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REVIEW

Antimicrobial resistance dynamics and the one-health strategy: a review

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Abstract

Antimicrobial resistance is a global threat that kills at least 75,000 people every year worldwide and causes extended hospital stays. In the coming 10 years, antimicrobial resistance is projected to have huge health and economic burden on countries, and the scarcity of available antibiotics further worsens the situation. Antimicrobial resistance results mainly from indiscriminate antibiotic usage in humans, animals and agriculture, and from the rapid emergence and dissemination of resistant pathogens. This issue is challenging for antibiotic stewardship, strict regulations on antibiotics usage, large-scale surveillance and responsible public behavior. This demands international cooperation and integrated efforts under the 'one-health' strategy. Here, we review antimicrobial resistance and the one-health strategy. We discuss the historical issue of using antibiotics. We highlight the effectiveness of hygiene in livestock rearing, careful antibiotic usage and large-scale surveillance of animals, humans and environment domains. We present strategies for mitigation of antimicrobial resistance, exemplified by the successful ban of triclosan which induced a significant decline of resistant pathogens. We emphasize the benefits of the global antibiotic resistance partnership and of the one-health participation of stakeholders from public, healthcare professionals and government to mitigate antimicrobial resistance.

Keywords Antimicrobial resistance · One-health · Antibiotics and agriculture · Animal health · Horizontal gene transfer · Environmental surveillance

Abbreviations

qnr	Quinolone resistance gene
bla	Beta-lactamase gene
mec	Methicillin resistance gene
sul	Dihydropteroate synthase gene for sulfonamide resistance
UN-FAO	United Nations Food and Agricultural Organization
GARP	Global Antibiotic Resistance Partnership
INSAR-India	Indian Network for Surveillance of Antimicrobial Resistance-India
NARMS-USA	National Antimicrobial Resistance Monitoring System-USA
ESAC-EU	European Surveillance of Antimicrobial Consumption-EU
SASCM-SA	South African Society for Clinical Microbiology-South Africa
PAHO	Pan American Health Organization
EARS	Net European Resistance Surveillance Network
GLASS-WHO	Global Antimicrobial Resistance Surveillance System-WHO

Introduction

There have been many stages of discovery and development in the knowledge and status of antibiotics usage and menace of antimicrobial resistance. After the initial discovery of

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Penicillin in 1928, many new antibiotics were found through intense industrial research during 1950–1970. However, regulatory constraints, long development phase, accruing financial inputs dampened the pharmaceutical interest into new antibiotics and fewer antibiotics were developed after the mid-1980s (Spellberg and Gilbert 2014).

On the other hand, indiscriminate antibiotics usage led to pollution by antibiotics and/or their residues across all niches such as food, soil, aquatic water bodies and sewage (Shi et al. 2020). These antibiotics originate from hot spots such as hospitals, pharmaceutical units, agricultural setups and livestock farms. High antibiotic concentration is linked to antimicrobial resistance often through horizontal gene transfer of antibiotic resistance determinants such as genes, transposons, integrons in deadly pathogens such as *Acinetobacter baumannii* (Gillings 2013), (Rodgers et al. 2019). Many such microbes pass through overlapping ecological niches between humans, animals and environment, thereby gaining resistance at even faster rate. Rapid emergence of resistant clinical pathogens is an imminent threat to public health, and 2.4 million people are predicted to die due to antimicrobial resistance in Europe, North America and Australia over next 30 years (Bianco et al. 2020).

Improved international mobility, immigration and economic exchange further lead to intercontinental distribution of resistant microbial phenotypes (Church 2004). Since 1950, many studies have reported increasing incidences of antimicrobial resistance (Davies and Davies 2010) and WHO has advocated research and antibiotics usage as per guidelines (WHO 2016). Subsequent research and attention to pharmaceutical neglect toward new antibiotics has been recognized, and efforts are directed toward aiding new antibiotic development and understanding the antimicrobial resistance landscape between animals, humans and the environment.

The interconnections and microbial exchange between ecological niches involving humans, animals and poultry, agriculture, environment and wastewater (sewage) cannot be neglected. This is frequently underscored by recognition of animal carriers and zoonotic sources during disease outbreaks (He et al. 2021). This scenario calls for adoption of a powerful emerging concept called ‘one health.’ It refers to a collaborative, inter-disciplinary and multi-domain approach of actions applied at local, national and inter-national scale. This collaborative approach needs to be implemented for antimicrobial resistance to tackle the omnipresence of drug-resistant microbes (Fisman and Laupland 2010). The underlying principles of ‘one health’ help to achieve long-term sustainability by strengthening human-animal bonds, providing safe food and water, sustainable agricultural practices, surveillance of disease, antimicrobial resistance and environment, alignment of government policies and regulations for efficient communication and global outreach. Direct outcomes of this ‘one-health’ approach would be interdisciplinary solutions emanating from strategic education, training, prevention, diagnosis and novel therapies against antimicrobial resistance (Fig. 1). The issue of antimicrobial resistance can only be dealt through knowledge and multi-thronged mitigation approaches, and thus, we discuss the overlapping landscape of antimicrobial resistance and stakeholders in

