# Impact of antibiotic resistance on sustainable development goals

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# Impact of Antibiotic Resistance on Sustainable Development Goals

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**Abstract**. The frightening spread of antibiotic resistance among infectious bacteria is one of the most important challenges facing health and the environment, which in turn burdens the economies of all countries of the world, and this in turn hinders the sustainable development goals of those countries. Moreover, Iraq is at the forefront of the countries where the ineffectiveness of most drugs is increasing as a consequences of the misuse of antibiotics represented in the overuse of antibiotics and not following the doctor 's prescription, as well as their overuse in anima1 feed and agriculture. Due to the importance of this topic and because it was not studied in Iraq, we designed this study to highlight the impact of antibiotic-resistance on sustainable development goals in Iraq.

## INTRODUCTION

The Sustainable Development Goals (SDGs) were published in 2015 by the UN within the program of "2030 Agenda for Sustainable Development" to serve as a global blueprint for a better, more equitable, more sustainable life on our planet [1]. The UN Earth Summit (Rio de Janeiro, 1992) and the UN Millennium Summit (New York, 2000) resulted in the antecedents of SDGs, the Agenda 21 and the Millennium Development Goals (MDGs), respectively [2,3]. The SDG initiative includes 17 well-defined goals from the fields of ecology, climate change, societal issues, economy, education and healthcare—that are frequently interlinked—with well-defined actions, targets and monitoring criteria to allow for the evaluation of the progress of these goals [4]. These goals were universally adopted by all UN member states, with the SDGs being continuously followed-up and reviewed by High-level Political Forum on Sustainable Development, seating annually. The deadline for attaining most of the SDGs has been set in the year 2030; however, others do not have a specific deadline [4].

In the field of health, there are several challenges facing or impeding the goals of sustainable development, the most prominent of which are water and air pollution, epidemics, and recently the spread of antibiotic resistance among pathogens [2,4].

The reduction in infectious disease morbidity and mortality may be attributed to a variety of factors; however, improved sanitation and public health, the introduction of vaccines and antibiotics are among the most significant [5,6]. The discovery and subsequent clinical use of antibiotics can be considered one of the game-changing achievements in medicine, revolutionizing the care of patients, who had previously succumbed to the onslaught of common or fatal bacterial infections, including (in reducing the incidence of) respiratory tract infections, Gastrointestinal infections, urinary tract infections, skin and soft tissue infections, bacteremia and others [5,6,7,8,9]. Since the 1950s, antibiotics have saved millions of lives (immunocompromised and immunocompromised patients) and allowed the development of complex medical interventions and specializations, which was not previously possible [7,10]. However, the emergence of bacteria resistant to these drugs has proven to be one of the most serious concerns for several years. The development of antimicrobial resistance (AMR) in bacterial pathogens is an expected result of evolutionary adaptation to these harmful agents [8,11,12]; However, the widespread use of these drugs has significantly accelerated this process [9,13]. Bacteria can evade the effects of antibiotics in several ways, including production of degrading enzymes (eg, β-lactamases), adaptation to alternative metabolic pathways (eg, folic acid metabolism), and target alteration (eg, modifications in ribosomal subunits or topoisomerase enzymes),

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deceased uptake of drugs (eg, outer membrane protein mutations), overexpression of efflux pumps or by production of a protective polysaccharide matrix or biofilm [14].

An increase in antibiotic resistance (ABR) use associated with increasing antibiotics uses that directly correlated with more unfortunate clinical outcomes, longer stays in the emergency clinic, excess mortality in affected patients and overweight and expenditures on the medical services framework. SDGs were distributed in 2015 by the assembled nations to fill it out as a global blueprint for a better, fairer, and more supportive life on our planet [17,18,19,20]. The SDGs contextualize antibiotics resistance as a cultural and public well-being issue worldwide; Also, advancing the development of ABR may constrain the achievement of many of the Sustainable Development Goals as The economic situation that drives the center of development on this planet (Figure 1) [1,15,16,21,22,23]. Figure (1) shows that the bad and excessive use of antibiotics, whether in poultry and fields as growth stimulants and others, leads to an increase in the proportion of incurable bacterial diseases, which in turn do not respond to the available antibiotics because they have developed resistance against them, and this is reflected in the health of the workforce and on the increase in import On the other hand, the treatments have exhausted the society healthily and economically, which in turn hinders the implementation of sustainable development plans [15,23].

