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Review Article

Emergence of colistin resistance in extended-spectrum beta lactamase producing *Enterobacteriaceae* isolated from food animals and its public health implication: A review

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ABSTRACT

Antimicrobial resistance as a result of emergence of extended-spectrum beta lactamase producing *Enterobacteriaceae* is a major health problem of human and animal that requires an intensive global attention. The production of beta lactamase enzymes remains as one of the major factors contributing to the development of resistance to beta lactams. These enzymes hydrolyze the beta lactam ring of the antibiotic and render it ineffective. Extended-spectrum beta lactamase producing bacteria have the ability to develop resistance to a number of antibiotics including the carbapenem and other third generation cephalosporins. In addition, the recent emergence and dissemination of the colistin resistance determinants *mcr*-1, *mcr*-2 and *mcr*-3 poses a serious threat to colistin as a drug of last resort in human medicine. In this review, we utilized words such as "colistin resistance and *Escherichia coli*", "*Klebsiella* and colistin resistance", "colistin resistance and *Salmonella*" as well as "detection of *mcr*-1 genes in *Salmonella* and *E. coli*". The extended-spectrum beta lactamase producing bacteria under *Enterobacteriaceae* that are resistant to colistin possess the ability to be transferred resistant determinants to other susceptible cells at a higher frequency. In this paper, the role of manure from food animals and how air travel contributes to the dissemination of *mcr*-1 haboring bacteria, resistance determinants and other metabolites that constitute a public health problem was also reviewed. It is concluded that these pathogens have significant consequences to the control of infection and plays key roles in treatment failure with colistin.

KEYWORDS

Antimicrobial resistance; Colistin; Emergence; Extented-spectrum; *mcr*-1

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INTRODUCTION

The emergence of multiple resistance Gram-negative bacteria that are resistant to colistin and other clinically relevant antibiotics having the potentials of shifting towards extensive drug resitance (XDR) and/or pan-drug resistance (PDR) is increasing largely worldwide (McGann et al., 2016; Yu et al., 2016; Liu et al., 2016; Olaitan et al., 2016; Moudgil et al., 2017). Antimicrobial resistance is one of the most important and serious threat to human and animal health in the 21st century. This has necessitated deliberate effort on the part of stake holders such as United States Centers for Disease Control and Prevention (CDC) and the World Health Organization (WHO) to recognize and quantify the magnitude of the threat (Moudgil, et al., 2017). Additionally, this catastrophe has been compounded by the fact that some countries do not have a good policy on the use of antibiotics in humans, as well as the frequent use of antibiotics in animal production (Liu et al., 2016; Torpdahl et al., 2017).

Regrettably, the last five decades saw, a significant decline in the discovery and development of new and novel antibiotics and a marked increase in bacterial strains resistant to the already available antibiotics (Torpdahl et al., 2017). These has greatly lead to increased concerns among stakeholders worldwide in order to come up with a strategy that will ensure the use of appropriate antibiotics for the treatment of multiple drug resistant Gram-negative bacteria most especially *Klebsiella pneumoniae*, *Pseudomonas aeruginosa* and *Acinetobacter baumannii* (Kempf et al., 2013; Liu et al., 2016). The spread of these resistant strains on a global scale poses a significant public health problem. This is because, it narrows down the cache of antibiotics both in quantity and in quality. It also creates a gap between antimicrobial resistance and development of antibiotics.

Colistin is a polypeptide antibiotics with wide spectrum of activity against Gram-negative bacteria especially those belonging to the *Enterobacteriaceae* family. Studies have shown that the most widely used polymyxin includes Polymyxin B and E, where colistin is classified under Polymyxin E (Skov and Monnet, 2016; Liu et al., 2016). These two classes of polymyxin even though share comparable biological activity, differ from each other by only one amino acid. Bacteria develop resistance to polymyxin by modifying the lipid A which leads to reduced susceptibility to Polymyxin (Kempf and Chauvin, 2016). Until recently, the mechanism of polymyxin resistance was observed to be chromosomally mediated, and involves the alteration of the two component systems which included, *pmr*AB, *pho*PQ, and in the case of *K. pneumoniae* a negative regulator *mgr*B. Thus, utilizing moieties such as phosphoethanolamine or 4-amino-4-arabinose to modify lipid A. Alternatively, in rare cases a complete loss of lipopolysaccharide is observed (Kempf et a., 2013). However, plasmid-mediated *mcr*-1 has been reported as one of the determinants of resistance to colistin and this plasmid gene can be transferred from cell to cell (Monaco et al., 2014; Liu et al., 2016). Hence, increasing our understanding to its spread and the consequence of frequent and indiscriminate use of colistin in human and veterinary medicine. Additionally, this finding further validate the role of horizontal gene transfer in the global spread of strains of *E. coli* and other extended beta lactamase producing bacteria harboring the *mcr*-1 and *mcr*-2 plasmid genes conferring resistance to colistin.