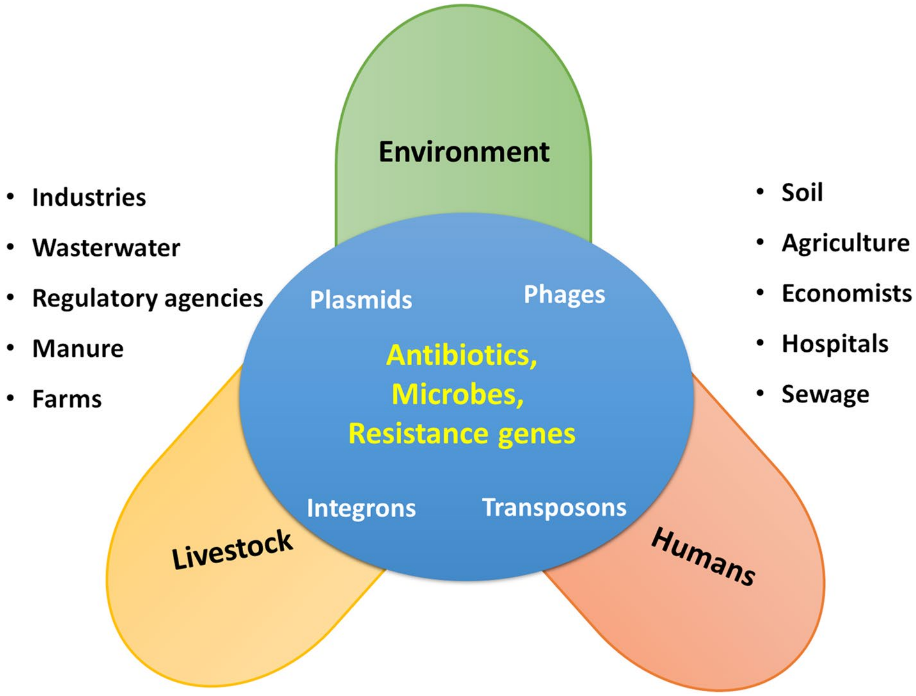

Fig. 1 One-health paradigm and stakeholders. ‘One-health’ refers to integrative strategies in design and implementation of legislation, policies and research, which facilitates communication between multiple sectors to achieve better solutions for public health. This holistic approach can aid in integration of information from different stakeholders such as regulatory agencies, economists, consumers and other contributors to provide sustainable solutions against antimicrobial resistance

this review. This article is an abridged version of the book chapter on antimicrobial resistance and One-health by Singh et al. (2020).

Antibiotics and antimicrobial resistance

Antibiotics in humans, veterinary and agriculture

Various antibiotics are used for the treatment of infections in humans and animals. Some of these antibiotics could be used in both animals and humans, whereas due to toxicity and/or different incidences of infection in humans, some of them are restricted only for use in animals (Church 2004), (Davies and Davies 2010), (Van Boeckel et al. 2015). Non-therapeutic usage of antibiotics has been found disproportionately more in animals, especially farm animals, as compared to humans because the antibiotics are added in their water and/or feed to prevent them from various infections (Cully 2014), (Van Boeckel et al. 2015). In farm animals, antibiotics are also used at sub-therapeutic levels as a growth enhancer (Landers et al. 2012), (Chattopadhyay 2014), a procedure called 'metaphylaxis' (Butaye et al. 2003). The period of metaphylaxis may range from 2 weeks to throughout the life of animals and increases their growth rate by up to 10% (WHO 2003). All such activities lead to the direct or indirect leakage of antibiotics in the environment and possess extreme threats to the human population.

What makes it more adverse is that certain antibiotics used on farm animals are reserved for human usage to treat terminal infection or infections caused by multi-drug-resistant pathogens (MDR) (WHO 2016). MDR pathogens have intrinsic resistance against many antibiotics, and they extensive usage of antibiotics increases their number in the farm waste, thereby creating more number of microbes showing resistance against more than one antibiotic (Tacconelli et al. 2018). According to a report published in the USA, it has been estimated that a large group of people may get affected by fluoroquinolone-resistant *Campylobacter* infections via chicken (Food and Drug Administration 2000). It has been reported from Canada and Europe, that poor hygiene and sanitation conditions lead to excessive use of antibiotics (Health Canada 2014; European Union 2015). Without compromising on economic front, antibiotic usage can be reduced largely by ensuring hygiene and routine vaccination (World Health Organization 2003; Tang et al. 2019). Under the guidelines of WHO, many countries have started good practices in their farm animals and have prohibited the use of certain antibiotics in their countries (Food and Drug Administration 2013; Health Canada 2014; European Union, 2015).