In Iraq, there is great interest in the study of antibiotic resistance, as hundreds of scientific researches have been carried out on the identification of ABR of pathogenic and symbiotic bacteria to which humans are exposed, and most of these multi-resistant bacteria have appeared in a fictional way. In our opinion, these studies were not feasible because they did not culminate in solutions and did not fall within the goals of sustainable development in Iraq. The aim of this review is to shed light on the direct or indirect impact of antibiotic resistance on the sustainable development goals through the negative impact of these ineffective antibiotics on the health and economy of the country.

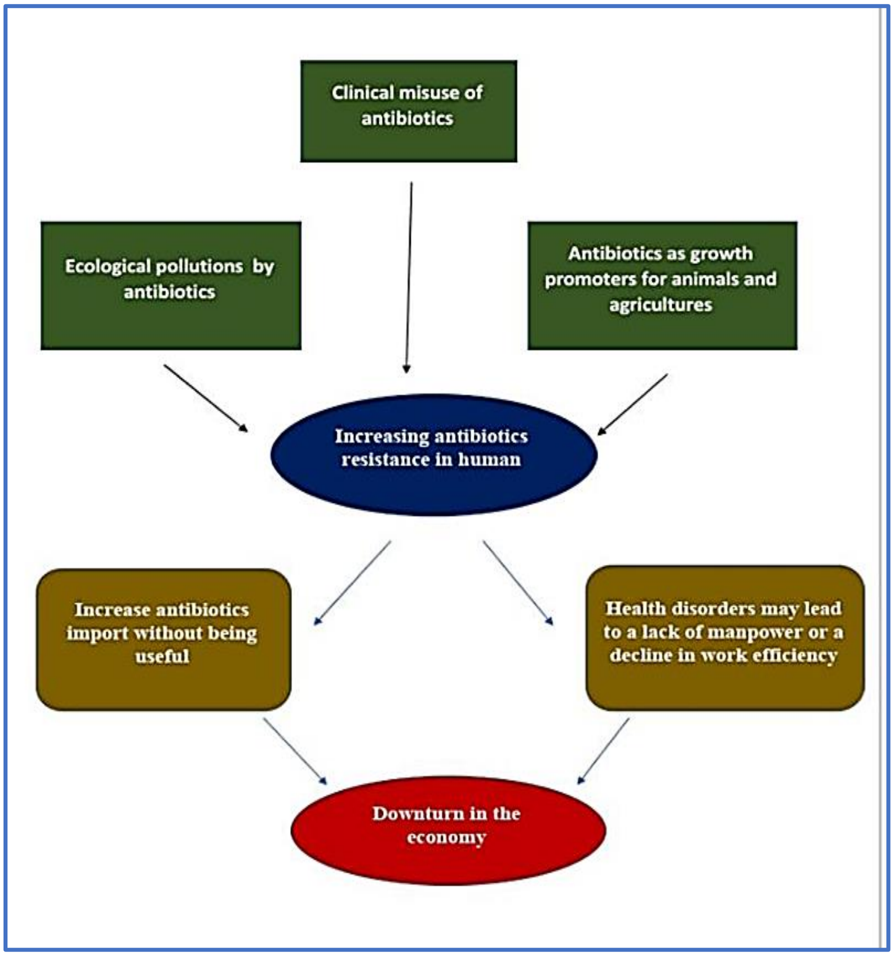

**FIGURE 1.** Effects of antibiotic resistance on SDGs throughout declined healthy and economy

# The Use of Antibiotics During the Corona Pandemic and its Connection to Sustainable Development

The current pandemic caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) or COVID-19 poses an immense threat to global public health. Since 15th October 2021, COVID-19 has infected almost 240 million people resulting in over 4.8 million deaths globally. Patients can develop severe complications associated with bacterial pathogens, which might be responsible for even higher mortality rates [24,25]. Antimicrobial therapy is important for managing confirmed COVID-19 cases with associated bacterial or fungal infections. However, the increased use of antibiotics and antifungals is somewhat counterproductive in the global effort to reduce antimicrobial resistance. A systematic review reported that increased use of antimicrobials while treating COVID-19 patients in Asia, Europe, and other regions is augmenting the threat of antimicrobial resistance (AMR) globally [26,27,28]. Lower- and Middle-income Countries (LMICs) (like Iraq) are prone to the twin burdens of increased risk from COVID-19 and AMR due to poorly resourced health programs, health care services and health governance, and ineffective regulatory and legislative mechanisms to control antibiotic use [29,30]. As countries have started administering vaccines and therapeutics, which are tackling the problems of the COVID-19 pandemic, the global threat of AMR remains unchecked. In LMICs, infection and fatality rates are higher, and mass vaccination has been challenged. The situation is worsening in low-resource settings, such as Iraq, where the uptake of vaccination is a major concern due to uneven distribution of vaccine and vaccine frequency. Vary, including seeking antibiotics without clinical confirmation of co-infection, suboptimal adherence and self-medication [27,28,31,32]

