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Scenario of Antibiotic Resistance in Developing Countries

Mohammad Mahmudul Hassan

Abstract

Antibiotic resistance is an emerging global concern. It is an increasing threat to public health sectors throughout the world. This devastating problem has drawn attention to researchers and stakeholders after a substantial economic loss for decades resulting from the ineffectiveness of antibiotics to cure infectious diseases in humans and animals. The spectrum of antibiotic resistance varies between developed and developing countries due to having variations in treatment approaches. Antibiotic therapy in the developed countries is usually rational and targeted to specific bacteria, whereas in the developing countries, most of the cases, the use of antibiotics is indiscriminate to the disease etiology. In developing countries, many people are not aware of using antimicrobials. They usually get suggestions from drug sellers and quacks who do not have the authorization to prescribe a drug. If registered doctors and veterinarians are asked to prescribe, then dose, course, and withdrawal period might be maintained adequately. Antibiotic resistance transmission mechanisms between agricultural production systems, environment, and humans in developing countries are very complex. Recent research makes a window to find out the global situation of antibiotic use and resistance pattern. The antibiotic resistance scenario in selected developing countries has been summarized in this chapter based on published literature (**Table 1**). This chapter describes the judicial use of antibiotics and discussed maintaining proper antibiotic dose, course, drug withdrawal period, especially on food-producing animals. The book contains a few recommendations, suggested by the national multi-sectoral surveillance committee to avoid antibiotic resistance organisms in livestock and humans in the developing countries.

Keywords: Antibiotics, Antibiotic resistance pattern, prescribed, registered doctors, developing countries

1. Introduction

After discovering the first antibiotic ‘Penicillin’ by Alexander Fleming in 1928, antibiotics played a notable role in saving millions of lives globally. Nowadays, the resistance of antibiotics has intensified significantly throughout the world [1]. Antibiotic resistance is a global problem in both developed and developing countries. The incidence of resistance has increased at an alarming rate in recent years and is expected to increase at a greater rate in the future as antibiotic agents continue to lose their efficiency [2], mostly in many developing or low-and middle-income countries (LMIC). Resistance bacteria do not respect national borders; the development of resistance in the most remote locations can impact the world in a concise time [1]. The widespread use of antibiotics for human and veterinary treatment has led to large-scale dissemination of bacteria with resistance ability to

antibiotics in the domestic animal-wildlife-environmental niche via food chain to humans in most developing countries, including Bangladesh [3]. Resistance bacteria are found in the stool and as intestinal flora of healthy individuals that are serving as reservoirs for resistance to multiple antimicrobials [4]. Antibiotics are a mainstay in the treatment of bacterial infections, and thus the worldwide increase in antibiotic-resistance bacteria is of major concern. The problem of antibiotic resistance is not restricted to pathogenic bacteria—it also involves the commensal microbiota, which may become a major reservoir of resistance strains of bacteria [5]. *Escherichia coli* is commonly found in the intestinal tract of humans and animals and can also be concerned with human and animal infectious diseases. Animal food products are important sources of *E. coli* as fecal contamination of processed animal carcasses at the slaughterhouse is frequently occurred. These resistance microorganisms and their possible resistance determinants may be transmitted to humans if these animal origin foods are improperly washed, cooked, or otherwise mishandled [6]. Although most isolates of *E. coli* are nonpathogenic, they are considered an indicator of fecal contamination in food. About 10 to 15% of intestinal coliforms are opportunistic and pathogenic serotypes and cause a variety of lesions in immunocompromised hosts such as animals and humans [7]. Among the diseases that they cause, some are often severe and sometimes lethal such as- meningitis, endocarditis, urinary tract infection, septicemia, and epidemic diarrhea in human, and yolk sac infection, omphalitis, cellulitis, swollen head syndrome, coligranuloma, and colibacillosis in birds [8]. Furthermore, salmonellosis is one of the most frequent foodborne diseases in humans in almost all countries, and *Salmonella enterica ssp. enteritidis*, followed by *typhimurium*, represent the most frequently isolated serotypes [9]. The most common disease syndromes caused by *Salmonella* serotypes in humans are typhoid fever and enteritis [10], and in avian species, *Salmonella* organism causes fowl typhoid and pullorum disease [11]. *Salmonella typhimurium* and *S. dublin* appear to be the commonest serotypes isolated from cattle, although the distribution of these 2 serotypes differs between countries, and the *Salmonella* organism predominantly causes bovine salmonellosis [12]. *S. aureus* causes superficial skin lesions and localized abscesses in a wide range of host animals. *S. aureus* causes deep-seated infections, such as osteomyelitis and endocarditis and more serious skin infections [13]. *S. aureus* is a major cause of hospital-acquired (nosocomial) infection of surgical wounds and, with *S. epidermidis*, causes infections associated with indwelling medical devices [14]. It also causes food poisoning by releasing enterotoxins into animal originated food. *S. aureus* causes toxic shock syndrome by release of superantigens into the blood stream. *S. saprophiticus* causes urinary tract infections in human, frequently in female population [15]. Over the past decade, the changing pattern of resistance against bacteria has depicted the need for new antimicrobial agents [2]. Developing countries are more vulnerable to antimicrobial resistance issues for their underprivileged health care infrastructure, unregulated agricultural production process, poor sanitation facilities and widespread misuse of antibiotics. In addition, weak monitoring system and improper implementation of legislative practices on antibiotic sell and uses in the agricultural production systems, increases the possibilities of resistant bacteria in the developing countries. The scenario of antibiotic resistance pattern worsen in developing countries as they use antibiotic indiscriminately in clinical treatments and food animal production system as well. With many bacterial causing diseases in human and animal in developing countries, this chapter will be focusing on three most common genera of bacteria viz. *Escherichia*, *Salmonella* and *Staphylococcus* that are posing threat to public health by gradually getting resistance against many antibiotics. The aim of this chapter is to identify the scenario of antibiotic resistance pattern in developing countries based on published literature (**Table 1**) and compile them to find out the overall spectrum of antibiotic resistance.