The risks associated with metaphylaxis of common classes of antibiotics used between humans and animals is clearly evident for third-generation antibiotics such as cephalosporins (WHO 2016). Upon widespread metaphylaxis of cephalosporins in animals, resistance across all cephalosporin antibiotics developed and spread to human pathogens. Now, it has been reported that the cephalosporin dosage had to be increased in humans as compared to animals (Food and Drug Administration 2012) and two genes, extended-spectrum beta-lactamases (ESBLs) and AmpC, which both confer resistance against these antibiotics, have been found on the bacterial plasmids in a highly mobile genomic region (European Medicines Agency 2009). ESBLs are a group of highly mobile antibiotic resistance genes providing resistance against beta-lactam group of antibiotics, and it poses major health risk to humans (Rawat and Nair 2010). Resistance in one class of antibiotics can also result in emergence of resistance against other antibiotics due to co-transfer of resistance genes, owing to their proximity in the genome, through plasmids. One such example is the carbapenems, against which common human pathogens like *E. coli, Salmonella* spp. and *K. pneumoniae* have gained co-resistance after overuse of cephalosporins (Nordmann 2014). Many studies have found similar ESBL-containing *E. coli* strains between animal, food and humans (Tadesse et al. 2017), (Odsbu et al. 2018), (Rizzo et al. 2019). The mode of dissemination of resistance genes between animals and humans has also been found to be through plasmids (de Been et al. 2014). Thus, excessive use of these antibiotics as metaphylaxis further aggravates the problem of resistant microbes in the environment (Canadian Integrated Program for Antimicrobial Resistance 2008) and urgently needs to be regulated. Many studies done in Japan, Denmark and Canada have shown the positive impact on the reduction of cephalosporin resistant microbes in food animals if it is not being used (Hiki et al. 2015), and a similar pattern was observed with the usage of fluoroquinolones in Australia (Nelson et al. 2007), (Rusu et al. 2015).

With the emergence of many multi-drug-resistant pathogens, the effectiveness of many general use antibiotics has largely reduced. Thus, certain antibiotics with high side effects in humans, such as colistin, are now being approved as last resort antibiotics against resistant pathogens. Colistin was only limited for metaphylaxis in food animals, and thus, high levels were being used. Its overuse in food animals led to many colistin-resistant pathogens and reports of horizontal transfer of colistin resistance gene (mcr-1) via plasmid (Liu et al. 2016) prompted the regulatory agencies of many countries to reduce colistin administration in food animals. Likewise, the extensive use of avoparcin, a glycopeptide antimicrobial, in food animals (Aarestrup et al. 1996) has created the problem for other candidates of the glycopeptide class of antibiotics. One such case is vancomycin (also a glycopeptide antibiotic), which is being used in case of multi-drug resistance and is now facing the problem of losing its effectiveness on humans as well as animals (Tang et al. 2014). Altogether, careful regulations need to be put in place for the use of veterinary antibiotics especially when they are highly potent and widespread surveillance of antibiotic seepage into the environment needs to be done.

Antimicrobial resistance, bacteriophages, animals and public health

The indiscriminate use of antibiotics has led to the increased prevalence of antibiotic resistance genes among pathogens (Fig. 2). In livestock, antibiotics are said to stimulate overall body development by improving digestion or preventing bacterial infections. This is postulated to be caused by suppression of unwanted intestinal bacteria which otherwise will cause infections leading to release of certain cytokines which reduces muscle mass (Liao and Nyachoti 2017), (Gonzalez Ronquillo and Angeles Hernandez 2017). In pork industry, China's use of the antibiotics for growth is four times higher than the USA (Cully 2014). Since antibiotics are often used for metaphylaxis in high levels, they are poorly absorbed in the animal body. Most of the antibiotics are excreted in feces which leads to emergence of resistant bacteria in the animal manure. In accordance, Denmark and the European Union have forbidden the use of 11 antibiotics since 1995, causing a decrease of up to 50% in antibiotic resistance (Hollis and Ahmed 2013).

