Antibiotic Resistance Genes: An Emerging Environmental Pollutant

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Abstract Antibiotics are the most effective group of antimicrobial drugs used for humans and veterinary therapy, but it is a rising trouble for the modern healthcare. However, the maximum use of antibiotics may be introducing the emergence and development of antibiotic resistance bacteria (ARB) and antibiotic resistance genes (ARGs), which increase the dissemination of resistance bacteria and genes in clinical and nonclinical environments. Horizontal gene transfer (HGT) and mobile genetic elements like plasmids, transposons and integrons are facilitating the environmental dissemination of the ARGs. The main source of antibiotics spreading is the uncontrolled uses of antibiotics, are not only used for the human therapy but it is widely used for the agricultural and livestock farming purposes. ARBs and ARGs have been extensively detected in wastewater, agricultural soil, animal manure and hospital waste, so that they must be consider as environment pollutant as well and that can contaminate the natural environment. This chapter gives an overview on the impact of antibiotics and antibiotics resistance genes as an environmental pollutant in different environment.

Keywords Antibiotics · Antibiotics resistance bacteria · Antibiotics resistance genes · Horizontal gene transfer · Environment pollutant

Abbreviations

ARB	Antibiotic resistance bacteria
ARG	Antibiotic resistance gene
HGT	Horizontal gene transfer

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WWTP	Wastewater treatment plant
MRSA	Methicillin-resistant *Staphylococcus aureus*
LGT	Lateral gene transfer
MGE	Mobile genetic element
GC	Gene cassettes
IS	Insertion sequence
CI	Chromosomal integrons
MI	Mobile integrons

1 Introduction

Antibiotics introduced in medical science as a medicine to treat and reduced the infectious disease causality and it was a biggest medical revolution of the 20th century. Penicillin was isolated by Fleming (1929) and it was the first commonly used antibiotics. In World War II, it was significantly used and reduced the death cases caused by the bacterial infections (Quinn 2013). Most of the antibiotics were discovered and introduced in the medical market form mid to last of 20th century and these molecules are still in use.

A large number of studies have demonstrated that the widespread use of antibiotics to treat microbial infections in humans, animals and less commonly in crop plants. Many antibiotics are also used for to promote growth and increase the feed efficiency in animal. After use, the proliferation of antibiotics residues, ARBs and ARGs introduced in the environment. ARGs have been detected in surface water (Reinthaler et al. 2003), groundwater (Chee-Sanford et al. 2001), sediments (Pei et al. 2006; Storteboom et al. 2010a) and wetlands (Cummings et al. 2010). The use of antibiotics is increasing day by day and the development and dissemination of antibiotics resistance genes among both the clinical and environment bacteria will be a consider a universal threat to human, animal and environmental health in the 21st century.

The antibiotic resistance can contaminate the environment because environmental bacteria develop resistance against the antibiotics which are used in the treatment of human and veterinary (Allen et al. 2010; Baquero et al. 2008; Martinez 2008; Riesenfeld et al. 2004; Zhang et al. 2009). In recent time, lots of interest has been expressed to the role of environmental bacteria because Many ARGs carried by pathogenic bacteria are originated in environmental bacteria (Martinez 2008), and ARGs have been found everywhere in a large range of environments (Zhang et al. 2009). Human antibiotic contamination may play a vital role in the distribution of clinical antibiotic resistance (Martinez 2009b; Wright 2010).

The antibiotics use in Livestock operations are very much responsible to increases the ARBs in animal workers (Bertrand et al. 2006; Boerlin et al. 2001), meat processors (Borgen et al. 2000). Now day's animal manure is widely used in