Country	Host	Bacteria			Author
		<i>Escherichia coli</i>	<i>Salmonella</i> spp.	<i>Staphylococcus</i> spp.	
Pakistan	Human	Amoxicillin, Ampicillin, Aztreonam, Cephalosporin, Cefotaxime, Ceftriaxone Ciprofloxacin, Floroquinol, Trimethoprim-sulfamethoxazole		Amoxicillin, Ampicillin, Amikacin, Cefoxitin, Chloramphenicol, Ciprofloxacin, Clindamycin, Co-trimoxazole, Doxycycline, Erythromycin, Fusidic acid, Gentamicin, Penicillin, Teicoplanin, Tigecycline, Levofloxacin, Linezolid, Vancomycin	[16–18]
	Poultry and poultry products	Ampicillin, Ciprofloxacin, Colistin, Tetracycline	Pefloxacin	Cefoxitin, Gentamicin, Oxacillin, Penicillin, Levofloxacin, Moxifloxacin	[19–22]
	Livestock			Amikacin, Amoxicillin, Cefoxitin, Ampicillin, Oxacillin, Augmentin, Cefotaxime, Chloramphenicol, Ciprofloxacin, Clindamycin, Enrofloxacin, Erythromycin, Fosfomycin, Gentamycin, Kanamycin, Linezolid, Ofloxacin, Penicillin, Rifampicin, Teicoplanin, Trimethoprim, Vancomycin	[23, 24]
India	Human	Amikacin, Ampicillin, Ampicillin, Augmentin, Cefepime, Cefoxitin, Cefoperazone, Cefotaxime, Quinolones, Ceftazidime, Ceftriaxone, Colistin, Cefuroxime, Cephalosporins, Ciprofloxacin, Co-trimoxazole, Ertapenem, Meropenem, Gentamycin, Imipenem, Nalidixic acid, Nitrofurantoin, Norfloxacin, Piperacillin, Streptomycin, Sulfamethoxazole, Tetracycline	Ampicillin, Azithromycin, Ceftriaxone, Cephalosporins, Chloramphenicol, Fluoroquinolones, Trimethoprim	Ciprofloxacin, Clindamycin, Co-trimoxazole, Erythromycin, Gentamicin	[25–35]
	Poultry and poultry products	Amoxicillin, Ampicillin, Cephalixin, Colistin, Cefoxitin, Chloramphenicol, Neomycin, Ciprofloxacin, Co-trimoxazole, Trimethoprim, Amoxicillin, Erythromycin, Rifamycin, Streptomycin, Doxycycline, Sulfamethoxazole, Nalidixic acid, Tetracycline, Gentamicin	Sulphamethizole, Chloramphenicol Amikacin Ceftazidime, Oxytetracycline, Nalidixic acid	Penicillin, Ciprofloxacin, Tetracycline, Erythromycin Ampicillin, Tetracycline Amoxicillin, Erythromycin Polymyxin-B, Cefoxitin Novobiocin, Oxacillin	[36–47]