It has been observed that manure enhances antibiotic genes transfer to bacteria infecting human populations and even exposes soil to it, causing a build-up of antibiotic-resistant genes in the environment (Zhu et al. 2013), (Pruden et al. 2012). These antibiotics along with metals used in livestock feed such as Cu, Zn, As, Cr, Cd, Pb and further generate a co-selection pressure on bacterial populations by hindering their growth and are positively correlated with antibiotic resistance genes (*sul*A and *sul*III) (Baker-Austin et al. 2006), (Zhang et al. 2012), (Seiler and Berendonk 2012). Even the unculturable portion of the microbiome of niches potentially houses antibiotic-resistant genes (Enne et al. 2008), (Zhu et al. 2013) and is speculated to act as sink for them. Further, it has been noted that human waste processed in sewage treatment plants results in less frequent antimicrobial resistance than untreated animal waste (Di Cesare et al. 2016).

Bacteriophages (bacteria-killing viruses) are an often ignored but important player in the antimicrobial resistance landscape. They carry many antibiotic resistance genes, and they can mobilize these genes similar to plasmids and integrons through horizontal gene transfer (Brabban et al. 2005). Phage-mediated transfer of resistance genes has been found responsible for conferring resistance against ampicillin in *Escherichia coli* (Colomer-Lluch et al. 2011), multiple drugs in *Salmonella enterica* (Schmieger and Schicklmaier 1999) and *Pseudomonas aeruginosa* (Blahová et al. 2000). Their attribute as vectors for gene transfer has been reported from many niches including sewage, which also has high numbers of resistant microbes and genes (*qnr*S, bla_{TEM}, $bla_{\mathrm{CTX\text{-}M}}$, bla_{SHV}, *mec*A, *sul*1) conferring multi-drug resistance (Colomer-Lluch et al. 2011), (Marti et al. 2014), (Calero-Cáceres and Muniesa 2016). More research needs to be done on the extent of involvement of phages, but their omnipresence and high capacity for gene mobilization between microbes

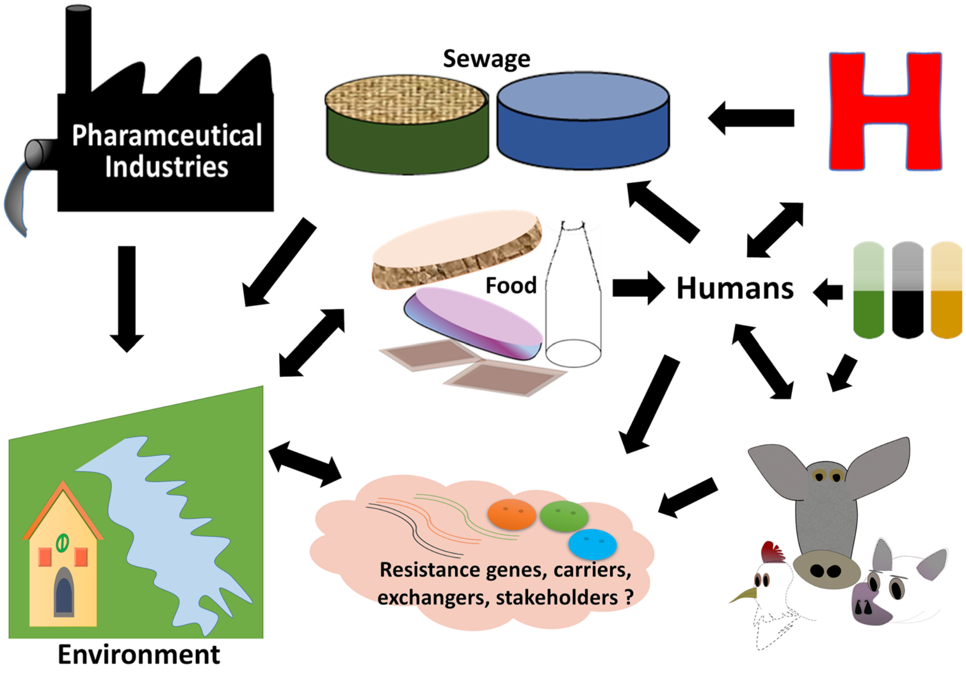

Fig. 2 Inter-connectedness and transferability between the different niches. Many routes of transmission exist for exchange of antimicrobial resistance determinants such as antibiotic resistance genes (ARGs) between animals, humans and the environment. Anthropogenic activities remain at the center of all major activities related to antimicrobial resistance

make them important in animal, human and environmental niches.