The use of colistin in humans, since its introduction in the 1950s, is restricted to the treatment of topical infection due to toxicity associated with systemic administration. Interestingly, 60 years later, Colistin is still being used as the drug of last resort for the treatment of multiple drug resistant Gram negative bacteria such as *E. coli, K. pneumoniae, A. baumannii and P. auroginosa* (Catry et al., 2015). This scenario creates a significant public health challenge with the emergence of strains that are not only resistant to colistin but, are capable of transmitting those resistance plasmid to other susceptible groups of bacteria (Liu et al., 2016). Additionally, increased resistance to this antibiotics is compounded by the frequent and in some cases indiscriminate use of colistin in Veterinary medicine for the treatment and prevention of gastrointestinal infections associated with intensive animal husbandry (Kempf et al., 2013). Initial report showed that in spite of the intensive use of this drug in veterinary medicine, there is no clear evidence to support resistance development to colistin. However, recent studies have provided evidence to the isolation of Gram-negative bacteria from animals that are resistant to colistin (Liu et al., 2016; Skov and Monnet, 2016). The authors also reported the carriage of *mcr*-1 a gene responsible for the development of resistance to colistin in *E. coli* strains isolated from 15% (78/523) raw meat samples and 21% (166/804) animals samples collected from 2011-2014 and 1% (/161322) samples from infected patients admitted to the hospital. In 2016, Solheim et al. (2016) also reported the occurrence of an *E. coli* strain carrying the *mcr*-1 gene isolated from 4951 *E. coli* isolates collected from 2006 to 2015. The authors also reported that the *E. coli* strain was isolated from diarrheic patient who travelled to India in

2014. Consequently, the isolate was also observed to possess the ability to transfer resistance *mcr*-1 gene to a susceptible strain. Hence, indicating the possible role of horizontal transfer of resistance determinants in the global dissemination of colistin resistance determinants as well as Gram-negative strains resistant to colistin. In another study, Xavier et al. (2016) reported the occurrence of a novel plasmid-mediated colistin resistance determinants *mcr*-2 from *E. coli* isolated from pigs in Belgium. In the same study, the authors also higher occurrence of mcr-2 plasmid genes (11/53) than mcr-1 (7/53).

Over the years, there is an increasing interest into the epidemiology of resistance to colistin in bacteria. The problems associated with the diffusion of colistin in solid agar medium has been previously reported (Tan and Ng, 2007). The European Committee on Antimicrobial Susceptibility Testing (EUCAST) recommended an accurate method for the determination of Minimum Inhibitory Concentration (MIC). However, a number of studies have shown that in *Salmonella*, resistance is based on serotypes. For example, *Salmonella enterica* serovar *Enteritidis* and *Salmonella enterica* serovar *Dublin* which are classified as the O-group (1, 9, and 12) have reduced susceptibility to colistin than other serotypes. The authors argued that this was possible because the O-antigen (surface LPS of the cell) plays a role in colistin susceptibility, hence, suggesting that the MICs in *Salmonella* should be performed at the level of serovar (Agersø et al., 2012). Manifestation of genetic variability described above can lead to under reporting of the actual occurrence of Gram-negative bacteria resistant to colistin, most especially in developing countries where there are no available and accurate diagnostic tools. This review article focused on the emergence of colistin resistance in extended-spectrum beta lactamase producing *Enterobacteriaceae* isolated from food animals and its' public Health implications.