Country	Host	Bacteria			Author
		<i>Escherichia coli</i>	<i>Salmonella</i> spp.	<i>Staphylococcus</i> spp.	
	Livestock	Meropenem, Imipenem, Ertapenem		Methicillin, Penicillin, Ampicillin, Kanamycin, Cefotaxime, Sulphadizine Amoxicillin	[48–51]
	Pet animals			Amoxicillin, Penicillin G, Methicillin, Cloxacillin, Ampicillin, Cephalothin, Cefuroxime, Ceftriaxone, Clavulanate, Neomycin, Streptomycin, Furazolidone, Nitrofurantoin, Ciprofloxacin, Erythromycin, Oleandomycin, Azithromycin, Doripenem, Lincomycin, Clindamycin, Sulfafurazole, Sulfadiazine, Chloramphenicol, Novobiocin, Vancomycin	[50, 52]
	Food and food products	Colistin, Cefotaxime, Ceftazidime, Gentamicin, Tetracycline, Amoxicillin		Oxacillin, Cefoxitin, Penicillin G, Cephalixin, Ampicillin, Methicillin, Kanamycin, Gatifloxacin, Ciprofloxacin	[53–56]
	Environment	Amoxicillin, Ciprofloxacin, Nalidixic acid, Ceftazidime, Cephalosporin, Penicillin, Cefuroxime, Erythromycin, Tetracycline, Ceftazidime, Cefotaxime, Gentamicin, Trimethoprim			[57–60]
	Bangladesh				
	Human	Colistin, Nalidixic Acid, Cefixime, Co-trimoxazole, Ceftazidime, Gentamicin, Amikacin, Imipenem, Ciprofloxacin, Azithromycin, Cefuroxime, Cefotaxime, Ceftriaxone, Meropenem, Nitrofurantoin, Levofloxacin, Meropenem	Ciprofloxacin, Ceftriaxone, Azithromycin, Clindamycin	Nalidixic Acid, Cefixime, Meropenem, Oxacillin, Gentamicin, Ceftazimid, Tocefoxitin, Etracylcin, Cefoxitin, Ciprofloxacin, Chloramphenicol, Clindamycin, Cefotaxime, Levofloxacin	[13, 14, 61–68]
	Poultry	Ampicillin, Tetracycline, Trimethoprim, Nalidixic acid			[7]

Country	Host	Bacteria			Author
		<i>Escherichia coli</i>	<i>Salmonella</i> spp.	<i>Staphylococcus</i> spp.	
	Food and food products	Erythromycin, penicillin, Vancomycin, Novobiocin, Tetracycline, Ceftriaxone, Ampicillin, Azithromycin, Bacitracin, Kanamycin, Nalidixic acid, Sulfamethoxazole	Ampicillin, Azithromycin, Erythromycin, Doxycycline, Sulphonamide, Azithromycin, Novobiocin, Oxytetracycline, Cephadrine, Amoxicillin, Erythromycin, Tetracycline, Erythromycin, Vancomycin, Rifampicin, Sulfamethoxazole, Bacitracin	Ampicillin, Chloramphenicol, Nitrofurantoin, Oxytetracycline, Oxytetracycline, Amikacin, Erythromycin, Oxacillin, Ciprofloxacin, Amoxicillin, Trimethoprim, Gentamicin, Penicillin, Erythromycin	[69–74]
	Environment	Ceftazidime, Gentamycin, Tetracycline, Imipenem, Ciprofloxacin, Chloramphenicol, Amoxycillin, Erythromycin, Azithromycin, Streptomycin, Norfloxacin, Cefepime, Cefixime	Ceftazidime, Gentamycin, Imipenem, Ciprofloxacin, Chloramphenicol, Cefoxitin, Tetracycline, Rifampicin, Ampicillin	Ceftazidime, Gentamycin, Azithromycin, Tetracycline, Imipenem, Ciprofloxacin, Chloramphenicol, Methicillin, Vancomycin	[75–77]
Thailand	Human	Trimethoprim/sulfamethoxazole, Colistin, Amoxicillin, Gentamicin, Cefazolin, Cefotaxime, Ceftazidime, Ceftriaxone, Cefixime, Cefalexin, Nalidixic acid, Ciprofloxacin, Norfloxacin, Ofloxacin, Doxycycline, Nitrofurantoin, Ampicillin, Oxacillin, Amikacin, Aztreonam, Cefotaxime, Meropenem, Piperacillin, Chloramphenicol, Amoxycillin, Cotrimoxazole	Trimethoprim-Sulfamethoxazole, Cefotaxime, Ceftazidime, Ceftriaxone, Ceftazidime, Norfloxacin, Nalidixic acid, Tetracycline, Gentamicin, Ampicillin, Ciprofloxacin, Chloramphenicol, Cotrimoxazole	Fosfomycin, Methicillin, Cefoxitin, Penicillin, Oxacillin, Mupirocin, Rifampicin, Cotrimoxazole, Ciprofloxacin, Chloramphenicol, Cefazolin, Clindamycin, Cephalexin, Trimethoprim, Amikacin, Ampicillin, Amoxicillin, Tetracycline, Cloxacillin, Cefotaxime, Meropenem, Piperacillin, Gentamicin, Ofloxacin, Erythromycin	[78–87]
	Livestock			Methicillin, Penicillin, Rifampin, Novobiocin, Tetracycline, Clindamycin, Oxacillin, Linezolid, Erythromycin, Cefoxitin, Kanamycin, Gentamicin, Trimethoprim, Ciprofloxacin, Levofloxacin	[88]
	Food and food products	Ampicillin, Cefotaxime, Cefpodoxime, Aztreonam, Ceftazidime, Imipenem, Gentamicin, Amoxicillin, Ceftriaxone, Nalidixic acid, Amoxicillin, Ampicillin, Cefepime, Amikacin, Doxycycline, Tetracycline, Ciprofloxacin, Co-trimoxazole, Colistin sulfate, Cefoxitin, Enrofloxacin,			[89, 90]