Another interesting study argues that street food indirectly exposes humans to antibiotics (Campos et al. 2015), owing to compromising practices in hygiene. This also relates to storage and purchase of raw materials from farms using cheaper farm practices, unregulated antibiotic use and diseased animals with high antibiotic levels (Pham Kim et al. 2013). One striking example of feed is the use of poultry litter as protein supplement for farm animals in South Africa, which is often contaminated with residues of antibiotics to which the poultry was exposed (Soto 2013). Food from animal origin can carry major proportions of antibiotic-resistant bacteria with about 47% of resistant *Salmonella* being isolated from meat and milk in Ethiopia (Ejo et al. 2016) and 14% of resistant *E. coli* isolated from chicken, milk and eggs in India (Laxminarayan and Chaudhury 2016). Unregulated antibiotic use can cause emergence of resistant pathogens like *Salmonella* spp., *Enterococcus* spp., *Yersinia enterocolitica, Listeria monocytogenes, Staphylococcus* spp. and many more (Phillips et al. 2004) which generally have higher recombination frequency and gene transfer ability, thus indicating fecal, soil and water contamination. Also the lack of quick and effective antibiotic resistance detection techniques, complex patterns of exchange of antibiotic resistance genes, unreliable prediction tools to understand the consequences of human mortality and morbidity, and fluctuating costs of care are associated with infections induced by such pathogens (Wegener 2012).

Residues of antibiotics such as tetracycline and chloramphenicol (Cameroon, Iran, Egypt) above their maximum residue limit (European Union standards) have been detected in muscle, heart and kidney of farm chicken (Daghrir and Drogui 2013), (Tavakoli 2015), (Guetiya Wadoum et al. 2016). Similarly, ciprofloxacin has been detected in eggs of terminally ill birds receiving antibiotic treatment (Billah et al. 2015), quinolones inside chicken and beef in Turkey (Er et al. 2013), amoxicillin in milk and eggs in Bangladesh (Chowdhury et al. 2015), sulfonamides and quinolones in milk in China, Malaysia and India (Cheong et al. 2010), (Zheng et al. 2013), (Kumari Anjana and Jayachandran 2017). This exposure of antibiotics to humans can lead to neuropathological problems, drug hypersensitivity, aplastic anemia, mutagenesis, disturbance of normal gut flora and many more such complications (Lee et al. 2001), (Nisha 2008), (Beyene 2015). European Union and other authorities have recommended a maximum residue limit for antibiotics in animal-derived food, but it is quite difficult to ascertain their safe level, thus monitoring antibiotic use and their clearance period from animal becomes crucial (Codex Alimentarius 2012). Many such guidelines on the use of medically important antibiotics in food-producing animals have been recommended by WHO in 2016 (Table 1) (Aidara-Kane et al. 2018). The historical linkage of antibiotic and antimicrobial resistance in the modern age could not be overstated, and direct effects of antibiotics and interconnected microbial entities on human health must be considered when probing the emergence and spread of antimicrobial resistance.

Antimicrobial resistance in soil and water bodies

Soil is a complex ecological niche and acts as source and sink for physical exchange between the living and nonliving components of the earth. Naturally, it also serves as a reservoir for antibiotic resistance genes and determinants coming from various sources (Fig. 1, 2) (Monier et al. 2011). Metagenomic studies of soil have shown that many antibiotic resistance genes exist which are yet to be fully characterized (Riesenfeld et al. 2004). Agriculture land may receive antibiotics washed off from other sources, but manure-supplemented soil especially with inputs from

Table 1 WHO recommendations on the use of medically important antimicrobials in food-producing animals

1	The Guideline Development Group (GDG) recommends an overall reduction in use of all classes of medically important antimicrobials in food-producing animals
2	The GDG recommends complete restriction of use of all classes of medically important antimicrobials in food-producing animals for growth promotion
3	*The GDG recommends complete restriction of use of all classes of medically important antimicrobials in food-producing animals for prevention of infectious diseases that have not yet been clinically diagnosed
4a	†The GDG suggests that antimicrobials classified as critically important for human medicine should not be used for control of the dissemination of a clinically diagnosed infectious disease identified within a group of food-producing animals
4b	†The GDG suggests that antimicrobials classified as critically important for human medicine should not be used for treatment of food-producing animals with a clinically diagnosed infectious disease

*Specific considerations: when a veterinary professional judges that there is a high risk of spread of a particular infectious disease, use of antimicrobials for disease prevention is justified, if such a judgment is made on the basis of recent culture and sensitivity testing results

†To prevent harm to animal health and welfare, exceptions to recommendations 4a and 4b can be made when, in the judgment of veterinary professionals, bacterial culture and sensitivity results demonstrate that the selected drug is the only treatment option

animal farms often contains high concentration of antibiotics (Marti et al. 2013), such as tetracycline residues and resistant microbes (Zhu et al. 2013). Antimicrobial resistance in soil is further aggravated if improperly treated wastewater which is a nutrient-rich niche for microbes is used for irrigation (Chee-Sanford et al. 2009; Oluyege and C 2015). Many antibiotics and resistance genes such as the $bla_{CTX\text{-}M}$ gene (confers resistance against cefotaxime) have been reported from soil near pig farms and even rice fields (Xiao et al. 2016).