MATERIALS AND METHODS

This review employed the use of a collection of fully published articles on the "emergence of plasmid-mediated colistin resistance in extended beta lactamase producing bacteria isolated from food animals". Literature searched was conducted from 15th November, 2017 to 14th December, 2017. In addition, the articles were filtered to capture relevant articles on the topic, for example, searches were made based on relevant articles published between 2012 to 2014 and then 2015 to 2017. The articles were retrieved from Thompson Reuter's web of science, Springer, Lancet, Scopus, Science direct, PubMed and Wiley through google scholar and Mendeley literature search. The search was also conducted on other scientifically relevant database such as African Journal Online (AJOL), Agricultural online Access (AGRI-COLA), Directory of Open Access Journal, Global Public Health and Science.gov. Articles related to the subject of discussions were retrieved. We utilized words and phrases such as colistin resistance and *E. coli*, *Klebsiella* and colistin resistance, colistin resistance and *Salmonella* as well as "detection of *mcr*-1 genes in *Salmonella* and *E. coli*". A total of about 200 articles focusing on colistin resistance in *Enterobacteriaceae* producing *E. coli* were pooled. However, for the purpose of this review, only articles cited met the inclusion criteria based on year of publication, Journal of Publication and relevance to topic of discussion. All articles used in these review were appropriately cited in the bibliography using Mendeley referencing guide.

RESULTS AND DISCUSSION

The use of colistin in animals, and its public health implications

In practice, colistin is used in animal husbandry either as feed additives for prevention of gastrointestinal infections or for treatments. However, in some animal species, oral administration of colistin is associated with poor absorption and bioavailability in the gastrointestinal tract. This creates a problem where resistant bacteria, resistance genes and other metabolites associated with colistin resistance are excreted in the feces. Thus, contaminating the environment with resistant bacteria as well as resistance genes which can be transmitted to other susceptible strains. The cycle continues and humans can get infected when feces from these animals are use as compost manure or in countries where there is poor regulation with respect to animal management systems, the animals contaminate the water bodies with their feces. Thus increasing the spread of colistin resistance determinants as well as pathogenic bacteria resistant to colistin (Wei et al., 2011; Liu et al., 2016; Van den Meersche et al., 2016; Kabir et al., 2017).

A number of studies have tried to establish the relationship between the amount of colistin in manures collected from animals raised in intensive management system and the quantity of the drugs found in treated animals. For instance, Van den Meersche et al. (2016) reported that, there is a correlation between quantity of colistin derived from the manure of treated pigs and the

quantity of the antibiotics used in farms where those pigs were raised. In another study, a prevalence of 1.6% of *E. coli* strains resistant to colistin collected from liquid pig manure have been reported (Hölzel et al., 2010). Costa et al. (2010) also reported a 10% prevalence of colistin resistant *E. coli* strains that were isolated from the environment around pig farms. These findings showed how indiscriminate and sustained use of colistin in animal husbandry contribute to the spread and dissemination of colistin resistant bacteria as well as the determinants of colistin resistance. Thus, constituting a significant public health problem through the emergence of pathogenic resistant bacteria. Even though, the isolation *E. coli* strains from the environment carrying the *mcr*-1 and *mcr*-2 genes have not been reported, there is a great potential of its isolation in the near future (McGann et al., 2016). It is important to ensure the maintenance of effective surveillance strategy that will help nip in bud the onset of these menace.

For instance, using China as a case study, the determinant of colistin resistance was reported in a surveillance studies carried out between April, 2011 and November, 2014. The study involved samples collected from food animals and interestingly, this gene was found in commensal and not pathogenic *E. coli* strains. This indicated the implication of frequent and indiscriminate use of colistin as a prophylactic agent as well as in treatment. Furthermore, it creates a serious public health problem, since the isolates where collected from food animals. Thus facilitating easy transmission of these resistant strains to humans and resistance genes to other susceptible bacterial strains. In addition, the finding of the survey showed that 20.6% of the isolates harboring the *mcr*-1 genes were isolated from pigs, 14.9% from raw meats while 1.4% from patients admitted to the hospital during the study period (Liu et al., 2016).

The authors further argued that in 2014 alone, an estimated 56.7 million tonnes of pork meat was produced and since China is one of the largest producers of pig, it also translates having cope with about 618 billion kg of manure each year. In addition, the country have to contend with about 29,000-87,000 tons of antibiotics residues in animal waste every year (Larson, 2015; Hao et al., 2015; Liu et al., 2016). Thus creating a favorable medium for widespread dissemination of colistin resistance determinants to other parts of the country and subsequently to other countries where China export meat and other meats product obtained from pork.

