

Antimicrobial Resistance: A Rising Global Threat to Public Health

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Abstract: The discovery of penicillin marked a revolutionary step in modern medicine, leading to the development of various chemotherapeutic agents that transformed the treatment of life-threatening diseases. However, the accelerating emergence of antimicrobial resistance poses a formidable global threat to public health, fueled by the indiscriminate use of antibiotics across various fields such as the health sector, agriculture, vet medication, etc. This review outlines the possible mechanism of resistance development in various pathogens such as efflux pumps, biofilm formation, downregulation of receptors, and mutation under species selection pressure. It addresses the role of the environment, that is often overlooked in the circulation of antibiotic remnants through animal waste, soil, the food chain, and the gene exchange process. The One Health framework integrates health with multidisciplinary surveillance and intervention strategies for an effective check on the phenomenon of antimicrobial resistance. Various current strategies have been considered, taking from antimicrobial stewardship to public awareness for addressing the current problem. There are various alternatives to conventional antibiotics discussed that can potentially minimise their usage and mitigate reliance on antimicrobial agents. This article provides a comprehensive overview to address the current issue with possible strategies and support future research to tackle AMR.

Keywords: Anti-microbial agents, Defined daily dose, DDD, MDR, Multi drug resistance, OH, One Health, AMR stewardship, AWaRe system

Introduction

The world stands on the brink of a potential pandemic due to unchecked antibiotic usage accelerating the spread of antimicrobial resistance. Antimicrobial therapy refers to the utilization of antimicrobial drugs for the cure, treatment, or mitigation of contagious diseases, including drugs like β -Lactam inhibitors, macrolides, streptomycin, anti-tubercular drugs, anti-viral drugs, etc.¹ No wonder they have been found to exhibit extensive applications across a broad spectrum of medical scenarios from the treatment of common infections to intricate and rare diseases that require specialized therapeutic interventions such as used in treatment of sepsis, which is the primary cause of acute kidney damage, organ transplants, cancer, and open heart surgeries in critically sick patients.^{2,3} However, over time, the continual utilization of these drugs leads to a phenomenon called antimicrobial resistance (AMR), where pathogens no longer respond to these drugs.¹ Although AMR is a naturally occurring phenomena, the extensive misutilization of antibiotics in veterinary settings and public healthcare systems provide a significant and growing risk by making the process faster. This makes the infection harder and more complex to treat. The disease becomes more challenging.⁴ In this way more higher category antibiotics will have to be employed in common ailments that might become ineffective in the case of other serious infections.¹ The strains of pathogens have become resistant that may include several factors like inappropriate uses, improper dosing frequency, food crops and poultry being treated with antibiotics for prevention of disease.^{5,6} Anti-microbial resistance (AMR) has been responsible for 1.27 million global deaths, leading to a significant increase in healthcare costs, reaching up to 1 trillion US dollars in 2019. The emergence of AMR has been driven by the misuse of essential antibiotics in humans, plants, and animals, which induces genetic variation in microbial species, making it more challenging to treat pathogenic infections. The report also depicted the

lack of proper surveillance and monitoring, of antibiotic consumption in low- and middle-income countries.¹ AMR comprises approximately 9% of total global deaths with an annual increase of 68% to 75% per year, linked to AMR directly or indirectly in 2022. Although there is a need of surveillance from the above facts, still there are several challenges for implementation among which data infrastructure and financial stability has been emphasized more.^{7,8} Thus, diving into this scenario there were many organizations who addressed this to be an alarming issue among which WHO gained prevalence. WHO incorporated AMR to be one of the top global concerns that needed to be accosted. They addressed it to be a part of the One Health (OH) concept. WHO has a Quadripartite coalition for addressing the OH situation and predicted that there will be 39 million possible deaths between 2022 and 2050, or 1.19 million deaths attributable to AMR annually in 2050 with misuse and overuse of antimicrobials in humans, animals, and plants.⁹ Apart from over utilization, AMR is also influenced by the type of area and whether people belong to urban or rural areas. It has been observed that there is a significant difference in distribution of AMR genes across different areas.¹⁰ This disparity may be attributed to differences in antibiotic access across these areas. Urban areas tend to have greater access to antimicrobial therapies compared to rural regions, resulting in pathogens being more likely to develop AMR genes against commonly used antibiotics in urban settings.¹¹ But there has been a shift in antibiotic consumption from high-income countries (HICs) to low- and middle-income countries (LMICs) that may be due to increased awareness of the harmful effects of AMR on health and our environment.

AMR is significantly influenced by environmental factors, thus there must be an interconnection with climate change (CC) that has the ability to indirectly worsen the AMR situation. Over time, AMR and CC have become most significant global health challenges, as recognised by WHO. Climate change is known to exacerbate human health issues, contributing to the overuse of antimicrobials, which indirectly accelerates the development of AMR. The impacts of global warming have led to increased surface temperatures, promoting the evolution of heat-resistant pathogens.^{12,13} Therefore, there are several non-biomedical factors as well, that play an important role in the responsible use of antibiotics, working in tandem to mitigate this global threat.¹⁴ Hence, WHO emphasizes the idea of monitoring the consumption of antibiotics and monitoring the environmental changes. Thus, gathering the required data becomes an important aspect for effective surveillance. Therefore, this article aims to collect and discuss the different aspects of AMR, its threats, and prospects in the near future.

Pathogens and AMR

WHO initiated the GLASS-Anti-Microbial Resistance surveillance system to monitor and analyse the development of new resistance cases, aligned with the WHO AWaRe classification system. The most common pathogens monitored within this framework include *Acinetobacter spp.*, *Escherichia coli*, *Klebsiella pneumoniae*, *Shigella spp.*, *Staphylococcus aureus*, and *Streptococcus pneumoniae*.¹⁵ WHO initiated the World AMR Week, held annually from November 18–24 to raise awareness against these pathogens.¹ Furthermore, several emerging and re-emerging infectious diseases, such as Ebola, Lassa fever, Nipah virus, Marburg virus disease, and SARS-CoV, have caused significant global health crises.¹⁶ These pathogens have developed resistance through mutations in their genetic material, which have been exacerbated by the widespread use of antibiotics in healthcare settings, self-medication, and the administration of sub-optimal doses.¹⁰ The resistance patterns observed in various pathogen strains are summarized in [Table 1](#).