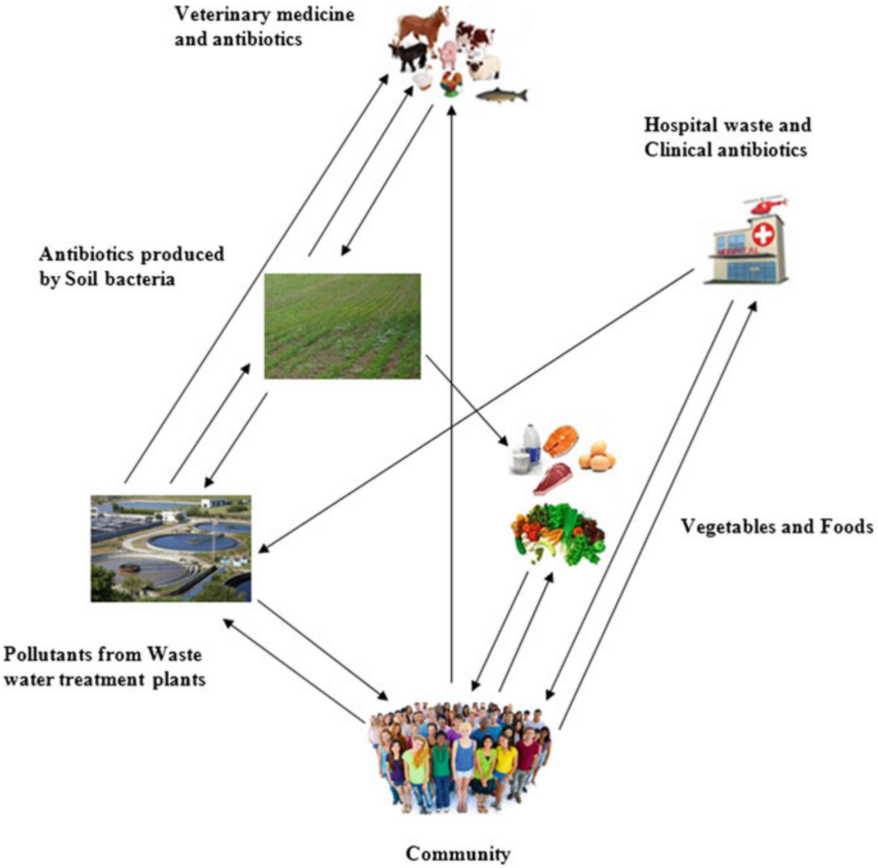

Fig. 1 Dissemination of antibiotic resistance bacteria and genes among different environmental conditions

agricultural fields and these antibiotic-treated animals are main source of antibiotics and antibiotic-resistant bacteria, and animal manure frequently increase the levels of antibiotics bacteria and genes in the soil. Dissemination of Antibiotic resistance bacteria and genes among different environmental conditions are presented in Fig. 1.

In the present chapter, we explore the dissemination of ARBs and ARGs in different environment like Wastewater Treatment Plants (WWTPs), Agro-ecosystems and Veterinary farming. Additionally, this chapter focuses on occurrence of ARBs and ARGs, because antibiotic resistance remains one of the major threats to public health.

2 Transmission of Antibiotic Resistance

Horizontal gene transfer (HGT) is mainly responsible for the transfer of genetic material between the bacteria (Davies 1997) and this process is also responsible for the transmission of antibiotics resistance among the pathogenic bacteria in worldwide (Levy and Marshall 2004). The main mechanisms of resistance gene transfer in a bacterium are plasmid transfer, transfer by viral delivery, and transfer of free DNA. The three mechanisms are responsible for facilitating the HGT are: Conjugation, transformation and transduction.

Transformation: Bacteria take up DNA from their environment.

Conjugation: Bacteria directly transfer genes to another cell.

Transduction: Bacteriophages (bacterial viruses) move genes from one cell to another.

The conjugation is a horizontal gene transfer process from donor cell bearing one or more conjugative plasmid to a plasmid free recipient cell through the construction of Conjugation Bridge (Lederberg and Tatum 1946). Conjugation could be seen to depend on the presence in the donor cell of a so-called fertility factor F, a relatively small autonomous DNA molecule. Bacteria can acquire antibiotic resistance genes from other bacteria in several ways and Conjugation is simple process which including genes encoding resistance to antibiotics (found on plasmids and transposons) from one bacterium to another.

Transformation involves the natural capability of uptake, integration, and functional expression of naked DNA such as plasmid or genome fragments from the environment and has the potential to transmit DNA between very distantly related organisms. Natural transformation is basically active uptake of free DNA by bacterial cell (Chen and Dubnau 2004; Dubnau 1999; Lorenz and Wackernagel 1994) also including human pathogens, such as *Acinetobacter* spp., *Haemophilus* spp. and *Neisseria* spp. Now it is very much clear that bacteria could exchange ARGs by using transformation and it has been responsible for the evolution of β-lactam resistant strains of *H. influenzae* and *N. gonorrhoeae*, as well as penicillin-resistant *S. Pneumonia* (Dowson et al. 1994; Saunders et al. 1986).