In many cases, the frequent and indiscriminate use of antibiotics is the major cause of the emergence of highly pathogenic resistant strains. However, studies have reported the isolation of *E. coli* strains resistant to colistin obtained from individuals without history of colistin usage (Olaitan et al., 2016). For example, in Laos Olaitan et al. (2015) reported the isolation of colistin resistant *E. coli* isolates from a boy without history of usage of colistin; however, the authors observed that the boy is the one feeding the family's pigs. Thus, suggesting the probable transmission of this pathogens from animals to humans via horizontal transfer of colistin resistance determinants. In Nepal, high rate of colistin resistance have also been reported from *Campylobacter* isolates obtained from pig carcasses (Ghimire et al., 2014). In another study, Figueiredo et al. (2015) reported a 7.2% prevalence of colistin resistance in *Salmonella* spp obtained from processed wine food. It is no news that *mcr*-1 genes are mostly isolated from *E. coli* strains collected from raw pig meat. However, high rate of resistance to colistin was also reported in other important food borne pathogens such as *Campylobacter* and *Salmonella*. Hence, creating major public health problems through increase in health care cost and prolonged hospital admission stay. Similarly, for the first time in humans, Olaitan et al. (2016) reported the occurrence of *Salmonella enterica* serotype *Newport* that is resistant to colistin. The authors further suggested that given the presence of factors predisposing to the transmission of resistance determinants, there is high potentials of isolating the organism in animals.

Even though previous studies have established the occurrence of *E. coli* and *Salmonella* strains harboring the *mcr*-1 gene from animals in Asia, Africa, North America, Europe and South America. There were however, reports that suggest that these pathogens actually harbored resistance genes long before they were first reported in 2015. For example, in a survey conducted by Shen et al. (2016) using isolates collected from 1970 to 2014 from chickens, showed that three *E. coli* isolates collected in the 1980s harbored the *mcr*-1 gene. Similarly, in another study conducted in Belgium using *E. coli* isolates collected from pigs from 2011 to 2012, the report showed that the isolates were also positive for the *mcr*-1. This is also consistent with other studies conducted in Germany in 2009 and France in 2011 where *mcr*-1 *E. coli* strains were isolated (Malhotra-Kumar et al., 2016; Falgenhauer et al., 2016; Perrin-Guyomard et al., 2016). The detection of bacterial strains harboring the *mcr*-1 and *mcr*-2 genes in several countries (**Table 1**), showed that almost every country is at risk of harboring bacterial strains harboring

the *mcr*-1 gene. Hence, there is need for proper surveillance of colistin resistance in bacteria obtained from food animals. This will go a long way in preventing the scourge of foodborne illnesses, reducing the length of hospital admission stay and cost of treatment with antibiotics.

The prevalence and epidemiology of colistin resistance

The major challenges of therapy in the 21st century due to limited treatment options occurs as a result of increase in the incidence of global antimicrobial resistance and the lack of the development of new antimicrobial agents (Doumith et al., 2016). This threat however, did not cause a reduction in the use of colistin as a drug of last resort for the treatment of severe infections caused by multiple drug resistant Gram-negative bacteria (Falagas et al., 2011). It is a well-established fact the resistance to colistin occured through point mutation, especially in genes that affect the synthesis of cell wall biosynthesis and lipid bilayer (Olaitan et al., 2014). However, the occurrence of plasmid-mediated colistin resistance determinants *mcr*-1 first in *E. coli* and then in *K. pneumoniae* obtained from raw meat, animals and human cases in the people republic of China **(Table 1)** showed the role of horizontal gene transfer in the dissemination of such resistance determinants. Colistin resistance development occured when the *mcr*-1 gene encodes a phosphoethanol-amine transferase and these results to reduced affinity to colistin (Liu et al., 2016).

Additionally, it was also observed that the presence of *mcr*-1 on a conjugative plasmid together with ISApl1 may facilitate the transmission of different plasmid back-bone between bacterial strains, genera and species. This scenario not only helps in the dissemination of resistance determinants, but has the potentials of transforming the XDR Gram-negative bacteria to PDR. The possible transmission of *E. coli* harboring *mcr*-1 from humans and animals in China has shown that these resistance determinants can be disseminated to other parts of the world. This also explains the occurrence of *mcr*-1 gene in South America, Asia, Africa and Europe (Arcilla et al., 2016; Doumith et al., 2016; Falgenhauer et al., 2016; Malhotra-Kumar et al., 2016; Suzuki et al., 2016; Torpdahl et al., 2017).