Mechanism of Resistance to Antimicrobials

AMR at the level of species can be defined as the consequence of mutations in the genes in most of the cases. But there exist several ways in which microorganisms exhibit resistance. Efflux pumps form the most widely presented mechanism for resistance in pathogens. The efflux genes are ubiquitously present and encode the physiological functioning of efflux pumps like stress adaptation, development, pathogenesis, and virulence of bacteria.¹⁷ It is found that AcrAB-ToIC codes for house-keeping the efflux pump is considered to be an important determinant of MDR phenotype in the *E.coli* pathogen.¹⁸ It is found that overexpression of AdeABC efflux pumps in *A.baumannii* contributes to the greater level of resistance towards the carbapenems along with carbapenem hydrolysing oxacillinases.¹² The particular mechanism becomes responsible for the increase in the minimum inhibitory concentration (MIC) of antibiotics. The effectiveness of the anti-microbials is enhanced on combination with efflux inhibitors and further on inactivation of genes encoding the transporters related to efflux pumps.¹⁹ The two component system (TCS) is a response system present widely in the prokaryotes which has been found to regulate efflux pumps in organisms. It is found that 17 response regulators are present in *E.coli* producing drug resistance.¹⁸ Drug affinity

Table 1 Worldwide antimicrobial resistant pathogens & their resistance. The list of several pathogens and their respective resistance mechanisms

Microbial Strains	Disease Condition	Resistance to Antimicrobials	Resistance Mechanism	Reference
<i>Bacteroides fragilis</i> *	Sepsis to surgical site, pelvic abscesses	Metronidazole, Clindamycin, Carbapenems	Efflux pumps on cell surface	[11]
<i>Acinetobacter baumannii</i>	Nosocomial infections, UTI	Carbapenems	Alterations in PBP, Efflux pump, β -lactamase enzyme	[12]
<i>Clostridium difficile</i>	Gastro-intestinal infection	Fluroquinolones, Cephalosporins, Clindamycin, Erythromycin	Efflux, Horizontal gene transfer mutation	[13]
<i>Enterobacter cloacae</i>	UTI, Septicemia, Pneumonia	β lactams, 3 rd generation cephalosporins, Fluoroquinolones	Porin channel alteration, Efflux pumps	[16]
<i>Klebsiella aerogenes</i>	UTI, RTI	β lactams, Carbapenems	Efflux pumps, Biofilm formation, inactivating enzymes	[16,17]
<i>Enterococci spp</i>	Nosocomial Infections	β lactams, Aminoglycosides, Glycopeptides	Efflux pumps, Mutation in ribosomal unit	[18]
<i>Staphylococcus aureus (MRSA)</i>	Nosocomial illness	β lactams, Tetracyclines, Macrolides, etc	Presence of mutated resistant genes	[19]
<i>Escherichia coli (MRSA)</i>	GI infections	Streptomycin, Tetracyclines	Horizontal transfer of resistant genes	[20]
<i>Pseudomonas aeruginosa</i>	Hospital acquired UTI, RTI	β lactams, Aminoglycosides, Fluoroquinolones	Transfer of mutant genes	[21]
<i>Salmonella typhi</i>	Typhoid fever, Salmonellosis	Cephalosporins, Azithromycin, Fluoroquinolones	Development of resistomes	[22]
<i>Vibrio cholerae</i>	Cholera	Clindamycin, β lactams	Efflux pumps, Catalase enzymes	[23]
<i>Mycoplasma spp.</i>	RTI, UTI, Genital infections	Macrolides, Fluoroquinolones, Aminoglycosides, Lincosamide	Mutations in amino acids	[24]
<i>Streptococcus pneumoniae</i>	RTI	β lactams, Macrolides, Fluoroquinolones, Sulfonamides	Alterations in PBP, Efflux pumps, Mutations, Catalase enzymes	[25]
<i>Plasmodium spp.</i>	Malaria fever	Quinine antibiotics (Chloroquine, Primaquine), Pyrimethamine, Anti-retroviral	Mutations in resistance proteins	[26]
<i>Mycoplasma tuberculosis</i>	Tuberculosis	Rifampicin, Macrolides, Pyrimethamine	Mutations in amino acids	[24]
Fungal species	Yeast infections, candidiasis	Azole, Triazole, Allylamines, Echinocandins	Point mutations	[27]

Note: *Name of species.

becomes diminished with down-regulation of PBPs in the cell wall. The alterations in PBPs in *A.baumannii* has led to low-level resistance to β -lactams.¹² MRSA and VRSA are those of the strains that inactivates the effectivity of vancomycin by alteration in the multiple proteins required to encode mobile transposons that recreate the peptidoglycan layer inhibiting the vancomycin along with sustaining the integrity of the cell wall.²⁰ Porin channel defect and Lipopolysaccharide changes in the cell wall has led to minimization of antibiotics activity, leading to development of resistant strains from third generation cephalosporins, fluoroquinolones, and penicillin categories of the drug.²¹ Bio-film formation or growth is considered as the most persistent and chronic form of AMR produced, accelerating the rapid spread of multi-drug-resistant strains. It is found that regulation of

efflux pumps is related to the formation of biofilm formation. From investigations it is found that there are six efflux pumps that are involved in biofilm formation. ESKAPE pathogens have acquired extensive, pan drug and multi drug resistance via biofilm formation.^{18,22} Catalytic enzymes such as β -lactamases are also responsible for reducing the susceptibility of antibiotics before they can reach the binding targets in the bacterial cell wall. They produce hydrolytic degradation of the antibiotics.²⁰ Among the catalytic enzymes cephalosporinases, carbapenemases, ESBLs (Extended Spectrum β lactamases) are the prominent sub-types to produce the resistance, where ESBLs exhibit plasmid-based antimicrobial resistance mechanisms. In some species such as gram -ve *Enterobacteriaceae* the hydrolytic enzyme being present in the periplasmic space works to neutralize the antibiotic drugs before they can reach to the PBPs.²³ Carbapenem resistance in *A.baumannii* is due to the presence of oxacillinases. Mutations is a massive challenge because they have the ability to alter disease phenotype that might potentiate transmissibility, virulence and overcome immune response for a pathogen lineage.²⁴ *Enterococci* possess plasmid, transposon, and chromosomal exchange mechanism additionally with lactamases to exhibit resistance to antibiotics. Single mutations within the protein of the 30s subunit of ribosome had led to peak level resistance for aminoglycosides.²⁵ Point mutations in the gyrA/gyrB (gyrase subunit A/B), parC, and parE (topoisomerase IV) makes *Salmonella typhi* immunize against fluoroquinolones exhibiting its mechanism by altering the binding sites.²⁶ Mutations in the promoter region of genes coding for transportation of substances across the cell can also restrict accumulation of antibiotic drugs in pathogenic cell leading to resistance.²⁷ The mechanism is also observed in *Plasmodium falciparum* where mutations introduced near the membrane spanning region of chloroquine resistant transporter on digestive vacuole causes the species to be resistant to chloroquine.²⁸ The process of mutation or horizontal transfer of genes in nature allows selection of novel alleles that has better survival rates in stress environmental conditions and further continuation of these variants causing resistance towards antimicrobials.²⁹ In the case of livestock, the most common pathogens to cause infections to have been reported are *Pseudomonas*, *Aeromonas*, *Paerugenosa*, *Enterobacter spp*, etc. Oxytetracycline and Enrofloxacin are the most common antibiotics used in farm animals.³⁰ Poultry farming being a backyard supportable food source had gained popularity as provenance of income. Salmonella infections are well linked to such a type of farming practices. Thus, larger use of antibiotics to prevent such infections to prevent small scale production losses has also led to widespread AMR among poultry farms.³¹ Antibiotic resistance through mutation in pathogens will depend on a) the rate of mutation supply, b) the level of resistance that is acquired through mutation, c) the fitness against drug concentrations by the bacteria, and d) the strength of selective pressure.³²