Country	Host	Bacteria			Author
		<i>Escherichia coli</i>	<i>Salmonella</i> spp.	<i>Staphylococcus</i> spp.	
		Erythromycin, Chloramphenicol, Ceftazidime, Trimethoprim			
	Environment	Penicillin G, Vancomycin, Erythromycin, Ampicillin, Tetracycline, Chloramphenicol, Streptomycin, Neomycin, Kanamycin, Cefazoline, Cefotaxime, Ceftazidime, Gentamicin, Nalidixic acid	Tetracycline, Ampicillin, Streptomycin, Tetracycline, Trimethoprim, Gentamicin, Ciprofloxacin, Nalidixic acid, Penicillin G, Neomycin, Vancomycin, Erythromycin, Kanamycin, Chloramphenicol	Methicillin	[91–94]
Nepal	Human	Amikacin, Ampicillin, Cefotaxime, Levofloxacin, Ciprofloxacin, Gentamicin, Ampicillin, Cefoxitin, Trimethoprim, Nitrofurantoin, Amoxycylav, Piperacillin, Ofloxacin, Cefotaxime, Colistin, Meropenem, Nitrofurantoin, Norfloxacin, Imipenem, Fosfomycin, Cefixime, Piperacillin, Cefoperazone, Nitrofurantoin, Meropenem, Co-trimoxazole, Ceftriaxone, Levofloxacin, Ceftazidime, Chloramphenicol, Nalidixic acid, Piperacillin, Tetracycline	Ciprofloxacin, Ampicillin, Chloramphenicol, Co-trimoxazole, Streptomycin, Nalidixic acid, Trimethoprim-Sulfamethoxazole, Ceftriaxone	Ampicillin, Ceftriaxone, Cefotaxime, Cefixime, Nalidixic acid, Piperacillin, Penicillin, Erythromycin, Clindamycin, Cefoxitin, Chloramphenicol, Ampicillin, Ciprofloxacin, Cotrimoxazole, Cefoxitin, Gentamicin, Tetracycline, Teicoplanin, Cephalexin, Cloxacillin, Erythromycin, Linezolid, Vancomycin, Ampicillin, Azithromycin	[15, 95–107]
	Poultry	Ampicillin, Amikacin			[108]
	Food and food products	Amoxicillin, Tetracycline, Cefotaxime, Nalidixic acid, Cotrimoxazole, Gentamycin	Tetracycline, Chloramphenicol, Nalidixic acid, Amoxicillin	Amoxicillin, Nalidixic acid, Cefotaxime, Tetracycline, Azithromycin, Cotrimoxazole	[109, 110]
Nigeria	Human	Cefuroxime, Cefotaxime, Amoxicillin, Imipenem, Ceftriaxone, Cefalexin, Ampicillin, Ciprofloxacin, Nalidixic Acid, Gentamycin, Nitrofurantoin, Kanamycin, Chloramphenicol, Pefloxacin, Ofloxacin, Streptomycin, Ceftazidime, Tetracycline, Amoxicillin, Trimethoprim, Co-trimoxazole	Ampicillin, Cefotaxime, Chloramphenicol, Trimethoprim-sulfamethoxazole, Ofloxacin, Ciprofloxacin, Co-trimoxazole, Tetracycline, Eftazidime, Ceftriaxone	Streptomycin, Gentamycin, Tetracycline, Cotrimoxazole, Erythromycin, Cloxacillin, Chloramphenicol, Augmentin, Imipenem, Ceftriaxone, Cefoxitin, Ciprofloxacin, Erythromycin, Cefalexin Co-trimoxazole, Nalidixic Acid, Ampicillin, Vancomycin, Azithromycin, Cefuroxime, Amoxicillin, Ceftazidime	[111–120]