Unsurprisingly, increasing levels of AMR threaten the attainment of the SDGs as this phenomenon considerably influences changes in society and healthcare: it can be said that the SDGs contextualize AMR as a global public health and societal issue [33]. This may have been worsened by the onset of the global severe acute respiratory syndrome coronavirus 2 pandemic, which has not only further substantiated societal inequalities and economic difficulties, but has also led to a considerable increase in antibiotic use worldwide for the treatment of patients; it is not yet known what will be the long-term repercussions of this pandemic in the context of SDGs [34]. Most notably, the use of antibiotics has increased substantially in intensive care units (therapeutically and prophylactically) in the management of patients suffering from coronavirus disease (COVID-19) [35]. Antibiotic consumption in Hungary (before the onset of the pandemic) may be considered as appropriate from a quantitative standpoint (per capita consumption), however, qualitatively (characterized by the ratio of broad spectrum/narrow spectrum agents used), this country performs among the worst in the EU, mostly owing to the high rate of fluoroquinolone consumption [36]. In addition, a study has highlighted that the unavailability of general practitioners in various geographical regions of Hungary also leads to worse antimicrobial use qualitatively. Among other antibiotics, the use of azithromycin has received substantial attention in COVID-19; while azithromycin has been known to have potent anti-inflammatory properties in the lungs (this has been described in patients with cystic fibrosis), some early studies on COVID-patients have also suggested this antibiotic as a potential treatment option with direct effects on the virus; however, the clinical evidence on this subject is highly controversial. Nevertheless, azithromycin has been included in many institutional and local treatment protocols (even though unnecessary use of this drug may also bring forth serious cardiovascular adverse events), both in Hungary and elsewhere around the world [37,38]. This will inevitably lead to the selection of resistant mutants in bacteria (e.g., respiratory tract pathogens, atypical bacteria) where azithromycin has therapeutic relevance, which may hinder appropriate therapy for future patients . It must also be mentioned that many other antimicrobial agents (e.g., hydroxychloroquine, ivermectin) were also proposed in the therapy of COVID-19, which has led to widespread attempts to procure these drugs by condition of people, going as far as looking for them in veterinary shops or pharmacies [39,40]. At the present time and at the level of the coming years, with the presence of COVlD-19 vaccines, the problem of using antibiotics during the COVlD-19 pandemic is gradually fading, and we do not believe that it will get worse during the next decade, with the possibility of providing appropriate vaccines and the epidemic receding. As COVlD-19 vaccines have saved the world from multiple problems that directly or indirectly affect the Sustainable Development Goals as in Figure 2.