The waste generated from farms, manures, irrigation water, drug manufacturing plants, hospitals, humans and antibiotic-contaminated ground surfaces often ends up in agricultural land which increases the level of antibiotics (Rodgers et al. 2019). Depending upon class of antibiotics, they degrade at different rates and thereby aggravate resistance against antibiotics (Du and Liu 2012) such as ampicillin, tetracycline, sulfamethoxazole, nalidixic acid and chloramphenicol (Carballo et al. 2013). The vegetables and fruits from these farming lands often pick up the antibiotics and resistant microbes present in the soil and pose risk of transmission of antimicrobial resistance to humans during transport and storage (Beuchat 2002), (Kumar et al. 2005). Although data for direct use of antibiotics in agriculture is limited, inputs from aforementioned antimicrobial resistance sources are often ignored and there is hardly any surveillance for resistance in agricultural land.

Water bodies such as freshwater lakes, rivers, artificial water systems and sea also act as dynamic reservoirs for antibiotic-resistant bacteria, antibiotic resistance genes and antibiotics owing to multiple edaphic and biotic factors (Ding and He 2010), (Cizmas et al. 2015) (Khan et al. 2019). Many resistance determinants such as ESBLs ($bla_{\text{CTX-M-15}}$, $bla_{\text{CTX-M-15}}$ $bla_{\text{OXA-58}}$) were found from rivers and drinking water sources, which exposes a large population to resistant microbes (Cacace et al. 2019). This is particularly worsened if animal farms, pharmaceutical plants, manure storages, wastewater treatment plants are in close vicinity of these water bodies (Kümmerer 2009). Very diverse and high numbers of MDR strains have often been reported from ground water and rivers across the world (Mulamattathil et al. 2014; (Wahome 2013). Certain mass gathering events such as religious congregations, sports, water parks, beach sports near water bodies witness a huge influx of resistant microbes such as *Enterobacter, Serratia, Klebsiella, Citrobacter* and *Pantoea* and inter-mixing of large populations in such hot spots also facilitates the spread of antimicrobial resistance (Khan, Memish, et al. 2010; Jani et al. 2018). These reports indicate toward the enormous effects of the antimicrobial resistance in the soil and water bodies and the role of environment as a source–sink pair for antimicrobial resistance. This demands for careful surveillance, strategic management of public events for effective control over spread of antimicrobial resistance.

Antimicrobial resistance and humans

Antibiotic consumption varies across the world owing to differences in incidences of infectious diseases, living standards, community hygiene and often broad-spectrum antibiotics are unnecessarily prescribed. Although new treatments alternatives such as use of probiotics (Hatakka and Saxelin 2008), probiotics surface proteins such as mucus binding protein (Singh et al. 2018) (Singh et al., 2017), fibronectin binding protein (Bisht et al. 2018) or oligosaccharides (Anand et al. 2018) have been proposed, they are still far from being commercial therapeutic success. This leaves fewer options to treat MDR strains, and extensive antibiotic stewardship of health professionals is needed. Antibiotic stewardship approach can be further augmented by increasing awareness in the general public about responsible usage of antibiotics. Humans can potentially act as most aggressive vectors for transmission of antimicrobial resistance, given their omnipresence, long distance travel, socializing and work. Human activities around antimicrobial resistance hot spots such as farms, drug manufacturers, hospitals, further load them with resistant microbes. Resistant pathogens can affect humans directly (Scallan et al. 2011), use them as transmission vectors (Spoor et al. 2013) and also utilize humans as niche for example 'human gut' for the exchange of antibiotic resistance genes among microbes (Willems et al. 2011). It is correctly reasoned that antimicrobial resistance in humans is linked to high exposure of antibiotics either by drugs or contaminated food or water. The antibiotic prescription pattern, market dynamics and disease state of patients decide antimicrobial resistance in humans, which directly affects patient's amicability for vital invasive procedures in cancer and transplantation (Friedman et al. 2016).

Many nations have taken steps to curb indiscriminate antibiotic usage at both pre-prescription and post-prescription levels, by strengthening public health and structured antibiotic stewardship (Garnacho-Montero et al. 2015) (Dyar et al. 2017). This has been further augmented by strict laws and regulations on the sale without prescription and over-the-counter antibiotics in many countries including Thailand, Mexico and Brazil (Santa-Ana-Tellez et al. 2013), (Holloway et al. 2017). Similar strides have been initiated in India (Laxminarayan and Chaudhury 2016) and South Africa (Gelband and Laxminarayan 2015) for strengthening of antibiotic stewardship program, tight regulatory control over antibiotics usage and data register of antibiotics sale (Masterton 2011), (Valsamatzi-Panagiotou et al. 2021). The direct effects of anthropogenic activities and fast transfer of antimicrobial resistance through food and drinking water to humans are easily perceptible. Apart from strategic antibiotic stewardship in hospitals, there is a need to adopt safe handling practices of antibiotic-polluted environmental samples originating from soil, water, etc.