Transduction involves transfer of DNA from one bacterium into another mediated by bacteriophages (Fig. 2). There are two types of transduction method: (1) Generalized transduction (2) Specialized transduction. Through specialized or generalized transduction, bacteriophages can transfer genes that are advantageous to their microbial hosts and endorsing their own survival and distribution (Modi et al. 2013; Lacey 1973). Transduction is also responsible for the transfer of some ARGs among clinical strains of *Staphylococcus aureus*, (Lacey 1973, 1984) and occurs among bacteria in natural water systems (Miller 1998; Miller and Ripp 1998).

The bacteriophage mediated mobilization or transfer of ARGs has been recognized in various bacterial species like the transfer of tetracycline and gentamicin resistance between *enterococci* (Fard et al. 2011), β-lactamase genes *Escherichia coli* (Billard-Pomares et al. 2014) and *Salmonella* (Schmieger and Schicklmaier 1999); or the transfer of antibiotic resistance plasmids in MRSA (Varga et al. 2012)

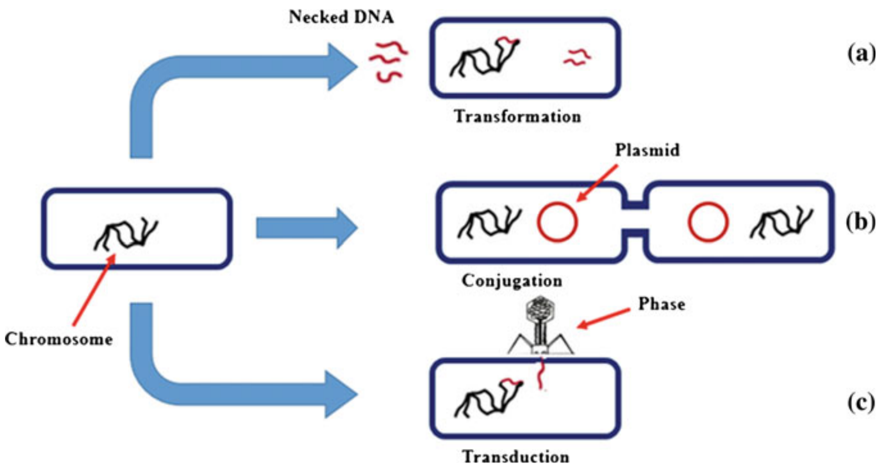

Fig. 2 Primary mechanism of Horizontal gene transfer in bacteria **a** Transformation: Necked DNA is taken up by the cell from surrounding environment **b** Conjugation: Transfer of conjugative plasmid through direct cell to cell link established by donor cell **c** Transduction: Bacteriophages move genetic materials from one cell to another by infection

but few studies have been reported that bacteriophage considered transfer genes between different bacterial communities (Fard et al. 2011; Jensen et al. 1998) and environment and play a major role in the dissemination of ARGs in microbial ecosystems.

3 Mobile Genetic Elements

Movement of foreign DNA within the genome or between bacterial cells is known as horizontal or lateral gene transfer (LGT), and the mobilization of DNA into the host bacterium is referred to as mobile genetic elements (MGEs) (Frost et al. 2005). Mobile genetic elements are a DNA segments which encode the enzymes and proteins that help in the movement of DNA. MGEs play a major role in bacterial evolution, infectious diseases, antibiotic resistance, bacterial symbioses, and biotransformation of xenobiotics and contribute very much to adaptation to new and changing ecological niches (Wiedenbeck and Cohan 2011). The three main processes transformation, conjugation and transduction are involved in the transfer of MGEs from one bacterium to another (Fig. 2). Intracellular mobility (DNA transfer within the genome) facilitated by transposons, gene cassettes, and integrons and Plasmids, bacteriophages, and conjugative resistance transposons can facilitate in the intercellular mobility (DNA transfer between the bacterial genome) (Bennet 2008).