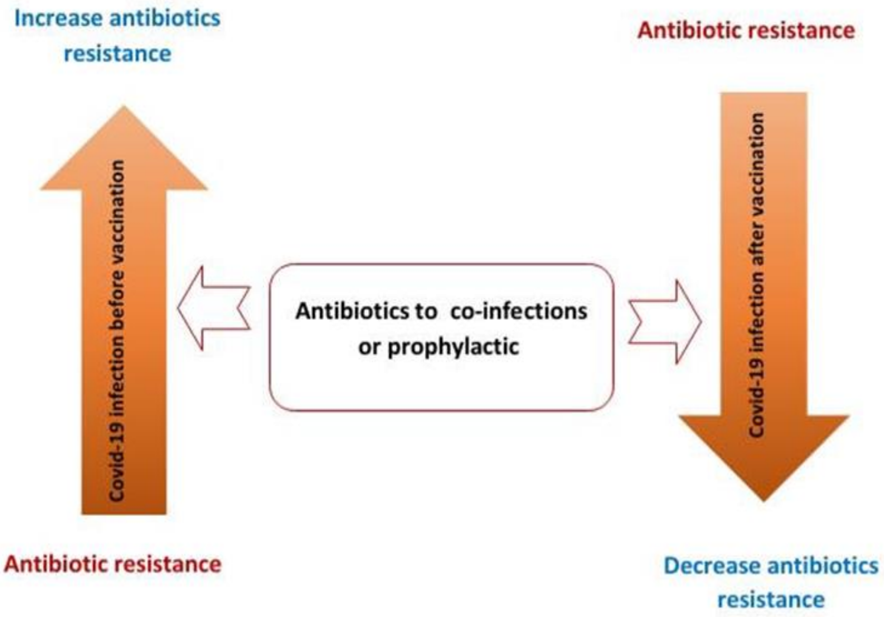

**FIGURE 2.** Effects of COVlD-19 vaccines on antibiotics resistance

## The Use of Antibiotics in Agriculture and Animal Feed and its Impact on Sustainable Development

The use of antibiotics is not only constrained to the clinical settings, as prescriptions involved in the therapeutic regimens for the eradication of diseases in humans. It is also employed in livestock farming, where antibiotics can be used for disease treatment of animals, and in sub-therapeutic levels in concentrated animal feed for growth promotion, improved feed conversion efficiency, and for the prevention of diseases [41,42]. Of great concern, the uses, types, and mode of actions of the antibiotics employed in agriculture and veterinary practice are closely related or the same (that may belong to the same general classes, function and act in similar ways) to those prescribed to humans. Clearly, the choice of antibiotics and the antimicrobial consumption pattern demonstrates geographical variation across the continents being influenced by the food animal species, regional production patterns and types of production system, intensive or extensive farming, purpose of farming (commercial or industrial or domestic), lack of clear legislative framework or policies on the use of antibiotics, as well as the size and socioeconomic status of the population, and the farmers in particular [43,44].

Due to the increased demand of animal protein in developing countries, intensive farming is instigated, which results in antibiotic residues in animal-derived products, and eventually, antibiotic resistance [45]. Antibiotic resistance is of great public health concern because the antibiotic-resistant bacteria associated with the animals may be pathogenic to humans, easily transmitted to humans via food chains, and widely disseminated in the environment via animal wastes. These may cause complicated, untreatable, and prolonged infections in humans, leading to higher healthcare cost and sometimes death. In the said countries, antibiotic resistance is so complex and difficult, due to irrational use of antibiotics both in the clinical and agriculture settings, low socioeconomic status, poor sanitation and hygienic status, as well as that zoonotic bacterial pathogens are not regularly cultured, and their resistance to commonly used antibiotics are scarcely investigated (poor surveillance systems)[46].

The Inclusion The Inclusion of nonessential antibiotics in animal feed for growth promotion purposes remains largely unregulated in the underdeveloped countries . The persistent use of these nonessential antibiotics in livestock farming can be attributed to the expansion and greater concentration of farmlands, inadequate governmental policies, and control over the use and sales of antibiotics, reduced use of infection control measures, and the unwillingness of farmers to execute delegated changes in farm practices [47]. Developing countries continue to employ the antimicrobial agent for growth promotion to maintain the healthy state of the animals, to increase productivity, and raise incomes for the farmers . However, these are contradictory to the Swedish agricultural data, as it recorded no loss of production after the ban exercise [48]. Altogether, Boeckel *et al*. [49] noted that on a global scale, the average antimicrobial agent consumed per annum of animal produced (per kg) varied across the animal species with values of 45 mg/kg, 148 mg/kg, and 172 mg/kg associated with cattle, chicken, and pigs, respectively. Equally, their mode of administration differs with the animal types. In this light, Apata [50] noted that antibiotics were added to water and feed for chicken in sub-therapeutic levels for growth promotion and prophylaxis. This had a devastating effect, as even healthy birds were unnecessarily exposed to antibiotics. Moreover, as these birds compete for food sources, eventually, there exists a difference in the doses consumed between the individuals, with one receiving a higher dose than others. This introduces another differential in the selective pressure on commensals, which could lead to the selection of resistant commensals that would eventually end up in the environment [51]. Singer *et al.* [52] accorded the administration of antibiotics in animal feed or water, in which the animals are reared in groups, making it difficult to isolate only the infected animals, as well as that the isolation process could be stressful to the animals and dangerous to the veterinarian who has to administer the antibiotic process. Contrarily, Sekyere [53], in their study, demonstrated the administration of antibiotics to pigs via the intravenous route for treatment, and in this case, shunned the exposure of healthy animals to antibiotics. However, this mode of administration might cause the accumulation of these drugs in adipose tissues, thereby posing a health risk to consumers of pork fat [54].

From the current presentation documented by the sources, we note that the use of antibiotics in agriculture or poultry contributes to the rise in antibiotic resistance among bacteria that will be transmitted directly from animals or plants to humans or indirectly through field products, and this increases the complexity of treating many diseases and thus targeting public hea1th , the economy and the environment, which are considered among the priorities of sustainable development as in Figure 1 and 3.

