU. About 76% veterinarians revealed that they did not have any reference materials for antibiotic residues and its withdrawal period related information and they reported printed materials as a preferred method of communication. Cattaneo *et al.* (2009) and Sawant *et al.* (2005) also reported similar findings of veterinarian's belief and communication needs. About 82% of the veterinarians did not maintain separate treatment registers for their private practices. About 68–92% veterinarians had awareness about Food Safety and Standards Authority of India (FSSAI), withdrawal period, antibiotic residues and antimicrobial resistance.

Antimicrobial usage data generated in this study will be useful to understand the drug use against various diseases in dairy animals and develop strategies to improve farming practices. Mastitis and other udder health related problems were the most common reason for antimicrobials use such as penicillins, cephalosporins and aminoglycosides both under organized and unorganized field conditions. Hence an effective mastitis management programs are required to reduce these antimicrobials use and to improve milk quality in dairy animals in the study area.

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