Consumption of Antimicrobial Agents

Global Consumption of Antimicrobial Agents

There are several factors that can affect the consumption of antimicrobial drugs in any region, that could be globally or by any country. People belonging to places with better health education and drug regulatory principles are less likely to have unnecessary antibiotic consumption. But it is observed that a person with insufficient medical information can participate towards AMR. Factors such as easy access to OTC (over the counter) drugs, unlawful accessibility to prescription drugs, lack of awareness, presence of children or old age majority, etc can lead to an increase in anti-microbial consumption for self-treatment or prophylaxis.³³ Globally, antibiotic consumption in children (<5 years of age) was 40.2 billion DDD in 2018 with an increase of about 46% from the year 2000 found through a longitudinal analysis technique using spatial modelling for common antibiotics like ampicillin and amoxicillin reported by caregivers for common ailments like fever, cough, diarrhea, etc.³⁴ COVID-19 pandemic had a disparate effect on antibiotic consumption across different income groups of people. For a study period of 2016–2023 for 67 reported countries, including the period of pandemic it was seen that there is an increase in the consumption rate of antibiotics in the MIC (Middle income countries) by 18.6% whereas, in contrast there was a significant decrease of 4.9% in HIC (High income countries), indicated in [Figure 1](#).³⁵

Consumption in India in the Health Sector

In India, a study on antibiotic consumption, based on private sales data from PharmaTrac, reveals that antibiotic consumption increased by 6.8% from 2011 to 2019, in alignment with DDD metrics and the WHO AWaRe classification system.⁵ There was a marked increase in antibiotic prescriptions during and after the onset of the COVID-19 pandemic, despite evidence suggesting a low incidence of bacterial co-infection. This period resulted in the consequent development of AMR against

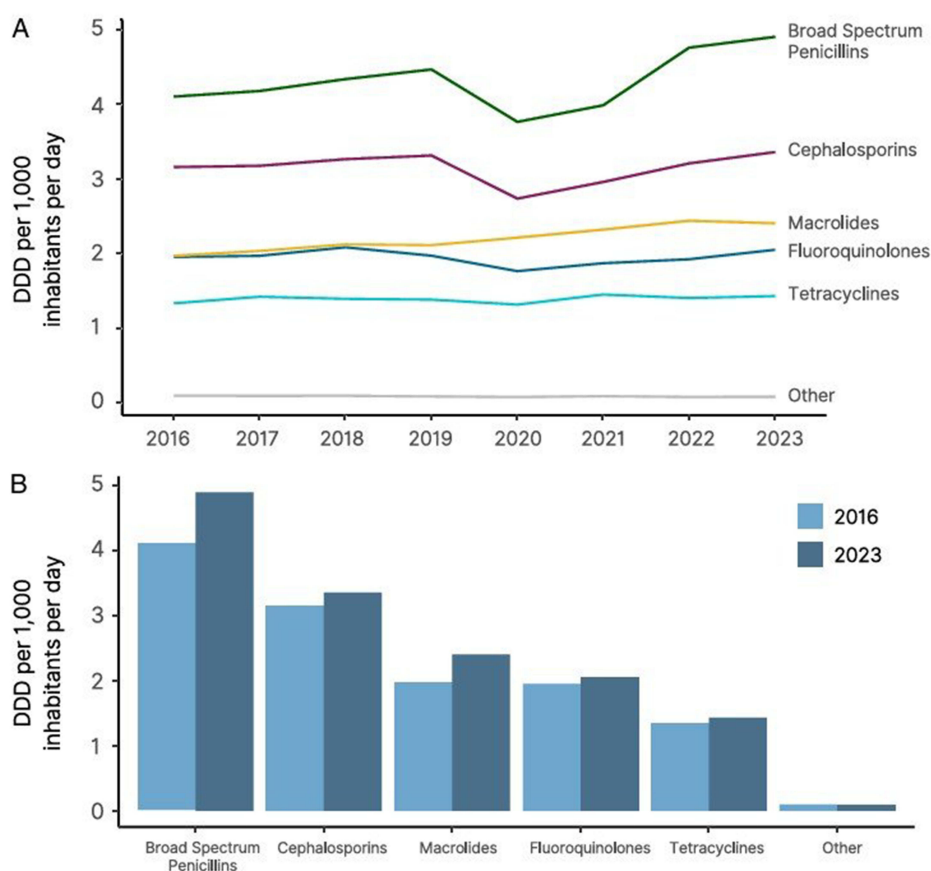


Figure 1 Global antibiotic consumption of top five antibiotic classes.³⁵ (A) Yearly changes in DDDs per 1,000 persons in a day for top five leading antibiotic classes by amount of consumption. Antibiotics different than the top five included in other categories. (B) Differences in antibiotic consumption in two different years (2016 and 2023) of the top five antibiotic classes by amount of consumption.

common pathogens such as *Acinetobacter baumannii*, *Klebsiella pneumoniae* (for Gram-negative bacteria) and *Staphylococcus aureus*, *Enterococcus faecium* (for Gram-positive bacteria) due to the frequent use of antibiotics.⁶ About 80% of antibiotics are dispensed in community pharmacies with the rest in other parts like hospitals. A study of four different regions of New Delhi, India, found that 41% of antibiotics were prescribed, with a trend that private sectors dispensed comparatively larger amounts than the public sector due to a lack of proper stocks in the latter, surveyed on the basis of Anatomical Therapeutic Chemical (ATC) classification and calculated as DDD per 1,000 patients.³⁶

Consumption in Farm Animals and Agriculture Around Different Parts of the World

Additionally, antibiotics are more frequently used in livestock and poultry for disease prevention than in humans, with China emerging as one of the top users after Brazil, India, Australia, and the USA.⁷ It has been claimed that the use of such antibiotics might get propelled by double into BRICS (Brazil, Russia, India, China & South Africa) countries, among which China grabs the front seat due to a shift into commercialization and large-scale farmsto meet the growing demand of food products. On a global scale, it is found that antibiotics consumed per annum per animal produced (in kg) differ for different animals (45 mg/kg in cattle, 148 mg/kg in chickens, and 172 mg/kg in pigs).³⁷ Most of the farms do not follow a fixed validated antibiotic feeding routine, they usually feed 1 week before breeding to until 2–3 weeks after breeding.³⁸ In a survey of the Red River Delta region of Vietnam, there are 45 antibiotics of 10 classes used in pig and poultry farming for therapeutic and prophylactic use, but the use is not regularised as per the drug supplier and is irrational, with larger doses than required.³⁹ In several countries, aquaculture is associated with wastewater management with land agriculture that uses manure and topical spraying on drugs to prevent diseases. Thus, there is a direct association of fishes with such drug matter as well as anti-microbial agents being directly used for fishes in

aquaculture.⁴⁰ In horticulture and apiculture practices it was seen that antibiotics were diligently used in order to prevent microbial infection in advance in farm animals as growth promoters at low doses for long durations, which is majorly contributing towards Multi-drug Resistance (MDR) strains.⁴¹ The unconsumed parts of such food matter can move into the environmental system, leading to the development of further antibiotic-resistant strains from soil bacteria.⁴² All these practices have contributed to human food becoming substandard in quality. But there is very limited evidence about foodborne transmission of AMR genes to humans. The transfer of genes is not easily traceable. Thus, complex transmission routes and frequent transfer makes it inconvenient to demonstrate whether there exists a reservoir of AMR genes that is being transferred to humans in the food chain through farm animals.⁴³ Thus, there are questions raised about the direct and indirect channelling of AMR genes to mankind. Still among these, there are studies and surveys that assuredly support the concern about the frequent use of antibiotics that may be therapeutic or non-therapeutic utilizations, which have detrimental effects on human health.⁴⁴ A joint report on integrated analysis of consumption of antimicrobials in humans and food producing animals released in January 2016 by the European Medicine Agency (EMA), European Food Safety Authority (EFSA), and European Centre of Disease Prevention & Control (ECDC) has greatly helped to monitor the alarming consumption of antibiotics, leading to a coordinated survey.⁶