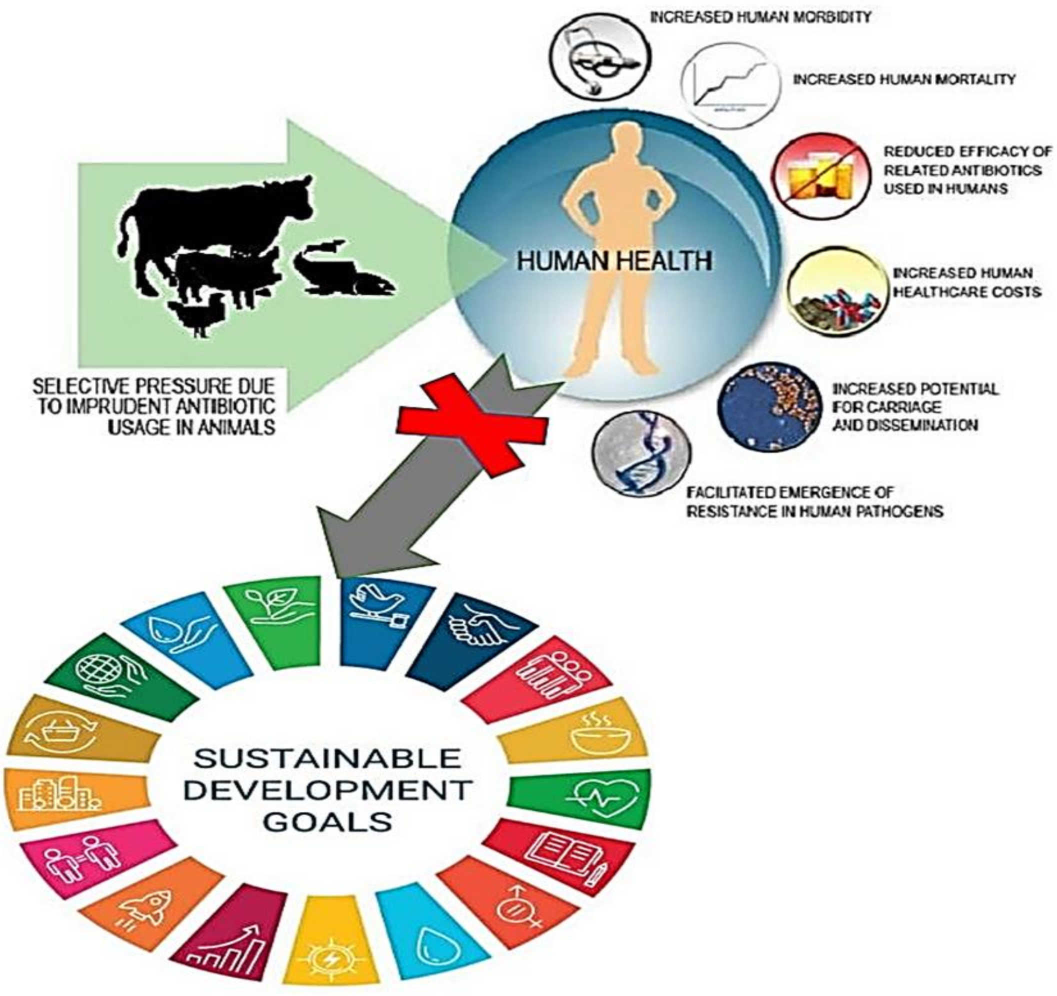

**FIGURE 3.** Effect of antibiotic in animal feeding on SDGs

## Animal - Derived Products and Antibiotic Pollution vs Public Health

In developing countries, food prepared and sold by street vendors is in vogue, and it is still emerging hastily in some countries, notably Iraq, Indonesia, Cameroon, and Democratic Republic of Congo [55]. These foods usually comprise of meat (beef, chickens, fishes) either raw, roasted, or cooked in sauce/stew, starchy foods and snacks, which are sold in restaurants located in public places (markets, schools, hospitals), on the ground in the streets, and along main roads [56]. It is for this reason that foodborne outbreaks are highest in developing countries, and dawdles as an issue of public health concern worldwide, because it is indicated as one of the significant food safety hazards concomitant with animal-derived foods [57]. Cooked foods sold on the street have a great socioeconomic impact; they create jobs and provide income to low or unskilled men and women, as well as serve as a major channel for the supply of food to financially handicapped individuals or poor and less privileged individuals. However, there is increased meat consumption to meet the protein demand of the population [55].