Research into the possible transmission of bacterial strains resistant to colistin from animals to humans is still at it infantile stage. This occurrence was observed despite the frequent and abundant utilization of this drugs in animal production and veterinary medicine for over 5 decades. Additionally, the problem was further compounded by the absence of adequate surveillance of colistin resistance in both human and Veterinary medicine. Even though, colistin resistance in animals is recently being recognized and described, a number of studies have actually reported increasing trends of resistance to colistin in pigs. For example, Boyen et al. (2010) reported the isolation of 10% porcine pathogenic *E. coli* in Belgium, while in Dutch, Timmerman et al. (2006) reported the isolation of *Salmonella* and *E. coli* strains that are susceptible to colistin. As interesting as the case maybe, other studies showed that in many European countries, the prevalence of bacteria belonging to the *Enterobacteriaceae* isolated from swine and poultry and that are resistant to colistin is very low (Kempf et al., 2013).

However, other studies showed that even though the emergence of multiple drug resistant bacteria in veal calves is of great concern to farmers, resistance to colistin in this production system is considered low and in some instance even absent (Di Labio et al., 2007). Similar case was also reported from *E. coli* strains isolated from poultry product, however, the occurrence of 2.1% colistin resistance from 328 isolates collected from broiler meat samples was reported (Lesho et al., 2013). While in Australia, the isolation of *Aeromonas* species resistant to colistin from clinical samples obtained from aquaculture is a common occurrence. A prevalence of 55.5% resistance to colistin was reported (Aravena-Román et al., 2012).

In Europe, PDR and XDR Klebsiella species have been reported as the most common causes of healthcare associated. In addition, the authors also reported the occurrence of bacterial strains resistant to colistin that are resistant to a number of other unrelated antimicrobial agents (Comandatore et al., 2013; Brink et al., 2013; Lesho et al., 2013). Furthermore, these strains have also been associated with high morbidity and mortality (Zarkotou et al., 2013; Catryn et al., 2015). Thus, indicating the stability of resistance plasmids conferring colistin resistance in this isolates. This further showed that even after withdrawal of these antibiotics, there is a probability of maintaining a sustainable resistance to colistin and where possible transmission to susceptible strains.

In China, the first isolation of *E. coli* strains isolated from chickens carrying *mcr*-1 gene was reported in the 1980s. However, first major outbreak was reported in 2009 and

Table 1: Occurrence of Colistin resistance spectrum in extended beta lactamase producing bacteria isolated from food animals and humans

S/N	Country	Sources of isolates	Bacterial	Method of determination	*mcr*	% Resistance	Reference
1	China	Feces, Pigs, poultry, dairy products	*E. coli*	MIC	*mcr*-1, *mcr*-2 *mcr*-3	33.3%, 11.7%, 12.9% and 0.2%	Liu et al. (2016), Shen et al. (2016), Yin et al. (2017)
2	Thailand	In patient	*K. Pneumoniae*	MIC-E test	*mcr*-1	14 isolates	Rolain et al. (2016)
3	Cambodia	Child	*E. coli*	-	*mcr*-1	1 isolate	Stoesser et al. (2016)
4	Vietnam	Pigs, chickens	*E. coli*	MIC	*mcr*-1	22.2%, 24.4%	Malhotra-Kumar et al. (2016), Nguyen et al. (2016)
5	Malaysia	Pigs, human	*E. coli*	Agar diffusion MIC	*mcr*-1	-	Liu et al. (2016), Petrillo et al. (2016), Yu et al. (2016)
6	Laos	Pigs and humans	*E. coli, K. pneumoniae*	MIC-E test and BMD	*mcr*-1	6.4%, 3.1%	Olaitan et al. (2014, 2016)
7	Japan	Cattle, poultry, pigs	*E. coli* and *Salmonella*	MIC-agar and BMD	*mcr*-1	1.0%	Han et al. (2002), Suzuki et al. (2016)
8	Nigeria	Inpatients	*K. pneumoniae*	MIC-E test	ND	1 isolate	Olaitan et al. (2015)
9	Algeria	Chicken	*E. coli*	MIC	*mcr*-1	2 isolates	Olaitan et al. (2016)
10	Egypt	Inpatient	*E. coli*	MIC_BMD	*mcr*-1	1 isolate	Elnahriry et al. (2016)
11	Kuwait	Inpatients	*Acinetobacter spp.*	MIC-Etest	-	12.0%	Al-Sweih et al. (2011)
12	Latin America	Inpatients	*E. coli*	MIC-Etest	*mcr*-1	9 isolates	Rapoport et al. (2016)
13	Switzerland	Inpatients	*E. coli*	MIC-BMD	*mcr*-1	2.6%	Bernasconi et al. (2016)
14	Italy	Inpatients	*E. coli*	MIC-BMD	*mcr*-1	8 isolates	Cannatelli et al. (2016)
15	Brazil	Inpatients	*E. coli*	MIC-Microscan system	*mcr*-1	1 isolate	Fernandes et al. (2016)
16	Germany	Pig , humans	*E. coli*	MIC	*mcr*-1	4 isolates	Falgenhauer et al. (2016)
17	France	Veal calve	*E. coli*	MIC	*mcr*-1	21% (106)	Haenni et al. (2016)
18	Denmark	Chicken	*E. coli*	MIC	*mcr*-1	6 isolates	Hasman et al. (2015)
19	UK	Pig	*E. coli*	MIC-agar dilution	*mcr*-1	43.1%,0.2%, 0.6%	Enne et al. (2008)
20	Belgium	Pig, veal calve	*E. coli*	MIC	*mcr*-1	12·4%	Malhotra-Kumar et al. (2016)