Integrons are genetic assembly platforms that capable in the integration, assembly and expression of gene cassettes (Davies and Davies 2010; Su et al. 2006; Mazel 2006; Kovalevskaya 2002). Integrons are natural gene capture systems that are located on MGEs like transposons and plasmid and play a major role in the dissemination of resistance genes (Hall and Collis 1995; Rowe-Magnus and Mazel 2002; Rowe-Magnus et al. 2002). The functional integron platform consists of a gene (intI) that codes for an integrase catalyzes the incorporation of gene cassettes (GCs) by sit specific recombination and a proximal primary recombination sequence called an attI site. The integrase mediates recombination between the attI site and a secondary target called an attC site. Integrons are divided into two major groups: chromosomal integrons (CIs), and mobile integrons (MIs). CI is also known as Super integrons, located in the chromosome of hundreds of bacterial species and they can carry up to 200 cassettes that mainly encode proteins with unknown function but MIs are located on mobile genetic elements and contain a limited number of GCs, usually encoding antibiotic resistance determinants and promote their dissemination among particular Gram-negative bacterial pathogen. Recently Class-1 integrons introduced as potential targets for source tracking of ARGs from anthropogenic environments because they are generally extensively more abundant in anthropogenic sources than in pristine environments. The majority of integrons which share a pool of gene cassettes are encoded resistance to antibiotics and the mobile resistance integrons are highly abundant in environment because most of the antibiotics are used in clinical and agricultural practice. Resistance genes and integrons are present in floc and sewage sludge (Drudge et al. 2012; Zhang et al. 2011), and considerable quantities are released in reclaimed water (Wang et al. 2014) or directly into rivers (Graham et al. 2011; Koczura et al. 2012). Resistance genes and integrons are also disseminated in effluent from hospitals and in wastewater from tanneries (Stalder et al. 2013). Further, the use of animal wastes as manure introduces resistance genes and integrons into agricultural soils (Binh et al. 2009; Byrne-Bailey et al. 2009, 2011; Cheng et al. 2013). Antibiotic resistance genes and integrons are now viewed as significant environmental contaminants and as markers for tracing sources of pollution (Pruden et al. 2006; Storteboom et al. 2010a, b).

The bacterial plasmids move many bacterial genes from one bacterial cell to another and the process called horizontal gene transfer. Specifically, conjugative plasmids that is able to promote their own transfer and the transfer of other plasmids from one bacterial cell to another. Plasmids carry a considerable variety of genes, including those that present antibiotic resistance and resistance to a number of toxic heavy metals, such as mercury, cadmium and silver. A resistance plasmid can carry one or more antibiotic resistance genes. Many resistance plasmids are conjugative, that is they encode the functions necessary to promote cell-to-cell DNA transfer, particularly their own transfer. WWTPs have been recognized as a reservoir for ARB and ARGs, including plasmids encoding resistance to antibiotics (Tennstedt et al. 2005; Schluter et al. 2008; Moura et al. 2010; Allen et al. 2010). Antibiotic resistance plasmids can harbour genes that confer resistance to most if not all clinically significant antibiotic classes such as macrolides, tetracyclines, cephalosporins, fluoroquinolines, aminoglycosides and β-lactams (Bennett 2008; Martinez 2009a; Szczepanowski et al. 2009).

Transposons are also belonging to the mobile elements called transposable elements that includes small cryptic elements called insertion sequences (IS elements), transposons and transposing bacteriophages that facilitate the movement of DNA fragments from one location to another on bacterial chromosome and plasmid (McArthur 2006). Tansposons are well structured modular systems that have different classes and are widely distributed among bacterial populations conferring various antibiotic resistance phenotypes. There are many transposons that are strongly related to antibiotic resistance such as Tn5 and Tn10 which encode resistance to kanamycine and neomycine, and tetracycline, respectively (Berg and Berg 1983; Merlin et al. 2011) but the Tn21 family of transposons represents one of the largest and first recognized groups involved in the accumulation and dissemination of ARGs. The Tn21 confers resistance to streptomycin, spectinomycin, and sulfonamides.