Antibiotics have been reported to accumulate and form residues at varying concentrations in the tissues and organs of food animals, as presented. Billah *et al.* [58] referred to these antibiotic residues as chemical residues or pharmacologically active substances representing either the parent compound or its degraded products, which are released, gathered, or stored in the edible tissues of the animal, due to their use in the prevention, treatment, and control of animal diseases. Undoubtedly, in Cameroon, Guetiya Wadoum *et al.* [59] demonstrated the presence of chloramphenicol and tetracycline residues in concentrations above the maximum residue limit (MRL) recommended by the European Union in 2010, in edible chicken tissues (muscle, gizzards, heart, liver, kidney) and eggs. Similarly, Billah *et al.* [58] detected ciprofloxacin in higher concentration in egg white, but in lower concentration in egg yolk during treatment of the birds. Also, Olufemi and Agboola [60] reported a high oxytetracycline residue in edible beef tissues of cattle slaughtered at Akure, in Nigeria, at violating levels beyond the MRL stipulated by WHO. However, of profound concern are circumstances in which diseased animals and animals undergoing therapy could be sold quickly to save funds, or could be slaughtered and used as food or feed for other animals. This causes difficulties in the prophylactic approach to handling epidemic diseases and health risks to consumers, as well as a negative influence on the environment. Van Ryssen reported the use of poultry litter as a feed to farm animals in South Africa, since it is considered as a bulky protein supplement [47,61].

Presence of varying concentrations of antibiotic residues in the different anima1-derived products in some developing countries. Ideally, no anima1 derived product should be consumed unless there is a complete absence of residual amounts of administered drugs. Nevertheless, the intriguing fact is that there are constant detectable levels of residues, identified via the help of markedly improved analytical methods. Therefore, the world regulatory authorities have set the MRL for various veterinary drugs that should be expected and considered safe in foods for human consumption [62,63]. Accor ding to Beyene [64], the diet, age and disease status of the anima1 added to the absorption, distribution, metabolism, and excretion of the drugs, the extra-label drug use and the improper withdrawal times, amongst others, are the risk factors responsible for the development of residues. In this light, farmers are supposed to adhere and implement the right dosages of the antibiotics, as well as observed their withdrawal periods to slaughter and market, in a bid to avoid illegal concentrations of drug residues in the anima1 products. The withdrawal period (clearance or depletion time) defines the length of time required for an anima1 to metabolize the administered antibiotics under normal conditions, and also, the time needed for the antibiotic concentration in the tissues to reduce to a safe and acceptable level described as tolerance. It can equally be referred to the time interval necessary between the last administration of the drug under normal conditions of use to anima1s and the time when treated anima1s can be slaughtered to produce foodstuff safe for public consumption. Depending on the drug product, route of administration and dosage form (even with the same active ingredients), the withdrawal periods vary from a day to several days or weeks, and according to the target animals[47,65].

It has been represented that the adequacy of individuals relates directly with the environment (i.e., their living space and its parts, including plants, anima1s, microorganisms, and others) and the idea of food that they gobble up. Contemplating the creating human people, the changing lifestyle conditions, the food lacks, and the more conspicuous solicitations for the elevated formation of anima1 proteins for human use across the globe, essential practices to upgrade the agrarian and current value are required [47]. Of interest is the essential usage of against disease specialists in cultivating to satisfy the necessities of the rising human people, as the use of hostile to bacteria in this setting has been connected with a couple of benefits. It is in this way speculated that, later on, basically all of the anima1s butchered and ate as food presumably got a chemotherapeutic or a prophylactic subject matter expert or the like [65]. Regardless, the usage of the se meats, milk, and eggs contaminated with hostile to disease developments typically massively influences the prosperity of individuals. These effects may be quick or underhanded, inferable from the high piece of the stores, which most likely accumulated over an excessively long period [65]. They can be shown as medicine exorbitant delicateness reactions, aplastic sickliness, malignant growth causing, mutagenic, immunologic and teratogenic effects, nephropathy, hepatotoxicity, aggravation of the standard vegetation of the processing parcels, a conceptive issue, as well as the improvement of against contamination safe organisms in the stomach [64,65,66].