Consumption in India in the Farm Sector

It is revealed that lack of awareness and knowledge in farmers of India has led to the inexorable spread of AMR in poultry and farm animals. For instance, consumption of antibiotic might greatly vary depending on the type, age, and body weight of animals, but India has been identified to have used about 114 mg of antibiotics per kg of meat in year 2020, ranking itself at 30th position in terms of usage.⁴⁵ Some of the uses revealed were 76% of farmers used antibiotics for prophylactic, 80% for metaphylactic and 8.33% for growth promotion in farm animals, which included sheep, goat, and dairy animals. Table 2 indicates the study made on quantity of different categories of antimicrobial agents that are used in animal farms of Telangana state, India.³⁰

Economic Impact of AMR

An important element of AMR's economic effect is the financial strain of controlling its hazardous outcomes. The added expense of AMR affected disease is far more burdensome and can outweigh the expense of managing the AMR. Strategies including enhancing national AMR surveillance, bolstering infection prevention and control, and raising awareness of the emergence of AMR and the prudent use of antibiotics or antimicrobials are the foremost priority of WHO with reference to WHO Action Plan 2015.⁴⁶ AMR has put a conspicuous macroeconomic and microeconomic impact by deteriorating production, loss of productivity and increased healthcare cost. By addressing AMR, we can

Table 2 Distribution of respondents based on their type of antibiotic use in farm adopted from³⁰

Antibiotics	Livestock & Poultry Farmers			
	Cattle & Buffalo (n = 60)	Sheep & Goat (n = 60)	Poultry (n = 60)	Total (n = 180)
Oxytetracycline	32 (53.33)	46 (76.66)	31 (51.66)	109 (60.55)
Enrofloxacin	26 (43.33)	42 (70.00)	36 (60.00)	104 (57.77)
Levofloxacin	11 (18.33)	22 (36.66)	30 (50.00)	63 (35.00)
Tylosin	15 (25.00)	13 (21.66)	23 (38.33)	51 (28.33)
Amoxicillin	19 (31.66)	15 (25.00)	19 (31.66)	53 (29.44)
Ceftriaxone	17 (28.33)	4 (6.66)	9 (15.00)	30 (16.66)
Streptopenicillin	29 (48.33)	26 (43.33)	11 (18.33)	66 (36.66)
Cefalexin	17 (28.33)	6 (10.00)	8 (13.33)	31 (17.22)
Trimethoprim + Sulfamethoxazole	21 (35.00)	19 (31.66)	24 (40.00)	64 (35.55)

protect economic stability, advance sustainable development, and cut the detrimental financial effects associated with global health problems.⁴⁷ In accordance with WHO estimates, the total global cost due to the AMR may rise to 1 trillion dollars by the year 2050. The World Bank suggests there will be a 1% decline in the world GDP by 2050, where low-income nations face a slump by 5–7%, leading to 100–200 trillion dollars of loss.⁴ The declining effectiveness of antimicrobial and antibiotic drugs have led to more expenditure in hospitals and healthcare centres. Budgets on healthcare being strained and becoming more challenging to treat an illness. People get ill frequently as a cause of AMR losing their work and thus indirectly affect the economic growth of a nation putting a global implication. Farmers due to AMR had to use more antibiotics.⁴⁸ One such scenario of epidemics is generated by pathogens in shrimp aquaculture that have resulted in massive economic loss in Asia & America. The losses can be further aggravated due to AMR. Reducing the chances of infection and ensuring prudent use of antibiotics can mitigate the losses by AMR.⁴⁹ Additionally, AMR has also increased the cost and difficulty in international trade and travel. Since countries due to spread of illness must put restrictions on travel of people and flow of products.⁴⁸ Thus, AMR becoming not only a health threat but also a global economic problem which needs attention as an alliance and a single made approach may not work out since every aspect related to AMR is intertwined. An organization called GARD (Global Alliance for Rapid Diagnostics) forms a node-to-node partnership, forming networks in North America, Latin America, Southeast Asia, South Asia, East Asia and Africa, and emphasizes a collaborative approach to unite research, innovation, and implementation of solution against AMR on a global scale.⁴

Role of Environment

Our environment, the surrounding in which we reside, has a great impact on our health. Lifestyle factors like what we ingest into our body and the hygiene we maintain decide our physical and mental wellbeing. Proper maintenance of the environment along with safe disposal of poultry, industrial, human and agro waste averts the chances of health-related illness.⁵⁰ Ensuring access to clean water and preserving the standards of hygienic food are critical measures to mitigate serious health malfunctioning and leads to minimizing the dependence on antibiotics.⁵¹ With growing populations, urbanization and evolving nations, development and food security largely depend on agriculture. The consumption of eggs, meat products, milk, and processed plant food has been increasing.⁵² Antimicrobials may also come from various non-point sources, most notably from agriculture, hospital, and industrial waste. It has been found that about 80% of the antimicrobials and antibiotics that have been used in animal husbandry are eliminated into the environment unmetabolized. This may move to the water bodies due to poor waste management, and eventually into soil bodies. Soil, which is a reservoir of microbes, becomes a source of resistant pathogens.⁵³ Therefore, antibiotics are circulating in the environment in their active forms.⁵⁴ There are evidence, theories, and documented facts about the intricate relationship between AMR & environmental factors. But these factors contribute to the selection and spread of resistant pathogens, further complicating efforts to address the global crisis of AMR. Still there are lags and the systematic national surveillance of AMR is slow in several nations, requiring attention.⁵²

Concept of One Health (OH)

It is very clear that antimicrobials make up a major part of our drug treatment methods available in our healthcare system against life threatening diseases. Thus, it is very natural to be dependent on them. But AMR is the greatest threat in the current scenario, which is highly unpredictable and we are unaware of its propensity of spread in our ecology.⁵⁵ Thus, it is a matter to be cautious for mankind. The concept of One Health (OH) was introduced during the emergence of severe acute respiratory syndrome (SARs) which was amplified in the “Manhattan Principles”.⁵⁶ The term got expedited during COVID. OH is a holistic and unified proposition that intertwines global threats such as AMR & CC, its effect on public health, food security, economical and social well-being, as well as biodiversity. It focusses to encroach balance and optimize health of animals, plants, or all parts which are involved in our surrounding diversity.⁵⁷ It is acknowledged that the use of antimicrobials invariably carries a significant risk of fostering AMR, that may be in human, agriculture, horticulture or production animals, leading to emanation of resistant gene pools.⁴¹ The bacterial resistant alleles evolve on the Darwinian principle of survival of the fittest. The evolution occurs mostly in areas where they are massively used like hospitals and community health centres and in animal farms, aquacultures even in highly polluted sewage and pharmaceutical wastewater.⁵⁵ Thus, it becomes necessary for all the components to get involved into this cycle to delay AMR and its consequences. The conceptualized approach of OH is complex in nature, which makes it difficult