MIC=Minimum Inhibitory Concentration, BMD=Broth Microdilution, mcr-1=Determinant of colistin resistance, E. coli=Escherichia coli Pathogenic,

5 years later, the prevalence of *mcr*-1 isolates have increased to 28% in isolates collected from chicken meat and 30% in isolates collected in chickens (Hasman et al., 2015; Liu et al., 2016). The reported prevalence of *mcr*-1 positive *E. coli* isolates in Europe, Japan and Nigeria ranges from 0% to 30%. However, a prevalence of 0% to less than 1% colistin resistance was also reported in majority of European countries (Harisberger et al., 2011; de Jong et al., 2011; Shen et al., 2016).

Several report showed that the prevalence of *mcr*-1 positive *E. coli* isolates is higher in imported chicken than in locally bred chickens (Hasman et al., 2015). Furthermore, In Tunisia, *mcr*-1 positive *E. coli* isolate have been isolated in healthy birds. It is important to note that the prevalence of colistin resistance differ between bird species. For instance, a study conducted in 11 European countries using isolates collected from turkey and laying hens showed that 7.4% of the isolates collected from turkey were resistant to colistin, while less than 1% of the laying hens were resistant to colistin (Harisberger et al., 2011). This is in contrast to the findings of similar studies conducted in Japan, where the author reported 1.7% prevalence of colistin resistance among laying birds (Hasman et al., 2015; Olaitan et al., 2016; Yao et al., 2016). The prevalence of colistin resistance from *E. coli* isolates collected from companion animals such as Dogs and Horses in Europe ranges from 0%-0.6% (Olaitan et al., 2016).

In addition, the prevalence of colistin resistance in *E. coli* strains isolated from pigs ranges from 0-52.4%, while 0-30% prevalence was reported among *E. coli* strains collected from ruminants. Evidence of vertical transmission of colistin resistance from breeder flocks to progeny have been reported in Vietnam (Nguyen et al., 2016).

The prevalence of colistin resistance from *Salmonella* isolates collected from poultry have been reported. In Europe, Iran, Spain and India, several authors have reported that the prevalence of colistin resistance in *Salmonella* collected from poultry ranges from 0% to 100% (Boko et al., 2013; Ranjbar et al., 2013; Quesada et al., 2015). This is lower than the 0-21% prevalence of colistin resistance in *Salmonella* isolates collected from pigs, ruminants, and Boars in Europe, Italy, Brazil and japan (de Jong et al., 2011; Zottola et al., 2013; Matayoshi et al., 2015). The global distribution of colistin resistance in *mcr*-1 carrying *E. coli* and *K. pnuemonieae* collected from food animals and humans is described in **Table 1.**

CONCLUSION

The rate which antibiotics are losing their effectiveness due to the emergence of extended-spectrum beta lactamase producing *Enterobacteriaceae* poses a serious threat to human and animal health. This is because, emergence of antimicrobial resistance reduces treatment options, increase the length of hospital stay and cost of treatment of antibiotics. In food animals, colistin is frequently used as oral medication for prevention and treatment of gastrointestinal tract infection. This has led to the emergence of and dissemination of colistin resistance determinants on a global scale. There is need for careful monitoring of the usage of colistin in animal husbandry as well as seek for alternative antibiotics that is effective, less expensive and competitive with colistin in the treatment of gastrointestinal infection.

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CONFLICT OF INTEREST

The authors declare that there is no conflicting interest with regards to the publication of this manuscript.

AUTHORS' CONTRIBUTION

AAB and RC conceived and drafted the manuscript, whereas, LT and RC critically reviewed the manuscript.

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