## Antibiotics' Introduction into the Environment

The unpredictable The indiscriminate and abusive use of antibiotics can result in higher concentrations of antibiotics in the environment, which can be termed as antibiotic pollution. The sources via which antibiotics can be released into the environment are diverse, including the human waste streams, and wastes from veterinary use and livestock farming [67]. Antibiotics used for prophylaxis or therapy in humans contaminate the human waste streams, likewise, the antibiotics used in animals for growth promotion, prevention, and treatment equally contaminate the animals' waste streams. Thus, these are considered as prime sources of antibiotic release into the environment. This is because the administered antibiotics are not fully metabolized, and are released unchanged into the environment, i.e., water, manure or soils. The amount and rate at which the antibiotics are being released into the environments depends on the specific antibiotic and its administered dosage, as well as the species and the age of the animals [68,69]. Nevertheless, these waste streams will contain both the antibiotics and resistance genes; both considered as pollutants, and their fate in the environment differ [70]. Furthermore, antibiotics and their metabolites contained in stockpiled animal manure may seep through the pile to surface and groundwater, and also into the soil. This is especially so for antibiotics with high water affinity or which are water soluble, thus making their spread and ecotoxicity in the environment faster, and widely with the aid of water fluidity [71]. In the same view, antibiotics can be introduced into the environment via soil fertilization with raw animal manure, irrigation with wastewater generated from farm activities, or via accidental release by runoffs from farms [72]. Interestingly, Hamscher *et al.* [15] noted that dust contaminated with antibiotics from farms could equally serve as another route of environmental release of these drugs. Chee-Sanford *et al.* [73] also emphasized the release of antibiotics into the environment via the dispersal of feed and accidental spill of products, as well as discharges. In addition, Sekyere [74] noted that pig farmers in some different districts in the Ashanti Region of Ghana do not secure their antibiotics, thereby making them freely accessible for use and abuse by unauthorized persons and children. Also, the farmers disposed of their used antibiotic containers by merely throwing them into

Drains, refuse dumps, or onto bare ground, instead of burying them as recommended. The author further mentioned that these antibiotics were stored under suboptimal environmental conditions, vulnerable to temperature fluctuations that could accelerate their decomposition, thereby causing a reduction in their concentration and efficacy during administration. Such circumstances promote antibiotic resistance of bacteria living in the gastrointestinal tracts of the animals, due to constant exposure to sublethal levels of these antibiotics, or could even cause prompt administration of an overdose of the antibiotics which is noted to be inefficient. More especially, in commercial and intensive poultry farming, antibiotics may be administered to the entire animal population in feed or water, rather than targeting only the diseased animals. Thus, resistance becomes unavoidable. Interestingly, antibiotics produced naturally by environmental microorganisms, to deter competitors from living space and food, are gradually accumulating in the environment [75,76]. Seemingly, antibiotics are released from their production facilities in high concentrations into the environment. Also, Sahoo and colleagues [77] noted that antibiotics could be found in the natural environment via improper disposal of out-of-date drugs from pharmaceutical shops, and unwanted, expired household pharmaceuticals. Accordingly, these antibiotics released usually consist of different types, and consequently, they do not degrade, all at the same time, i.e., they degrade at different rates in the environment over time by the main elimination processes, including sorption, photo degradation, biodegradation, and oxidation. Albeit, other applied methods, such as adsorption, filtration, coagulation, sedimentation, advanced oxidation processes have been implemented [78,79]. Specifically, several findings have demonstrated the use of composting, and anaerobic and aerobic digestion to cause the reduction of the antibiotic's level in manure, wastewater, and sludge, but these processes vary in efficiency with the category of the antibiotics, the conditions employed for composting, as well as the type of livestock manure [80]. Nonetheless, the presence of these antibiotics in the environment may create selective pressure resulting in antibiotic resistance and also the removal processes, reduce the concentrations of these antibiotics, allowing time for the exposed bacteria to develop resistance which may be presented as stress adaptation, co-selection, cross-resistance, and cross-protection. Moreover, the use of antibiotics urges susceptible bacteria to these antibiotics to develop resistance in a bid to survive. In this view, bacteria prevaricate the inhibitory or bactericidal activities of the antibiotics, and execute resistance by either modifying or altering the target sites (ribosomes) for binding by antibiotics, with the help of ribosomal protection proteins which bind to the ribosomes, thereby preventing the binding and interference of protein synthesis [47,77] or neutralizing antibiotics via enzymes produced by adding acetyl or phosphate groups to the precise site on the antibiotics, or finally, via changing of membrane permeability due to the presence of efflux pumps on the cell membrane. Furthermore, the sensitive bacteria tend to survive in an antibiotic polluted environment by acquiring antibiotic resistance genes from other bacteria or phages (lateral gene transfer), undergo mutations in specific antibiotic gene targets, and by altering of the bacterial surfaces [47,69,80]. However, more show about effect of environmental pollution by antibiotic resistance on SDGs appeared in Figure 4.