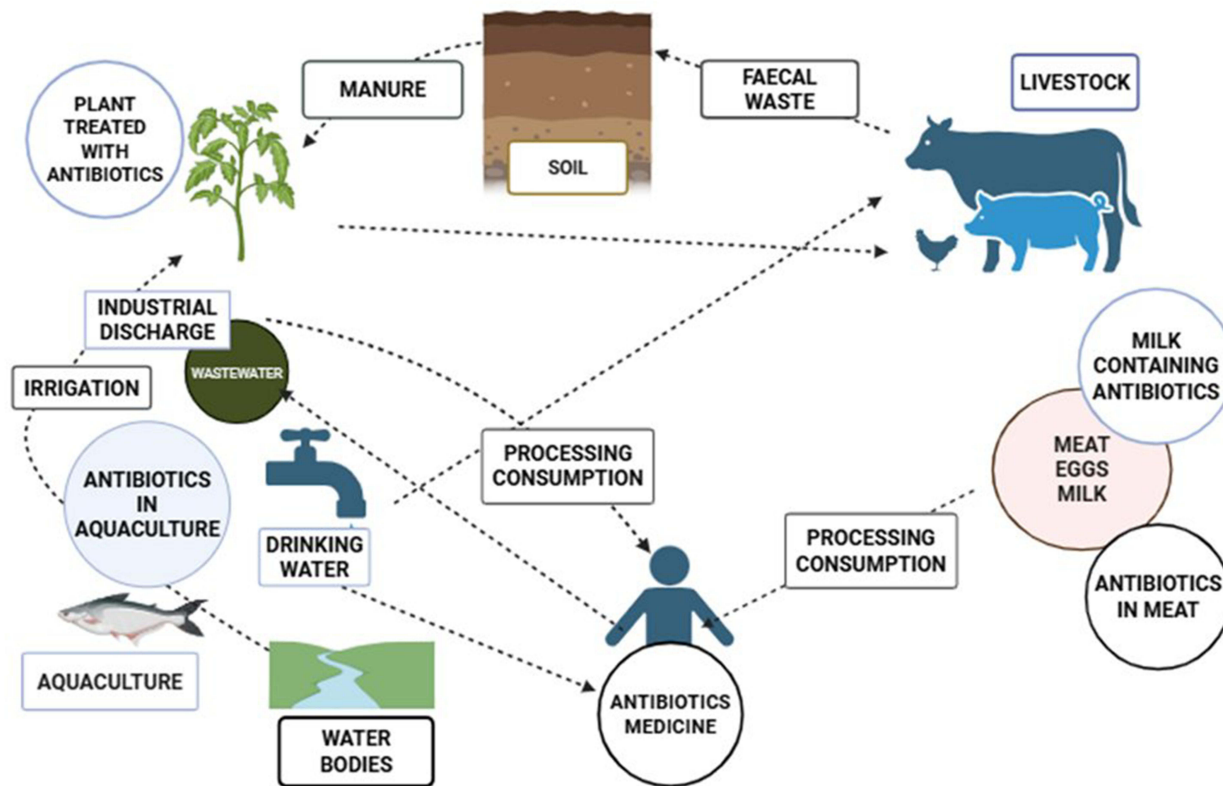


Figure 2 Antibiotic exposure to different components of the environment. The figure represents the interconnection between different components of the environment and circulation of the antimicrobials and their increasing concentrations.

to achieve in a global level. But, all the responsible elements of this cycle or domain involve altogether to reduce the presence of antimicrobials in the environment, making it more practical to achieve. The interconnection of the elements and the cycle of antimicrobials is interpreted in Figure 2. The approach of OH recognizes the association of human, animal, and environmental health. Integrated surveillance systems are essential to monitor AMR across the food chain.⁵⁸ OH is a multidisciplinary and collaborative approach emphasizing that the health of humans, animals, and ecosystems is interdependent. It has been a cornerstone in combating AMR by addressing its drivers in both healthcare and agricultural practices. WHO's Quadripartite Collaboration on One Health – involving the WHO, FAO, OIE, and UNEP – aims to mitigate AMR risks by fostering cooperation among sectors (WHO, 2021).⁵⁹

Alternatives to Antimicrobial Agents

The emergence of novel alternatives is a need of the hour. All 12 pathogens have been identified as a great threat, and are divided into different classes as critical pathogens, high priority, and medium priority. There is also a category of MDR (Multi-Drug Resistant) bacteria. It requires use of nanotechnology and computational methods to deal with such a precarious threat. Apart from them, there are alternative therapies such as monoclonal antibodies, Anti-Quorum sensing, darobactins, vitamin B6, bacteriophages, drug repurposing, and discovering newer antibiotics with a broader spectrum of action. In this direction, nanoparticles would produce a sustained and delayed action of antibiotics.⁶⁰ In-silico methods of computational approach is the greatest weapon to develop novel anti-microbial agents which enables predictions such as pharmacophore identification, data mining, and structure–activity relationship.⁶¹ Some of the approaches are.

CRISPR Cas9 System

The CRISPR system is a pivotal part of the immune system. They are potentially utilised for targeting virulence in pathogens by a new area of gene editing biotechnological tools for therapeutic purposes. Antimicrobial agents developed via this mechanism produce action based on a gene sequence. Thus, the modularity and ease of this method can help tackle AMR, unlike traditional antibiotics.⁶²

Phytochemicals

Phytochemicals in plants have great antioxidant and anti-inflammatory properties essential for self-defensive action against microbes, extreme weather conditions, UV radiation, animals, etc. These chemicals have potency to be developed into great synergistic alternatives of antimicrobials. Similarly, essential oils and oleoresin natural extracts act as a source of such phytochemicals.⁶³

Metal Nanoparticles

Microbial pathogens, unlike antibiotics, cannot develop resistance against metal particles like silver (Ag) and gold (Au) which have anti-microbial properties targeting different components. There are research evidences for Au & Ag nano particles having potential antibacterial properties against gram negative bacteria like *E.coli*.⁶⁴ Inhibition of virulence factors like adherence factor, invasion factor, polysaccharide capsule, toxins, etc., rather than only killing of pathogen would produce less emergence of resistant genes.⁶⁵

Monoclonal Antibodies Therapy

Monoclonal antibody (mAb) therapy with the mechanism of toxin neutralization is one such novel approach in which an extensive study has been done. They have a great advantage of low toxicity and long serum half-life. Selection of mAbs with appropriate specificity for non-overlapping epitomes will show better efficiency in neutralization of pathogenic toxins and will prove to be an alternative strategy against AMR.⁶⁶ There are several such approaches that are being targeted to affect both the internal and external environment of pathogens without the emergence of AMR. Development of an antibody–drug conjugate such as combination of an anti-microbial agent with an opsonic anti-body, as done by Genentech, produced anti-staphylococcal activity by phagosome.⁶⁷

Quorum Sensing (QS) Inhibitors

Bacteria produce resistive action by formation of biofilms in response to antimicrobial agents and biofilms are developed by quorum sensing, producing more massive strains of resistant genes. Thus, for disruption of such biological response there are therapies which target and demolish the QS signalling system called as QS inhibitors halting the formation of such resistant biofilms.⁶⁸