Country	Host	Bacteria			Author
		<i>Escherichia coli</i>	<i>Salmonella</i> spp.	<i>Staphylococcus</i> spp.	
	Poultry	Tetracycline, Ampicillin Nitrofurantoin, Chloramphenicol, Penicillin, Ampicillin, Amoxicillin, Cloxacillin, Augmentin, Tetracycline, Streptomycin, Gentamicin, Erythromycin, Cotrimoxazole, Nalidixic Acid		Penicillin, Ampicillin, Amoxicillin, Cloxacillin, Augmentin, Tetracycline, Streptomycin, Gentamicin Chloramphenicol, Ofloxacin, Erythromycin, Cefuroxime, Cefoxitin, Amoxicillin, Ceftriaxone	[121–123]
	Livestock	Cloxacillin, Penicillin, Teicoplanin, Sulphadimidine, Ampicillin, Tetracycline, Nalidixic acid, Trimethoprim	Amoxicillin, Enrofloxacin	Ampicillin	[124, 125]
	Environment	Ceftazidime, Cephalexin, Ceftriaxone, Cefotaxime, Cephalexin, Tetracycline, Lipocaine, Augmentin, Ceftazidime, Cefuroxime, Ampicillin, Chloramphenicol, Amoxicillin-clavulanic acid, Ciprofloxacin, Ampicillin, Augmentin, Gentamicin	Gentamycin, Ofloxacin, Amoxycillin, Ciprofloxacin, Tetracycline, Pefloxacin, Lipocaine, Ceftazidime, Ceftriaxone, Cefotaxime, Cefotaxine, Cephalexin, Augmentin, Cefuroxime, Ampicillin, Colistin, Ofloxacin, Cotrimoxazole, Ciprofloxacin, Nitrofurantoin Trimethoprim, Ceftazidime	Ceftazidime, Cephalexin, Ceftriaxone, Cephalexin, Tetracycline, Lipocaine, Amoxicillin	[126–132]
Brazil	Poultry		Amoxicillin, Ceftiofur, Ciprofloxacin, Gentamicin, Chloramphenicol, Tetracycline, Sulfafurazole, Enrofloxacin, Sulfonamide, Spectinomycin, Trimethoprim		[133, 134]
	Human		Ampicillin, Ampicillin, Ceftriaxone, Ceftiofur, Chloramphenicol, Ciprofloxacin, Enrofloxacin Tetracycline, Trimethoprim		[135]
	Food and food products		Sulfonamides, Streptomycin, Tetracycline, Gentamicin, Ceftriaxone, Trimethoprim		[136, 137]

Table 1.
Summary of antibiotic resistance scenario of three bacteria in different samples from selected developing countries.

2. Main text

2.1 Practical scenario of antibiotic resistance pattern in developing countries

An organized literature search approach was used to detect all published studies reporting resistance bacteria in human samples and foods of animal origin in some selected developing countries. PubMed, Science Direct, and Google Scholar were searched for relevant studies published until 2019. The search terms have been adopted into outcome, population, descriptive, and area categories. Based on the study objectives, specific Boolean words were developed using “AND” and “OR”. Some modification has been conducted based on the search engine requirements, and advanced search criteria have been used to search Google scholar. The papers were downloaded using the Chattogram Veterinary and Animal Sciences University (CVASU) library network. The Boolean words of each category were combined using “AND”, whereas “OR” was used to join the term within a category. Data was extracted and recorded for study location, citation, first author, title, time of study, year of publication, type of specimen, sample size, number of positive specimens, amount of antibiotics, specific antibiotic sensitivity or resistance level percentages, methods of detection used, culturing techniques and resistance genes. Resistance of *E. coli* was mostly seen in humans and poultry compared to *Salmonella* and *Staphylococcus*, and the most resistance drug was Ampicillin and Ciprofloxacin in Pakistan. Furthermore, resistance of salmonella was seen in human samples with Ampicillin, Trimethoprim, and Ceftriaxone. Pefloxacin was resistance to *Salmonella* in derived from poultry. Resistance staphylococcus were observed in cattle, buffalo, poultry, and table egg to antibiotics Penicillin, Ampicillin, Oxacillin, Ciprofloxacin, Trimethoprim, Gentamicin, Linezolid, Erythromycin, Clindamycin, Amikacin, Vancomycin, Chloramphenicol and Cefoxitin. In India, resistance of *E. coli* was mostly seen in poultry, and the human was in second position and the drugs: Ciprofloxacin, Ampicillin, Amoxicillin, Trimethoprim, Gentamicin, Co-trimoxazole and Sulfa-methoxazole were found resistance. The highest resistance of Salmonella was detected in poultry with a higher level of Oxytetracycline. In the case of *Staphylococcus* spp., excessive resistance was seen in poultry and cattle with commonly used antimicrobials: Oxacillin, Penicillin G, Ampicillin, Methicillin, Amoxicillin, Erythromycin, Methicillin, Cloxacillin, and Kanamycin. In Bangladesh, the highest antibiotic resistance of *E. coli* was seen in human, and the most resistance drugs are Tetracycline, Ampicillin, Nalidixic acid, Trimethoprim-Sulfamethoxazole, Ciprofloxacin, and Ceftriaxone. Moreover, *Salmonella* resistance to Azithromycin, Ampicillin, and Erythromycin was detected in humans. Resistance of *Staphylococcus* was observed in humans, and the most resistance antibiotics are Ciprofloxacin, Gentamicin, Chloramphenicol, Tetracycline, and doxycycline. In Thailand, the highest resistance of *E. coli* was noticed in human and pig, and the most resistance antibiotics are Ampicillin, Ceftazidime, Tetracycline, Gentamicin, Ciprofloxacin, Norfloxacin, Clavulanic acid, Doxycycline and Colistin sulfate. Research revealed that resistance *Salmonella* was detected in the Thai human population alongside highly resistance antibiotics: Ampicillin, Tetracycline, Ciprofloxacin, Chloramphenicol, and Trimethoprim. On the other hand, resistance *Staphylococcus* was found in humans with higher drug resistance, and the antibiotics were Doxycycline, Gentamicin, Cefoxitin, Ceftriaxone, Methicillin, Tetracycline, Erythromycin, Penicillin, and Cefoxitin. In Nepal, higher resistance of *E. coli* was identified in humans, and many bacteria became resistance, including Doxycycline, Gentamicin, Cefoxitin, Ceftriaxone, Methicillin, Tetracycline, Erythromycin, Penicillin, and Cefoxitin. Besides, resistance salmonella was recognized in humans and foods with resistance antibiotics such as Ampicillin, Ciprofloxacin, Chloramphenicol,