4 Reservoirs of Antibiotic Resistance Genes

4.1 Wastewater Treatment Plants

Most of the studies prove that antibiotics resistance bacteria are present in the wastewater treatment plants and it is the main source of both ARBs and ARGs (Munir et al. 2011; Rizzo et al. 2013). Figure 3, shows the route of dissemination of ARGs and ARBs from WWTP into different environmental conditions. The waste water treatment plants are the reservoir and suppliers of antibiotic resistance genes and also hotspot for the horizontal gene transfer because WWTPs receive sewage and bacteria from various sources or different natural environments (Rizzo et al. 2013). Antibiotics can enter WWTPs through human excretion, farm animals and direct disposal of medical and industrial wastes and it is a serious threat to spread of resistance, may be pathogenic bacteria resistance pathogen and antibiotic resistance bacteria (Martinez 2009a). Basically untreated water, treated water and sludge are the main reservoir of the ARGs. Although most of the studies have reported that the quantities of ARGs in treated wastewater effluents are significantly higher than the surface water (Lachmayr et al. 2009; Rodriguez-Mozaz et al. 2015; Czekalski et al. 2014). During the treatment process in WWTPs some antibiotics are removed (Batt et al. 2006), but not all antibiotics are completely removed (Giger et al. 2003). For example, β-lactam and vancomycin genes have been found in natural environment in very low quantity but resistant bacteria and genes encoding resistance against certain β-lactam and vancomycine have been reported in WWTPs. Resistant and multi-resistant bacteria, such as *Escherichia coli*, *Pseudomonas aeruginosa*, *Acinetobacter* spp. and *Enterobacteriaceae* are present in many processes of WWTPs (Kümmerer 2009). One of the study (Tsai et al. 1998) shows that the

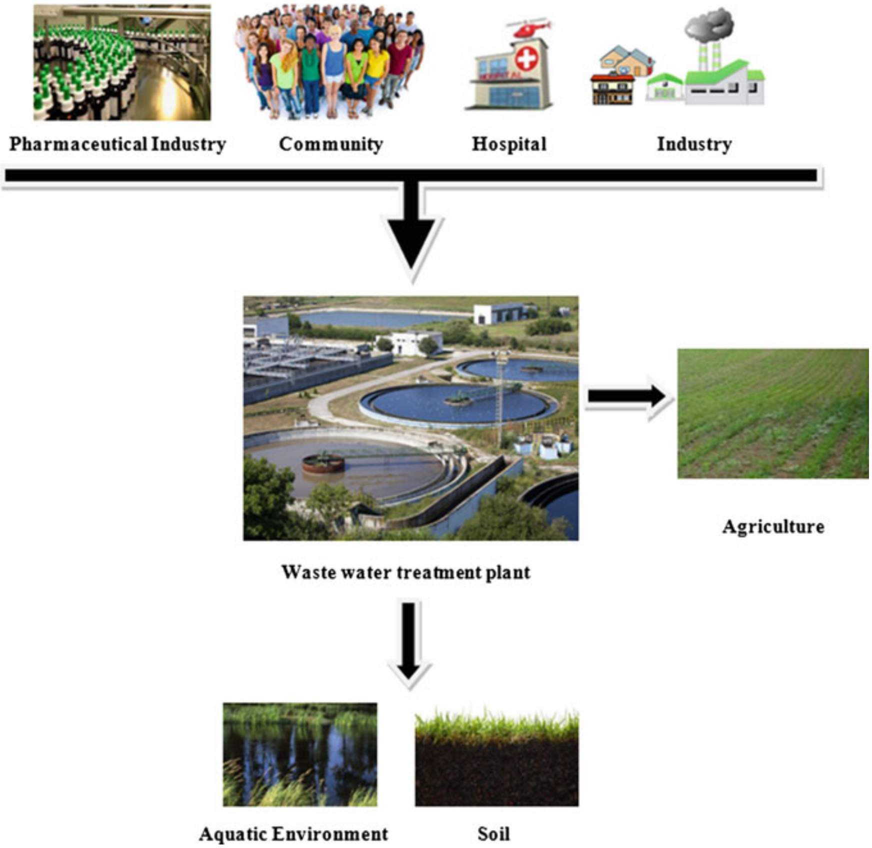

Fig. 3 The route of dissemination of ARGs and ARBs from WWTP into different environments