Target Inhibition

Teichoic acids are glyco-polymers constituting the envelopment of gram-positive bacterium playing a critical role in the pathogenesis, cell division, resistance to antibiotics, etc. Therefore, the inhibition of biosynthesis of lipoteichoic acid can meet the purpose of destroying the bacterial activity of *S.aureus*.⁶⁹

Substitution with Similar Molecules

Synthetic mimics of antimicrobial peptides (SMAMPs) are the molecules that can imitate the properties of antimicrobial peptides which can be peptidomimetic oligomers or other small molecules. These can be cost beneficial and toxicity overcoming alternatives to antimicrobial peptides.⁷⁰

Immunomodulators

Immunomodulators have the potential to prevent the downregulation effect of the pathogens in our body. They can strengthen the action of antibiotics. These include cytokines, interleukins, interferons, oligodeoxynucleotides, glucans, peptides, etc.⁷¹

Vaccination

Vaccines are another prospective approach to put AMR on check by preventing over-exploitation of antimicrobial agents. Vaccines reduce the risk of secondary infections that are accompanied mostly after viral infections. PCV9 vaccine used for pneumococcal disease has worked fine against penicillin resistant pneumococci and clotrimazole resistant pneumococci. Typhoid vaccines that include Vi polysaccharides and another Ty21a used orally. WHO approved toxoid complementing with Vi vaccine in 2017 for the age group of 6 months to 2 years. Measles is associated with acute respiratory infections, but vaccination has rechannelled the possibility of 21 million deaths of children between 2000 and 2017.⁷²

Novel Diagnostic Approach

Bacterial coinfection was a common threat that occurred during the COVID-19 pandemic. Most hospitalized patients were exposed to hospital acquired or ventilator associated pneumonia, even mucormycosis (black fungus). Patients were provided with large doses of antimicrobials even with low rates of microbial infections, without proper diagnosis, which is why AMR consequences have broadened during the reign of coronavirus infections.⁷³ Under such a grave situation, biosensors offer emerging advances to detect the infection of pathogens or bacterial infection and thus form a great weapon for proper diagnosis of any disease. Compared to the traditional forms of diagnostic methods, biosensors can be time efficient, economical, and more sensitive and specific in operation. Biosensors consist of three major parts: receptor, transducer, and detector.⁷⁴ There have been unique developments about the recognition elements that are employed by the biosensors.

Aptamers

Antibodies are one of the common elements, but aptamers are defined structures that are oligomers of ssDNA, RNA, XNA, or peptides that form complementary base pairs used in biosensing. SELEX (Systematic Evolution ligands by exponential enrichment) is the technology that has been created based on aptamers that are deeply studied for developing the biosensors.⁷⁵ Incorporation of DNA aptamers on Fe oxide nanoparticles led to an increase in the detection sensitivity.⁷⁴ Recently novel biosensing methods are mostly found based on DNAzyme, molecular imprinted polymers (MIP), and aptamers.⁷⁶

Bacteriophages

Bacteriophages are a novel approach as well for bacteria disclosure due to its advantage over conventional techniques like ELISA (Enzyme linked immuno-sorbant assay), PCR (Polymerase Chain Reaction), fluorescence assay, RIA (Radioimmunoassay), and Electrophoresis that are laborious and costly on larger scale. Whereas bacteriophages show better accuracy and have reduced time of analysis.⁷⁶ They are also resistant to physical and chemical variation like temperature, pH, organic solvents, etc. They can produce high titers of progeny phages and have the innate ability to differentiate between live and dead cells. Lytic bacteriophage 12600 has an efficient specificity towards *Staphylococcus aureus* ATCC 12600 strains.⁷⁷

Optical Biosensors

Optical biosensors consist of transducers based on the phenomenon of fluorescence, luminescence, reflectance, absorption, refractive index, etc. The detection is on the changes that occur on the interface, thus it is insensitive to the unbound materials.^{77,78}

Piezoelectric Biosensors

There are piezoelectric biosensors that sense the small changes in the masses by utilizing changes in the piezoelectric crystals. Similarly, there are biosensors based on electro-chemical and electrical phenomenon detecting the changes in potential and electric current.⁷⁹

Transistor Biosensors

Biosensors that are based on field effect transistors (FET) are being widely deployed and are highlighted for efficiency and time preservation characteristics. Broadly implemented structures in the biomedical field are the ion-sensitive field efficiency transistors (ISFETs) and metal oxide semi-conductor field efficiency transistors (MOSFETs). These are based on differences of applying the gate voltage, design, material of the gate, and channel region.⁷⁸ In the coming years, amalgamation of FETs with nanomaterials A3B5 heterostructures and oxide heterostructures have potential to construct more sensible and competent detection of pathogenic bacteria.⁷⁹ An interaction is created in between the gate and the charged molecules, altering the ion terminal of the ion selective membrane because of accumulation or depletion of charged biomolecules. The phenomenon causes a change in the conductance which becomes the mode of sample analysis. When a voltage is applied between the source and drain, a current starts to flow in the semi-conductor's channel, the respective state is known as turn-on state. In the case of negatively charged species like *E.coli*, molecular interaction takes place at the transistor gate due to the occurrence of binding interaction, detected by the surface mannositides. The interaction depicts the amount of voltage that is required to make the FET move into turn-on state. The charge, that is negative charge of *E.coli* here produces a positive shift that can be represented into a graph of voltage vs current.⁸⁰

Global Surveillance

The first global report was issued by WHO on April 2014, representing the extent of AMR and the gaps present in its systematic surveillance from national and international surveillance networks. In the year of 2015, WHO launched the Global Action Plan (GAP) to combat the issue of AMR. The aim was to ensure proper use of antimicrobials, eliminate the problem of AMR by addressing the root issues as deep as possible, to raise awareness for the issue among the community.⁶ It comprises three key workstreams: a) Surveillance, Evidence, and Laboratory Strengthening (SLE), b) Control and Response Strategies (CRS), and c) National Action Plan, Monitoring, and Evaluation (NPM).¹ This framework supports the evaluation of antimicrobial stewardship programs and assesses the effectiveness of related policies. Therefore, it has become a global imperative to overcome the barriers for effective AMR control.¹⁵ Surveillance plays a crucial part in the monitoring of serious health threats like AMR, which helps keep a check, aids research, along with assists public policy and communication. It involves timely collection of data and its analysis, which is the aim of various global action plans launched by governing bodies worldwide.⁸¹ Data monitoring is done from local, hospital, and community data acquisition at a global level with the global surveillance system can provide novel and identifiable trends about AMR and would also allow policymakers to design new strategies which would be effective at international level to counter the threat of AMR.⁸² In AMR monitoring, bioinformatics has exceptional benefits for surveillance of AMR genes and tracking them through in-silico methods and even tracking new resistant microbial populations.⁸³ A study revealed the potentially harmful genes such as bla_{NDM} in *Enterobacter* spp. that necessitates attention to AMR in livestock coming under frame of One Health concept.⁸⁴ Global Antimicrobial Resistance & Use Surveillance (GLASS) launched by WHO nurtures the surveillance process and frames strategies for AMR. GLASS was the first ever approach made by WHO initiative to standardize AMR and antimicrobial consumption data gatherings. It analyses the trend of AMR among population. The surveys include disease prevalence and antimicrobial consumption reports. The study analysis extrapolates the country level infection rates and existence of resistance. There are community level studies which frequently use a small sample size. With these, the data may be scarce and include bias and such small level studies may not represent AMR globally due to various disparities.⁸⁵ Studies for quantifying AMR should not be limited to antibiotic susceptibility, but it requires a comprehensive addressing to the variations of demographic and clinical profiles across the globe in order to get more insight of the situation.⁸⁶ The surveillance data also keeps an eye on the rate of death caused by the AMR and estimates the possibility of further crisis and chances of dodging the increasing percentage. There are regional surveillance networks that work along with GLASS such as CEASAR, EARS-net,