Prevention and regulation of antimicrobial resistance

The issue of antimicrobial resistance needs to be tackled both at prevention and mitigation levels, which needs awareness in general public, tight regulatory measures and responsible antibiotics usage. Sensitization of the public toward antimicrobials could be done through radio, television and awareness campaigns by non-governmental organizations and can result in success stories such as of 'triclosan.' Earlier, triclosan was a widely used antimicrobial in many countries, but it was banned for use when its role in antimicrobial resistance became public and public pressure mounted on the government (McGinley 2016). Healthcare systems could benefit from antibiotic stewardships, identification of critical control points and strict adherence to regulatory measures (Uchil et al. 2014). A major preventive measure to mitigate antimicrobial resistance is surveillance, further augmented by use of high-throughput technologies such as next-generation DNA sequencing and inclusive classification systems such as Rescon (resistance readiness condition), which links severity and spread potential of antimicrobial resistance (Martínez et al. 2015). This applies directly to resistance determinants and mobilizing elements like plasmids, transposons and integrons and also to other environmental stress factors like heavy metals, temperature (Vorholt 2012). Other omics technologies further resolve information about antibiotics levels, mobile genetic elements, resistance genes and their expression patterns coupled with actual antibiotic residues present in the niche (Spicknall et al. 2013).

These approaches are important to identify patterns and overlapping ecological factors involved in emergence and spread of antimicrobial resistance including those due to biofilms, phyllosphere and water bodies (Calero-Cáceres et al. 2014). Overall, this helps in precise statistical prediction of abundance and mobilization of resistant genes and accessory genetic elements, spread between humans, animals and environment and predictive model to aid in the design of mitigation strategies and critical regulatory policies against antimicrobial resistance. These surveillance measures are not effective in standalone countries, and thus, inter-continental partnerships between regulatory agencies of different countries are being strengthened (Rogers Van Katwyk et al. 2020). Some examples are GARP (Global Antibiotic Resistance Partnership)—(Ganguly et al. 2011), (Leung et al. 2011), INSAR-India, NARMS-USA, ESAC-EU, SASCM-South Africa, PAHO (Pan American Health Organization) and EARS-Net (European Resistance Surveillance Network), GLASS – WHO. All of these networks focus on information exchange and partnership in research and action for efficient tackling of antimicrobial resistance (Berendonk et al. 2015). These preventive measures need a boost from another front, which is the development of novel and potent antibiotics augmented with improved drug delivery strategies to bypass biofilms (Singh et al. 2021). Reducing the mass usage of antibiotics by imposing extra charges on non-human antibiotic usage and strict regulations to encourage raising animals in clean, hygienic conditions would also help the overall effort (Hollis and Ahmed 2013). However, all such efforts need to be integrated under 'One-Health' approach across the world with further consideration of other ecological factors and niche diversity to customize the prevention and mitigation plan against antimicrobial resistance. The effectiveness of high-throughput surveillance and public awareness is paramount, and we need to consider the interplay of ecological factors in the antimicrobial resistance landscape. The discernible need for worldwide networks to fight against antimicrobial resistance is also a pertinent concern, and recent efforts by many countries need to be continued and strengthened.

Antimicrobial resistance and the one-health approach

The 'one-health' concept offers multiple benefits in systematic dealing with the menace of antimicrobial resistance. A big concern in the antimicrobial resistance issue is the acquisition of resistance by human pathogens from their non-pathogenic relatives in the environment (Forsberg et al. 2012). There are many direct evidences for human–animal–environment interrelatedness, and inclusive strategies such as 'One health' have to be adopted for effective control and mitigation of antimicrobial resistance. The 'one-health' approach is directly beneficial for humans when applied to surveillance network and public awareness programs where it facilitates precise understanding of the pattern and active dynamics of antimicrobial resistance. For example, documentation of resistant microbes from human origin in an area provides ideas about endemic patterns of such resistant microbes (Critchley and Karlowsky 2004). This information could be utilized for prioritizing antibiotic susceptibility screens for infection in incoming patients and would promote evidence-based antibiotic prescription by physicians. Furthermore, the sensitized physicians themselves can encourage patients to adopt good hygiene practices, safe disposal of animal waste and general behavior during zoonotic disease outbreaks, thereby leading to low infections and robust addressal of public health issues.