Co-trimoxazole, Nalidixic acid, and Amoxicillin. However, antibiotics such as Amikacin, Gentamicin, Ciprofloxacin, Amoxicillin, Tetracycline, Erythromycin, Cefotaxime, Oxacillin, Cefoxitin and Co-trimoxazole recorded resistance against *Staphylococcus* in Nepal. In Nigeria, the highest resistance of *E. coli* was reported in human and resistance antibiotics were Tetracycline, Ceftazidime, Cefotaxime, Ceftriaxone, Ciprofloxacin, Gentamycin, Sulfamethoxazole, Penicillin, Ampicillin, Amoxicillin, Cloxacillin, Augmentin and Amoxicillin. Moreover, resistance *Salmonella* was found in the water source in the environment to antibiotics Ampicillin, Cefotaxime, Ceftazidime, Ciprofloxacin, Sulfamethoxazole-trimethoprim, and Tetracycline. Moreover, the resistance *Staphylococcus* was seen in humans and the environment, and the resistance antibiotics were Ceftriaxone, Gentamicin, Erythromycin, Co-trimoxazole, Chloramphenicol, Tetracycline, Streptomycin, Cephalixin, and Ampicillin. Finally, in Brazil, antimicrobial-resistance (AMR) *E. coli* were recorded in water source, and the resistance antibiotics were Ampicillin, Cephalixin, Amoxicillin, and Polymyxin. On the other hand, resistance salmonella was detected in poultry with resistance antibiotics such as Gentamicin, Sulfonamide, Trimethoprim, Ampicillin, and Chloramphenicol, Ciprofloxacin, Enrofloxacin, Tetracycline, and Ceftriaxone. A great majority of antimicrobial classes that are already resistance to the bacteria are used in humans and animals, including domestic animals, poultry and other birds, and commercial farm fishes. These findings of AMR in the agricultural production system, environment, and humans from developing countries pose a threat to the global context.

2.2 Tale of AMR in developing countries

Antibiotics are considered to safeguard against infectious diseases caused by pathogenic bacteria, but unfortunately, antimicrobial resistance becomes a burden in humans, animals, and the environmental niche worldwide. It happened due to the indiscriminate, inappropriate, and unregulated use of antibiotics in animal and agricultural production systems and humans. In developing countries, AMR is overburdened by antibiotics as growth promoters by the farmers, feed dealers, drug sellers, and the lack of approved legislation by the respective government authorities [138]. However, some countries have written and approved legislation, but appropriate implementation and systematic monitoring are not noticed. Multi-drug resistance (MDR) bacteria are increasing day by day at every corner of developing countries and escalate treatment costs. In a recent WHO report, it is speculated that about 10 million people will die, and 100 trillion USD from the world economy will be lost for AMR by 2050 if no effective measures are taken [139]. Humans are mostly suffering in developing countries due to the ineffectiveness of antibiotics to microbes. *E. coli*, *Salmonella* spp. and *Staphylococcus* spp. are now resistance to the commonly used antibiotics and some higher generation antibiotics such as 3rd generation cephalosporins. This might be due to cross-contamination with hospital equipment, animal originated food, and mixing of medical and veterinary hospital effluents in the environments [16, 26, 31, 67, 78, 97].