and ReLAVRA.⁸⁷ One of the causes of high incidence of AMR in LMIC can also be due to a lack of accurate and sufficient data available to generate the report of the current situation of AMR in those countries. And, thus, they lack in framing policies, community level participation, and global collaboration to eliminate the matter.⁸⁸ The excellence and representativeness of data rely on numerous factors like quality of laboratory, diagnostic capacity, staff management, and information technology.⁸⁶ In order to evaluate the trend and occurrence of AMR, the WHO suggests a two-pronged approach: a) synthesizing nationally representative standardized data emphasizing passive surveillance of AMR in clinical samples in suspected patients with infections, and b) an active periodic national level survey.⁸⁵ The factors that influence the surveillance are 1) the capacity of staffing, trained personnel, laboratory facilities, transportation, and infrastructure, 2) the data infrastructure, referring to the method of data collection, standardization, and its assurance of quality, 3) the framing of policies, 4) engagement of stakeholders that include appropriate individuals, entities, organizations, and influential personalities, 5) sustainability of economic elements such as cost and funding that are necessary to conduct the surveys, and 6) representativeness of data, etc.⁷ Incorporation of AI tools for management of such a large data collection can become a boon.⁵ This helps guide the effectiveness of national and community level statute and affects health decisions.⁸⁹ Bioinformatic tools like AMRColab have been designed for users for detection of AMR genes for convenience for comparison and visualisation of pathogenic genes without much bioinformatics training. Similarly, QAAPT is another such AMR monitoring bioinformatics tool that facilitates statistical outputs, data curation, and integration with lab systems, making it more accessible for individuals with limited software expertise.^{90,91}

Policy and Regulations

Quadripartite organization of OH policy issued a “call to action” (CTA) for encouraging collaboration and associations to put OH policies into action at all levels. The action plan formulated seven priorities: press releases, facing difficult challenges at different society levels, synthesizing policies and strategies, updating work force, prevention of pandemics, gaining knowledge, and economic stability with investment.⁸⁸ Several countries have redoubled their efforts to create and carry out national action plans to address AMR. The most emphasized one is pertaining policies to encourage sensible use of antimicrobial agents and vaccination drives leading to infection prevention and control.⁹² Policymaking is a crucial task, because only introducing them is not enough – the implementation is vital. The large number of stakeholders involved in the AMR reduction make policymaking a complex task. The policies need to be coordinated across nations and addressed properly among the makers to be effective. Successful AMR addressing nations employ multi-faceted strategies with distinct objectives.⁹³ In India, National Health Programmes such as RNTCP (Revised National Tuberculosis Control Programmes) and AIDS control programmes advise on the proper and sound use of antimicrobial and antiviral drugs. There is a hospital-based sentinel system for monitoring the AMR in the patients with coordination with national level centres.⁹⁴ PK/PD modelling during the clinical and preclinical trials can help formulate policies and regulations for the use of newer antimicrobial agents.⁹⁵ Pharmaceutical companies must be regulated concerning information that is being communicated to the consumers and financial incentives to the physicians. Antimicrobial misuse and overuse in animals and plant originated food sources needs monitoring, with enacting laws and regulations.⁹⁶ Limitations must be advised on the sale of antimicrobial drugs at a community pharmacy to curb the misuse of state funded drugs.⁹⁵ Secluded and remote interventions have minimal or no impact, thus having low success rates. For implementation into the health system, proper information and amendable legislative structure are required, along with strong leadership and political impact.⁹⁶

Antimicrobial Stewardship

Antimicrobial stewardship refers to best fit selection of drug, dosage, and duration of therapy with a low chance of propagation of AMR. It aims to promote the use of antimicrobial agents only when its requirement is necessary.⁹⁷ The advent of Multi-Drug Resistant (MDR) strains has caused new problems for patients, with hospital acquired infections all around the globe. Therefore, antimicrobial stewardship becomes crucial for the effective treatment of infections, preventing the misapplication and overexploitation of antibiotics.⁹⁸ Antimicrobial stewardship necessitates the idea of mentoring the correct utilization of available health resource. Like preceptorship, stewardship requires effective guidelines and strategies. The criteria of guidelines included by the Society for Healthcare Epidemiology of America & Infectious Disease Society of America (IDSA) include a) monitoring the consumption and level of AMR, b) initiating and implementing the guidelines for control and required use of antibiotics, c) adapting the CDC (Centre for Disease

Control & Prevention) guidelines into hospitals, d) formulating local and community level policies, e) implementation and enforcement of policies and guidelines, and f) periodic evaluation of the applicability and outcomes of the strategies.⁹⁹ There are several factors that can act as constraints for antimicrobial stewardships. Inadequate training of responsible personnel, poor wages, frequent staff turnover and lack of proper orientation of the plan contributes as a barrier to stewardship programmes. Sponsorships and time constraints are highly responsible for an effective antimicrobial stewardship agenda.¹⁰⁰ Healthcare providers of all tiers have a critical role to play in accomplishment of this idea. Proper education and screening of patients before coming into any conclusion of drug therapy can prevent the unnecessary use of antibiotics. Patient history evaluation has an important role to play in this direction.⁵⁰ Certain kinds of medicines have an obvious chance of developing resistance on long-term usage. Thus, it is the responsibility of medical advisors to counsel and educate the patients about the outcomes and restrict self-medication practices.⁹⁷ Encouraging the idea of prevention is better than cure among communities by promoting hand hygiene, emphasizing optimum nutrition and vaccinations. As per studies done in developing countries, there is a 95% prevalence of multi-drug resistance in countries like Pakistan which makes treatment of complex diseases like tuberculosis, malaria, and acute respiratory infections burdensome.¹⁰¹ Interventions by antimicrobial programmes are framed to four categories, which enable us to provide guidelines to the antibiotic usage, structural guidance to antimicrobial therapy with proper diagnostic tests, restrictive prevention of self-medication and requirement of medical professional approval and persuasive educating and increasing awareness with proper feedback.¹⁰⁰ There are studies that put light on budgetary constraints as one of the crucial obstacles of antimicrobial stewardship. Thus, despite awareness, there is a lack of institutional commitment to stewardship.^{97,100} But, according to a survey conducted in India, more than 70% of medical prescribers expressed a positive attitude in increasing their understanding to the use of antimicrobial agents, indicating the value of recurring training. Regimens like DOTS (Directly Observed Therapy Short course) became one of the most successful programmed therapies that aimed to make the patient complete the course and prevent the drug resistance to occur and their becoming a good illustration of antimicrobial stewardship and appropriate application of policies and utilization of plan.¹⁰² Although the NMC (National Medical Council) has attempted to introduce such training programmes into undergraduate and postgraduate curricula, still there are very few programmes being practiced in reality.¹⁰³