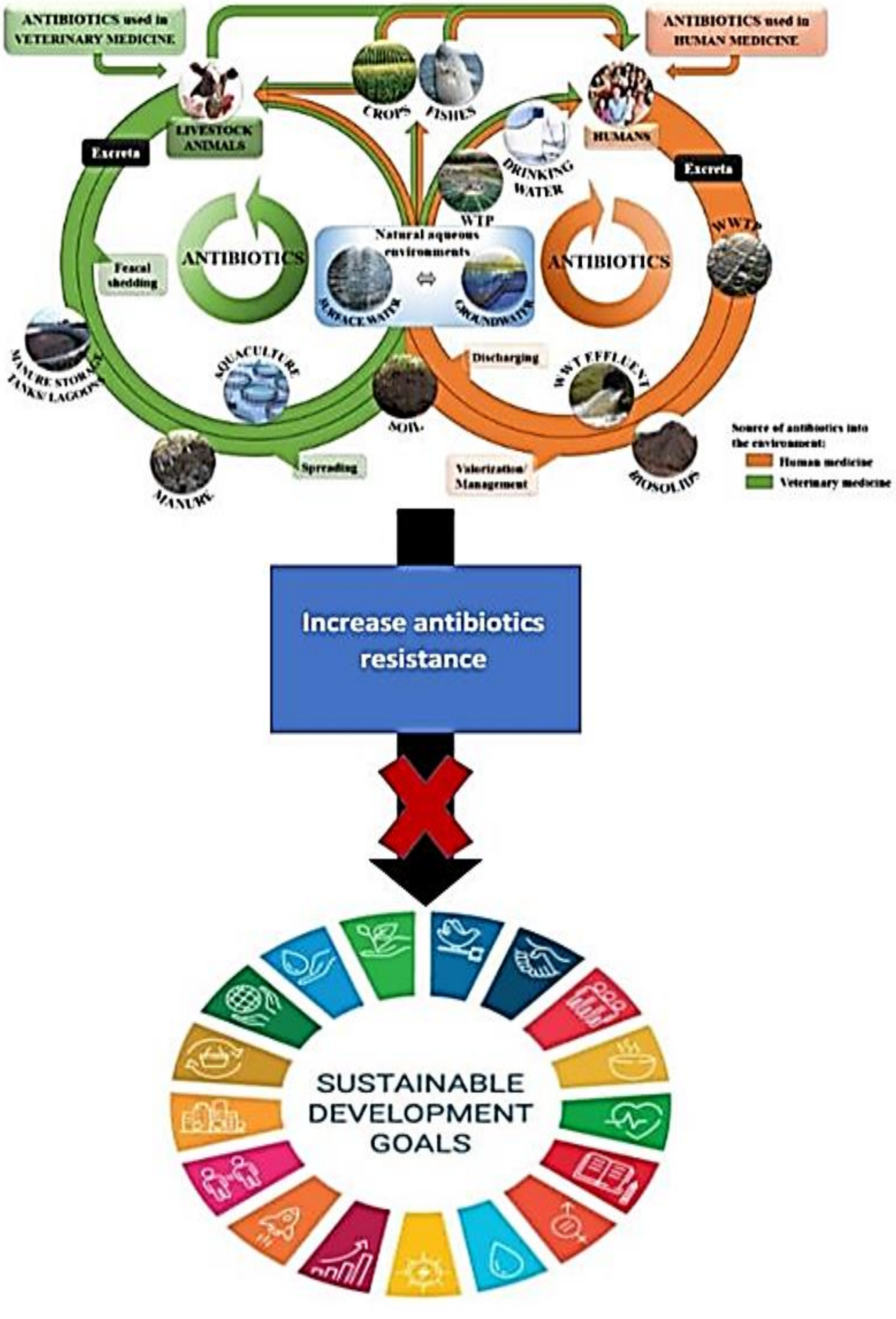

**FIGURE 4.** Sources of environmental pollution by antibiotics resistance bacteria

## CONCLUSION

Antibiotic resistance is perhaps the main issue holding back the SDGs worldwide, but studies on this topic are very limited. The most important reasons for the development and increase of antibiotic resistance is the overuse of antibiotics in fodder and agriculture, in addition to their misuse in the medical aspect. Through this brief review, we noticed that the rate of antibiotic resistance is increasing alarmingly in Iraq, whether at the medical level, poultry or the environment, and this in turn contributes to the decline in the health level and thus the economic level in most countries of the world, and thus we have offended the sustainable development goals that we seek to achieve

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