Salmonella species are very frequently appeared in activated sludge from hospital waste treatment facilities and it is a potential source of infectious organisms. Some recent studies have inspected the tetracycline resistance in activated sludge WWTPs (Guillaume et al. 2000; Auerbach et al. 2007; Kim et al. 2006; Al-Ahmad et al. 2009). The study (Guillaume et al. 2000) has occurred different tetracycline resistance determinants and one more study (da Costa et al. 2006) has investigated the presence of various multi-resistant enterococci in urban sewage and sludge in WWTPs in Portugal and showed that treatment procedure of these bacteria in wastewater treatment plants did not prevent dissemination to the environment. Another study showed that the blaTEM, qnrS, ermB, sul-I and tetW and vanA resistant genes have been detected in both the hospital effluents and in treated and without treated effluent of urban wastewater treatment plants (Narciso-da-Rocha et al. 2014; Rodriguez-Mozaz et al. 2015). The mobile genetic elements can promote the horizontal gene transfer and induce the occurrence of ARGs in different environmental compartments (Schwartz et al. 2003). The aforesaid studies are showing the importance to find out the efficient solutions for minimising antibiotic resistance spread. In this situation, disinfection process can be a best way to control the diffusion of antibiotic resistance into the environment, mostly in reuse of treated wastewater for agricultural purpose (Fatta-Kassinos et al. 2011; Ferro et al. 2015). Till now few works have been done regarding the effect of disinfection processes mainly chlorination and UV radiation, of ARGs removal (Guo et al. 2013; McKinney and Pruden 2012; Munir et al. 2011; Yuan et al. 2015; Zhuang et al. 2015).

4.2 Agricultural Soil

Soil is a large reservoir of microbial diversity and the majority of antimicrobial compounds used today in human and veterinary health care have been isolated from soil microorganisms.

Most of the antibiotics used in agriculture are given as growth-promoting and prophylactic agents, rather than to treat infection. In all over the world antibiotics are used between 60 and 80% of the total antibiotics production in animal husbandry (Silbergeld et al. 2008). These antibiotics are used as growth promoting agents and are frequently detected in animal manure. The animal manure is a main reservoir and source by which ARBs and ARGs first enter the environment. When soils are treated with animal manure, the antibiotic resistance bacteria carrying ARGs are introduced in the soil because manure enhanced the horizontal gene transfer process in which ARGs are transferred to soil bacteria (Jechalke et al. 2014). Anthropogenic activities can transfer ARB and ARGs from natural environments to soils is generally associated with horizontally transferred elements like class-1 integrons, while selective pressure that can also increase the abundance of native ARGs. The study has (Forsberg et al. 2012) strongly suggested that mobile genetic elements such as plasmids and integrons carry ARGs between soil and human microbiomes. Moreover, the physical properties of soil can also play an important role on the activity and stability of both antibiotics and ARGs in soil matrices.

One study quantifies four broad-spectrum β-lactam AR genes (blaTEM, blaSHV, blaOXA and blaCTX-M) and class-1 integron genes (int1) in soils from manured (M) versus inorganic fertilised (IF) fields and the ARGs levels were significantly higher in manure versus inorganic fertilizer in soils. This was supported by another study that investigated the integron gene cassette diversity in manure-amended field and compare with without manure treated filed, detected class-1 integrons harbouring the aminoglycoside resistance gene aadA in manure-amended soils but not in without manure treated soil. The aadA genes were also abundant in the manure, confirming that aadA gene localized on class-1 integrons are introduced via pig manure into agricultural soil (Binh et al. 2009). The aforesaid studies indicate that application of antibiotic-containing manures expands AR levels in amended soils.

Now days treated wastewater irrigation is progressively more popular in arid and semi-arid areas of the world, applied in agricultural sector but WWTPs encompass a huge collection of environmental and clinically relevant ARB and ARGs, which can be detected in influent, activated sludge and discharged effluent, potentially enhancing AR reservoirs in the downstream environments like river and lake. The wastewater biosolids contains high concentration of ARBs and ARGs are regularly applied to agricultural soil as fertilizers. The study (Negreanu et al. 2012) evaluated the long-term effects of treated wastewater irrigation on AR in agricultural soils, using standard culture-based isolation methods and culture-independent molecular analyses and the study indicated that ARB levels in the treated wastewater itself were significantly higher than those measured in the freshwater.