In highly populated developing countries where there is a shortage of physicians, the people seek to take drugs, including antibiotics, by their own decision or prescription from drug sellers or quacks. Even in the rural area, it is hard to find a licensed doctor or veterinarian to treat people and animals and keep faith in a quack or village doctor. Those quacks, health assistant village doctors, and drug sellers prescribe different antibiotics even for common symptoms such as colds, coughs, and diarrhea, where a simple, supportive treatment course would be enough. Self-medication, both in the human and veterinary sectors, is another major problem for generating antimicrobial resistance. In some cases, licensed doctors and

veterinarians are biased to treat antimicrobials due to various pharmaceutical companies [138]. Those unnecessary prescriptions and a broad spectrum of antibiotics in animals and humans have already brought a great disaster in most developing countries [29]. Poor sanitation and hygiene are essential factors for transmitting resistance organisms from animals (mainly food and pet animals) and environment to humans. Countries like Bangladesh, Brazil, India, and Nigeria are mostly suffering from sanitation and hygiene management issues for growing AMR [140]. There is a chance of nosocomial infection in hospital settings, as many hospitals have no facilities for waste disposal and wastewater treatment [14]. There is also a high risk of spreading resistance microbes from patients to their surroundings, especially to caregivers or family members.

Poultry meat is one of the topmost widely accepted food worldwide as a cheap protein source, and more than 90 billion tons of chicken meat produce each year. A large variety of antimicrobials are used in poultry production systems for disease prophylaxis and used as growth promoters to increase growth and productivity [8], which accelerate the expansion of resistance in pathogens and different commensals. Therefore, human health is a great concern with the emergence of resistance pathogens from poultry and AMR residue from poultry meat and eggs [18, 74]. Food producing animals or livestock has, also affected by AMR due to not maintaining proper dose, treatment interval and duration in therapeutics, metaphylactic and prophylactic treatment, and withdrawal periods of different antimicrobials. Growth promoter is another influential factor-like poultry production system in most developing countries [88, 124, 135]. Human-livestock interaction is another vital factor for transmitting resistance microorganisms from food and pet animals to humans or vice versa.

An agreement should be maintained among the scientific community to stop the excessive use of antimicrobials in food animal production system. Thus, it will help to limit the AMR on human health. Otherwise, AMR in food animal pathogens will unavoidably effect on treatment failure of livestock and poultry diseases. As a result, pathogen transmission on the environment will increase, and production loss will be soared, and the economy of developing countries will be hindered. In developing countries, the environment is also contaminated with high levels of resistance organisms and AM residues derived from human, livestock, and poultry waste [124]. Hospital, both human and veterinary wastewater, is the potential source of AMR.

Water is the mainstream potential reservoir of antimicrobial resistance as wastewater contaminated rivers, ponds, and other water bodies. Medical and veterinary hospital effluents (with different types of resistance organisms) were directly drained to the nearby water bodies and contaminated the fishes ultimately consumed by humans. Poor sanitation and hygiene management bring pathogens close to each other's species and accelerate the horizontal resistance gene transmission [140]. Ceftazidime, Cefpodoxime-resistance bacteria were isolated in Nigeria. Moreover, Azithromycin, Tetracycline, Gentamicin, Ciprofloxacin, Cefotaxime, Chloramphenicol, Cefoxitin, and Oxacillin resistance *Staphylococcus aureus* found in both human and veterinary hospital drainage water in Bangladesh [14, 121]. Research in Thailand detected Cefazoline, Cefotaxime, Ceftazidime, Gentamicin, Tetracycline, Chloramphenicol, Kanamycin, and Nalidixic acid resistance *E. coli*, which indicate the vulnerability of AMR in the environment [94]. In food animals in developing countries, antibiotics are frequently used in food and water to the entire group for a prolonged time and often at sub-therapeutic doses. These conditions favor the selection and spread of resistance bacteria within and between animals as well as to humans through food consumption and other environmental pathways.