Public Awareness

The emergence of AMR is greatly influenced by insufficient knowledge by healthcare workers. It is the prime responsibility of the healthcare provider in different levels like primary, secondary, and tertiary health sectors to educate people and grow their awareness about serious threats like AMR. The duty comes hand-in-hand to ensure rational usage of antibiotic and antimicrobial drugs, with correct dose, time, and duration of therapy along the correct route of administration.¹⁰⁴ One of such management systems is observed in Zambia, where awareness campaigns and IPC (Infection Prevention & Control) activities are carried out by nurses, pharmacists, microbiologists, biomedical scientists, physicians, and environmental specialists.¹⁰⁵ In India, the National Action Plan (NAP) was launched in April 2017 under the Indian Ministry of Health & Family Welfare that set its priorities to AMR aligning to a comprehensive Global Action Plan (GAP) by WHO. The first most stratagem was to increase comprehension and awareness about of AMR by training, education, and efficient communication, whereas the NAP 2024 prioritizes a regional approach to revise antibiotic usage, with the following expected outcomes:^{106,107}

- a. International collaboration with food regulators and policy regulations against AMR.
- b. Country-specific and sector-specific awareness modules.
- c. Nationwide strategy planning and capacity building for food operators.
- d. Strengthen AMR surveillance and laboratory potential.
- e. Incorporate AI-based AMR and AMU monitoring tools.
- f. Gain more knowledge about the role of Whole Genome Sequencing (WGS) and Antimicrobial Susceptibility Testing (AST) in AMR monitoring.
- g. Alternatives for antibiotics to minimize the extensive utilization.



Figure 3 Measures to prevent AMR. The figure represents the key strategies to overcome AMR.

The value of an effective communication cannot be underrated. For any mass program to gain its pace and success lies in the hands of the public, that may be use of antibiotics or vaccination programmes. In this direction, an excellent example is the COVID 19 vaccination that was a great accomplishment worldwide.¹⁰⁸ Figure 3 represents the all required measure to tackle AMR efficiently.

WHO AWaRe System of Classification

The introduction of the AWaRe system of classification brought a paramount modification in the essential list of medicines in the year 2017 by categorizing the antimicrobial agents into three classes. The system aimed in strengthening the surveillance with integration to GLASS and decreasing the unnecessary prescription of antibiotics to curb AMR.¹⁰⁹ In contrast to the classification system of AWaRe, Access(A) category consist of drugs that are narrow spectrum with least potential to develop resistance, whereas Watch(Wa) class had drugs whose consumption needed to be restricted due higher chances of resistance development and Reserve(Re) consist of newly developed drugs that are kept as backup as an ultimate option only if the pathogen is confirmed.¹¹⁰ India is emerging to be the hotspot of AMR due to the widespread practice of polypharmacy and inappropriate use of antibiotics for minor infections.¹¹⁰ The studies have indicated an imbalance in the use of the antibiotics where the one belonging to the Access of WHO remains to be utilized <50% which are recommended for first-line treatment options, whereas the Watch category of antibiotics consumption is as high as 68.2% more susceptible to develop resistance.¹¹¹ The Access antibiotics are continuously being prescribed for non-infectious conditions, undermining the intended role and growing the intensity of resistance.¹¹² This distorted use, even after WHO's recommended criteria, is largely driven by poor diagnostic infrastructure, obligating the healthcare providers to rely on empirical treatment.¹¹¹

A study adopted the WHO AWaRe system and used a modified Delphi approach to achieve the expert consensus of antibiotics in the UK and proposed a UK-AWaRe system of classification that reflects its local resistance patterns and prescription practices.¹¹³ Thus, there is a requirement of sustained antimicrobial awareness system in the coming days, designed as per the local patterns to minimize the environmental dissemination of resistant variety of microorganisms.¹¹⁴

Conclusion

The escalation of AMR presents to be a multifaceted global health challenge. This review highlights the existence of several resistant strains of pathogens along with their diverse mechanisms of resistance that evade the efficacy of antimicrobial agents. The emergence and spread of AMR is a complex interplay of multiple interconnected factors. The misuse and mishandling of the antibiotics in healthcare and agricultural sectors being the primary drivers of AMR along with other factors such as inadequate waste management supports the existence of AMR in the environment. A large number of data have been provided that discuss the amount of antibiotics that are being consumed in our day-to-day life in different income level countries suggests the need of proper vigilance. These unmonitored practices contribute the continuous release and circulation of antimicrobial agents and their remnants in the environment, with each step further compounding resistance through cumulative exposure. Thus, it's imperative to minimize and make judicious use of these pharmaceuticals not over utilizing their potential. OH by WHO endorsed the interconnectedness of food security, animal health, agriculture, and animal husbandry in the transmission of AMR. Farmers involved in horticulture, agriculture, apiculture, or animal farm are required to adopt practices that eliminate or reduce the antimicrobial uses. It would be rightful to prevent the use of such drugs with proper sanitation, hygiene, and avoidance of stressful conditions in farms. Veterinarians must be insightful while prescribing such medications. Similarly for human proper hygiene and sanitation at the community level can be constructive. It is the sole responsibility of healthcare workers to inform people about this issue and promote stewardship activities. Governmental level programs, a strong policy framework, and active surveillance activities and bioinformatics tools for monitoring must be supported with a survey of their respective local patterns.

This article also discussed several novel approaches for minimizing their use and alternatives of treatment that can prevent the further dissemination of AMR. Advanced and novel diagnostic techniques abetted with AI for medical prognosis can facilitate disease identification, hence averting the administration of inappropriate antibiotics for treatment and mitigation. And, to ensure there is no defer in treatment of diseases due to already existing resistant drugs, it is crucial and necessary to develop novel antibiotics that replace them and restrict the AMR-related death rate. Approaches made to not only aim in direct combat of specific pathogens but also for immunization of our body systems using biotechnological tools with concepts of monoclonal antibodies and stem cells to enhance the natural defence mechanism of our body show a promising picture for the future. Although the debated prevention plans, research advancement, and action strategy seem to be an optimistic approach for AMR, still further work is essential to fully comprehend its intricacies and formulate sustainable solutions for a protracted period.

Although this review provides a foundational overview with an aim for future intervention and cross-sectoral AMR solutions, it is still important to acknowledge certain limitations that may affect the generalizability. This review has mentioned certain limited contextual data about the consumption pattern across countries and worldwide, but the actual figure or specific data remains. These small scale data remain to be insufficient to predict the real scenario and current state of affairs. The future recommendations for this review holds opportunity for how efficient the alternative treatment approaches can be in healthcare and work against AMR threat. Alongside there may be a need to dig into other socioeconomic factors that might be affecting AMR and related data analysis could be done that depicts their effects.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising, or critically reviewing the article; gave final approval of the version to be published: have agreed on the journal to which the article has been submitted, and agree to be accountable for all aspects of work.

Disclosure

The authors declare they have no competing interests in this work.

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