Using quantitative real-time PCR, (Knapp et al. 2010) showed a significant increase in the relative abundance of selected ARGs in archived soils from Holland from the 1940s when antibiotics were first used, to the present time. Over the past 15 years a huge number of antibiotics from a broad range of classes, including macrolides, lincosamides, sulfonamides, chloramphenicol, florfenicol, fluoroquinolones, tetracyclines have been detected in agroecosystems (Campagnolo et al. 2002; Hamscher et al. 2002; Kolpin et al. 2002; Halling-Sorensen et al. 2003; Aga et al. 2005; Batt et al. 2006; McKinney et al. 2010; Watanabe et al. 2010; Bartelt-Hunt et al. 2011; Pruden et al. 2012; Zhang et al. 2013). Although we have enough amounts of data generated on the occurrence of veterinary-use antibiotics in agroecosystems but our understanding of their overall distribution is still quite limited.

4.3 Livestock's Farming

The main interest regarding the use of antibiotics in animals are for various reasons, including disease treatment, prevention, control, and growth promotion/feed efficiency. The transmission of ARGs between farm animals, the wider environment and humans are resented in Fig. 4. Antibiotics are extensively used as a growth promoter in livestock farming and play a major role in the emerging public health crisis of antibiotic resistance (Preston 1987; Nagaraja and Chengappa 1998; Gaskins et al. 2002). ARBs related to livestock's can be transmitted to humans through the environment (Graham et al. 2009) and food products (Price et al. 2005) and to agricultural workers by direct contact (Smith et al. 2013). Although most of the antibiotics are used in agricultural purposes but relatively little interest has been paid to how antibiotic use in farm animals contributes to the overall problem of antibiotic resistance. In European countries, antibiotics are widely prohibited as growth promoters in animal husbandry (Singer et al. 2003; Kümmerer 2009; Cabello 2006) but in developing countries the situation is totally opposite because the demand of animal proteins are very high and the consumption of antimicrobials are very unregulated.

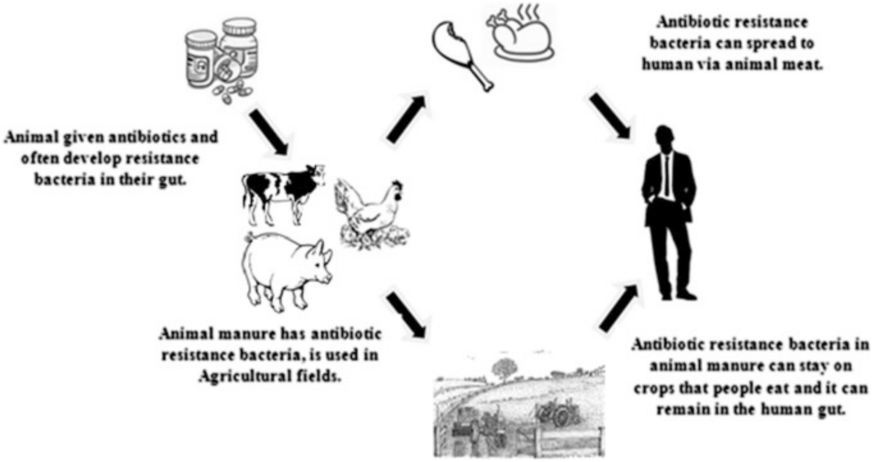

Fig. 4 Diagrammatic representation of transmission of ARGs between farm animals, the wider environment and humans

The workers who worked in Farm and slaughterhouse and those in close contact with them are directly at risk to infect with resistant bacteria through close contact with infected animals. Most of the studies have been proven that the transmission of antibiotic bacteria from animal to farm worker. The study (Levy et al. 1976) first reported the direct transfer of resistance bacteria form animal to farm worker, who got the same tetracycline resistant *E. coli* strain in the gut flora of chicken caretakers as in the chickens receiving tetracyclinelaced feed.