Although not considered as measure of antimicrobial resistance, the antibiotics and their degraded products largely drive resistance in all niches (Subbiah et al. 2016) and are sometimes responsible for activating biofilm formation, motility and stress response in microbes (Romero et al. 2011). There are myriad types of applicable regulations and stakeholders in areas related to human, animals and environmental health, which handle the issue of antimicrobial resistance with different levels of seriousness. The regulation on use of last resort antibiotics (for humans) such as carbapenems and colistin in agriculture settings is very relaxed and allows mass level usage (Pereko et al. 2016). Less regulatory oversight into agricultural systems and their neglect toward recognizing it as reservoir of antimicrobial resistance further worsens the situation. The risks estimated due to pathogens arising from these domains directly affect humans involved in handling agriculture products during production, transport and even the disposal of agricultural wastes. Careless antibiotic prescription to animals without giving any consideration for resistance against carbapenems and colistin in case of veterinary pathogens still ends up being part of the animal–human–environment interplay and aggravates the development of resistance. The antibiotic administration pattern at individual animal and herd levels also differs, and integrated approaches to understand long-term effects in the context of antimicrobial resistance must be considered.

Across many developing nations, hunting of wild animals for food also referred as 'bush meat' has been linked with infections including, e.g., Ebola virus (Peterson 2003). Low vaccination, frequent mixing of animal–human habitats and poor hygiene in such countries further drive infections and concomitantly complicate the issue of antimicrobial resistance. Such situations have prompted many agencies such as WHO and UN-FAO (United Nations Food and Agricultural Organization) to join hands and design strategies using the 'one-health' approach to deal with endemic diseases such as echinococcosis, bovine tuberculosis, rabies and brucellosis in Africa while considering animal interactions (Aidara-Kane et al. 2018). Similar strides have been initiated by UN-FAO and WHO to tackle the risk of avian influenza (influenza virus A) in humans by collaborative efforts of veterinarians and physicians (OFFLU-OIE/FAO 2019).

Given the multidimensional issue of antimicrobial resistance and overlapping spheres of its sources, treatment regimen and control of regulations demand inclusive mitigation under the 'one-health' framework. This framework collates information from all stakeholders and fills knowledge gaps (Fisman and Laupland 2010) to compare regulatory standards for resistant strains isolated from human, animal and environmental sources. This facilitates clarity in mitigation strategy and design of logic-based risk mitigation policies for precise administrative and structural support in dealing with antimicrobial resistance (McLain et al. 2016). The one-health model can effectively mitigate the issue of antimicrobial resistance and is equally applicable to developed, developing and under-developed countries (Gebreyes et al. 2014) which is necessary for a sustainable control of mankind over antimicrobial resistance. The overreaching arc of 'one health' to provide effective control over the confounding factors of antimicrobial resistance is widely recognized. It is prudent to work within the integrated framework of 'one health' and mitigate antimicrobial resistance in a sustainable and long-term fashion.

Conclusion

Numerous studies have established overlapping interactions between humans, animals and the environment, especially in the context of emergence and spread of antimicrobial resistance. Frequent outbreaks of zoonotic diseases and their clear association with both environmental and human domains underscore their interwoven relationship. Clinicians, veterinarians and regulatory agencies have achieved wonderful milestones in infectious diseases, but quantifiable and integrated measures against antimicrobial resistance between human, animals and environment are largely missing. Due to this, even though the link between these ecological domains is obvious, only few predictive models exist which could inform about their source–sink–reservoir relationships during most disease outbreaks. A big reason for this knowledge gap is due to focus on human research and complete ignorance of other stakeholders spanning the animal, plant and environmental niches. This ignorance has been rampant at almost all levels including relaxed regulations, indiscriminate antibiotic usage, surveillance, control and research.

Recent studies on the rapid rate of exchange of antimicrobial resistance determinants between these spheres of life further underscore futility of all domain-limited efforts and demands inter-sectoral focus for tackling antimicrobial resistance. Recent research has shown that strict regulatory control, antibiotic stewardship, novel antibiotic development and widespread surveillance have to be adopted. The multi-domain nature of the issue of antimicrobial resistance demands its handling through an inclusive approach called 'one health,' which provides integrated solutions with multi-sectoral representation at the level of surveillance, detection and targeted mitigation. This deals comprehensively with the biotic and abiotic confounding factors involved in antimicrobial resistance and provides sustainable solutions. One-health approaches are useful for all countries at different economic levels and are particularly suitable for effective implementation in low- and middle-income countries that often tend to have high disease burden and worse situations of antimicrobial resistance.

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Declarations

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