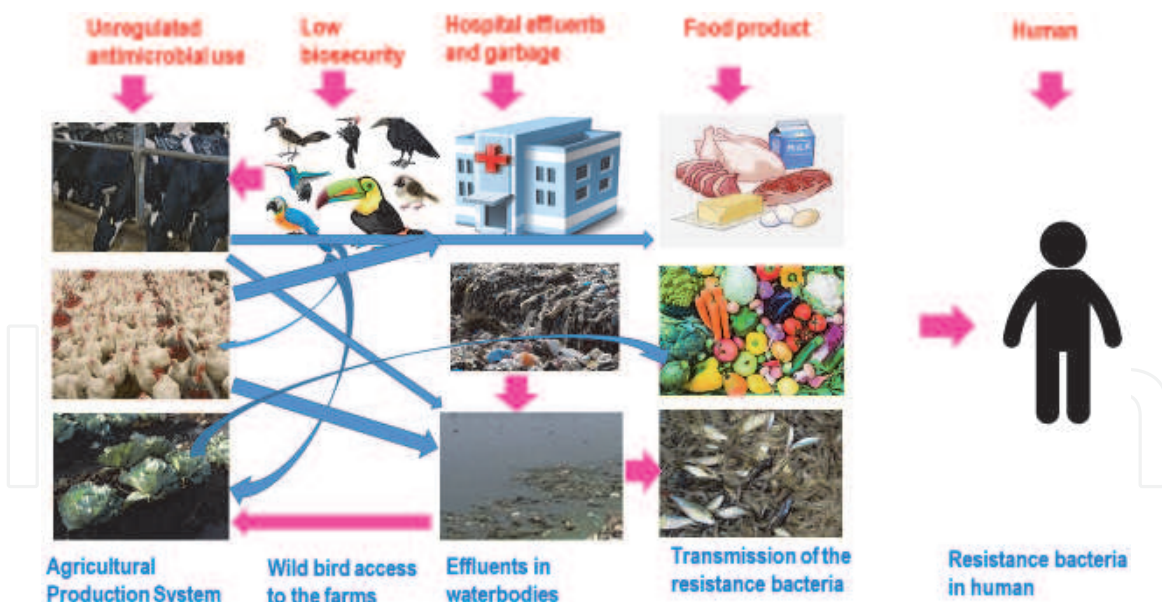


Figure 1.
 Complex transmission dynamics of AMR between agricultural production system, environment, and human
 (credit: MM Hassan; created by using online materials).

To reduce the AMR in developing countries, proper rules and regulations for antibiotic use in humans and animals should be followed. Only registered physicians will prescribe antibiotics for humans; livestock and poultry farming will be conducted with veterinary supervision. Buying and selling antimicrobials should be restricted without prescription. National surveillance with a multi-sectoral committee in the “One Health” concept would be a useful measure for monitoring antibiotic use in animals and humans.

2.3 Transmissions dynamics of AMR in developing countries

Due to the unregulated use of antibiotics in agricultural production systems in developing countries, bacteria become resistance to single or multiple antimicrobials. These resistance bacteria or genes are transmitted directly from agricultural food products such as meat, milk, egg, fish, and vegetables to humans. Hospital effluents, garbage, livestock effluents contaminated with resistance bacteria drained to the nearby water body where fishes raised, and this water is also used in the crop fields for their productions. It is another way to transmit resistance bacteria from crops and fish to humans. The fate of AMR bacteria in the agricultural production system and environment is still unclear. Could AMR bacteria and mobile genetic elements carrying the resistance genes further evolve after their transfer to the environment? There are knowledge gaps regarding the magnitude and dynamic nature of spread regarding antimicrobial resistance bacteria and antimicrobial resistance genes within and between different ecological niches on farms, which deserve to be considered when assessing antimicrobial resistance bacteria’s transmission the food chain. Moreover, the transmission pathway of resistance bacteria between the agricultural production systems, environment, and humans in developing countries is very complex and given in **Figure 1**.

3. Conclusions

Antimicrobial resistance has shown a profound surge in developing countries as well as around the globe. In developing countries, antibiotic resistance on different

microorganisms, especially *E. coli*, *Salmonella* spp. and *Staphylococcus* spp. are skyrocketing in different agricultural production systems, environments, and humans due to the poor management and practices, which is truly terrifying. Further studies are required based on the international standard to evaluate AMR nationwide in every developing country. It is essential to sketch a proper multi-sectoral surveillance plan to research, diagnose and execute necessary steps for combating against multi drugs resistance hitch. There is a need for detailed system biology analysis of resistance development *in-situ*. Metagenomic analysis of bacterial pathogens from diverse sources, including hospitals, veterinary clinics, agricultural production systems including live animal production, marketing, processing, and waste water plants, might underline bacterial pathogens' evolution for integrin-mediated resistance gene transfer in resistance evolution. One Health approach by each government among all stakeholders could promote better exercise and antimicrobial stewardship.

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Conflict of interest

Not exist.

Author details

Mohammad Mahmudul Hassan

Department of Physiology, Biochemistry and Pharmacology, Faculty of Veterinary Medicine, Chattogram Veterinary and Animal Sciences University, Khulshi, Chattogram, Bangladesh

*Address all correspondence to: miladhasan@yahoo.com

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