In boiler production gentamycin is commonly used antibiotic but it is not approved in United States as a growth promoter although it remains the most widely used antibiotics in boiler production (Luangtongkum et al. 2006). Some of the antibiotics resistant genes found in food bacteria have also been identified in humans, providing indirect evidence for transfer of antibiotic resistance genes by food handling or consumption. Most of the food-borne pathogens such as *Escherichia coli*, *Salmonella, Enterococcus* and *methicillin-resistant Staphylococcus aureus* (MRSA) are showing the homologous relationships between bacterial resistance genes in humans and farm animals and there is ample of evidence these pathogens can spread resistance genes between animal and people. The rise of antibiotic-resistant bacteria among farm animals and consumer meat and fish products has been well documented (Kümmerer 2009; Lee 2003; Zhao et al. 2003). Some of the antibiotic resistance genes identified in food bacteria have also been identified in humans, providing indirect evidence for transfer by food handling and/or consumption. Expert opinion suggests that global consumption of antimicrobials in animals is twice that of humans (Aarestrup 2012).

5 Impact of Antibiotic Resistance Genes on Human and Environmental Health

Antimicrobial resistance is a worldwide problem in human and livestock farming. The major risk factor involves to increase this situation is broadly use of antimicrobial compound that play a main role in the dissemination of resistant bacteria and resistance genes in animal and humans (Van de Bogaard and Stobberingh 2000). Most of the antibiotics are used for the prevention and curing of infections in human and animals as well as for promoting faster growth of livestock (Dolliver and Gupta 2008) and partially metabolized products are then discharged in sewage treatment plants or directly in water along the excreta. The intensive use of antibiotics in hospitals and agricultural cause the dissemination in aquatic and soil environments and with the help of selective pressure these compounds may affect the treatment of human disease (Thiele-Bruhn 2003; Segura et al. 2009).

The European Union banned the feeding of human related antibiotics to livestock for growth promotion but in after few years the ban was expanded to all antibiotics and related drugs. Similarly, many countries have restricted the use of antibiotics in animals those are still use in therapy of human infections but many developing countries are still using these drugs in very high amount. For example, the class of β-lactam antibiotics is widely used groups of antimicrobial in human and animals but the emergence and dissemination of ESBLs has caused a major concern in several countries and the utilization of quinolones for aquaculture has been banned in several countries, because those antibiotics can remain active in sediments for long periods and spreading the resistance against the quinolones. These infections have a great impact on public health due to an increased incidence of treatment failure and severity of disease.

The household waste and hospital effluents have been shown to be rich in resistance genes and affect the diversity of resistance bacteria because these wastes are discharge in wastewater (Czekalski et al. 2012; Thevenon et al. 2012; Vignesh et al. 2012; Tacão et al. 2012; Schwartz et al. 2003; Santoro et al. 2012). These contaminations in aquatic environments contribute to the spread of human pathogens along with the dissemination of antibiotic-resistant bacteria. The overexposure to antibiotics is leading to increasing levels of resistance in the human.

Antibiotic-resistant bacteria is not only found in pathogenic bacteria but also in the wildlife (environmental organisms of terrestrial and aquatic habitat) and these are very important to human health because of the increasing importance of some zoonotic species of the genera *Salmonella, Campylobacter*, *Listeria*, *Staphylococcus*, *Enterococcus and Escherichia*, which are known to exhibit high levels of acquired antibiotic resistance (de Jong et al. 2013; Garcia-Migura et al. 2014; Brooks et al. 2014).

Transfer of resistance genes from environmental bacteria to human pathogen is basically the main risk for the public health and *Escherichia coli* have been recognized as a major player in the dissemination of antibiotic resistance (Henriques et al. 2006; Zhao and Dang 2012). Freshwater environments are well-known systems for the distribution and evolution of antibiotic resistance (Baquero et al. 2008; Figueira et al. 2011; Tacão et al. 2014). Water bodies are sites of genetic exchange through horizontal gene transfer where environmental bacteria interact with microbes originated from humans and other animal sources. Aquatic ecosystems may become a threat to human health when they are affected by pollutants carrying resistant bacteria (Baquero et al. 2008).

6 Conclusion

The occurrence and dissemination of antibiotics resistance is a growing problem in different environments like clinical, veterinary, husbandry and agricultural that needs to be paid much more attention regarding to the major factor responsible for the origin and spread of such pollutants. The antibiotic resistance genes are now widely spread through the biosphere and affect the global microbiome because antibiotic contamination promotes the mobilization of resistance genes between the environments. Now it's time to pay more attention to these pollutants which are spread through different sources and active in the environment.

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