

Antimicrobial Resistance: A Growing Serious Threat for Global Public Health

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Abstract

Antibiotics, among the most significant discoveries of the 20th century, have prevented infectious diseases from claiming millions of lives. However, their widespread use and misuse have created strong selection pressure, enabling microbes to develop antimicrobial resistance (AMR) to many drugs. Over time, AMR has spread primarily through human-to-human contact, both within healthcare settings and in the community. It is driven by a complex interplay of healthcare and agricultural factors, including the excessive use of antibiotics in livestock feed, which significantly contributes to the emergence and spread of resistance. Antimicrobial-resistant bacteria are now increasingly common, posing a serious global public health threat. Treatment options for resistant infections are limited, leading to higher healthcare costs, as well as increased morbidity and mortality. Furthermore, the development of new antimicrobial agents has not kept pace with the growing demand. To combat AMR, coordinated global efforts are essential. Key strategies include surveillance, responsible antibiotic use, improved access to quality healthcare, and strong regulatory measures to prevent a potential post-antibiotic era.

Keywords: Antibiotics, antimicrobial resistance, mechanisms of resistance, drivers of resistance, measures to combat resistance

INTRODUCTION

Antibiotics, once celebrated as the “magic bullets” of the 20th century, now confront a significant obstacle from antimicrobial resistance (AMR). A phenomenon where microorganisms, such as bacteria, viruses, fungi, and parasites withstand drugs, designed to eliminate them. Infections caused by AMR are more difficult to treat, increasing the likelihood of severe illness and mortality. Antimicrobial agents, which encompass antibiotics, antivirals, antifungals, disinfectants, and food preservatives, function by eradicating microbes or inhibiting their growth [1]. Antimicrobial resistance (AMR) occurs

when drugs, such as antibiotics, antifungals, or antiparasitics, lose their effectiveness in treating infections. This situation complicates disease management, increasing the likelihood of transmission, disability, and mortality. The improper use and excessive consumption of these medications contribute to resistance, posing risks to human, animal, and plant health, as well as affecting surgical procedures, agriculture, and food safety [2].

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Antimicrobial resistance (AMR) poses a significant global health risk, resulting in approximately 4.95 million fatalities each year. The excessive use of antibiotics, particularly in animal feed, has exacerbated this issue, resulting in multidrug resistance (MDR) that endangers both human health services and the livestock sector by

making standard treatments ineffective [3]. The World Health Organization identifies climate change as the leading health risk, projected to result in 250,000 deaths each year between 2030 and 2050. Antibiotic resistance develops naturally through mutations or the transfer of genes, a process often intensified using antibiotics. Extended spectrum β -lactamase (ESBL) genes contribute to resistance against third-generation cephalosporins, currently affecting approximately 14% of the global population and increasing by 5.4% each year. The rising resistance also poses a threat to last-resort medications, such as carbapenems and colistin, while the presence of non-antibiotic antimicrobials in the environment further exacerbates the issue [4].

Antimicrobial resistance (AMR) is an escalating worldwide health challenge resulting from both the excessive use and inappropriate application of antibiotics, which gives rise to drug-resistant pathogens. This “silent pandemic” poses a threat to contemporary medical practices and necessitates immediate intervention. Improving the use of antimicrobials, particularly in veterinary medicine, is essential for managing the proliferation of multidrug-resistant bacteria [5]. Coordinated global efforts are crucial in addressing the growing issue of antimicrobial resistance, but significant policies are still not enforced. The movement of people across borders speeds up the dissemination of resistant pathogens, as demonstrated by the transmission of New Delhi Metallo β -lactamase-1 (NDM-1) from India to Western countries, underscoring major risks to public health, economies, and international commerce [6]. The increase in resistance among gram-negative bacteria is primarily fueled by mobile genetic elements on plasmids that can swiftly transfer between bacterial populations. Standardized methods for plasmid typing are enhancing our comprehension of their host ranges and worldwide spread. The issue of antimicrobial resistance presents a significant challenge, with a rise in antibiotic usage in livestock projected to reach 67% by 2030, placing considerable strain on global healthcare systems [7].

TIMELINE OF MAJOR ANTIBIOTICS DISCOVERIES AND ANTIBIOTIC RESISTANCE

Paul Ehrlich discovered synthetic prodrugs named salvarsan and neosalvarsan in 1910 to treat syphilis, indicating the beginning of the current antibiotic era. Gerhard Domagk's discovery of prontosil, a sulfonamide prodrug, eventually took their place. Selman Waksman made significant contributions to the study of soil bacteria in the 1930s and found several antibiotics, including streptomycin for tuberculosis. He described antibiotics as substances that microorganisms make to eradicate other microorganisms. The “Golden Age” of antibiotics, which lasted from the 1940s to the 1960s, began in 1928 when Alexander Fleming isolated penicillin from *Penicillium Rubens*. At that time, most today's antibiotics were found. However, the use of antibiotics has been accompanied with resistance [8]. The 1945 discovery of cephalosporin, a β -lactam antibiotic that entered clinical use in 1964, was successful in treating infections that were resistant to penicillin. Five generations have been created throughout time, and the most recent one has action against gram-negative bacteria that produce ESBLs. But there is now opposition to previous generations. Since its discovery in 1950, tetracycline has been used extensively to treat infections, particularly those of the gastrointestinal tract. *Pneumococcus* developed resistance to the third-generation fluoroquinolone levofloxacin in 1996. Introduced in 1944 to treat TB, streptomycin is currently facing challenge. Antibiotic resistance was discovered to be genetically transmissible by conjugation, transformation, and transduction by the middle of the 1950s [9].

SUPERBUGS

The term “superbugs” describes highly drug-resistant microorganisms that worsen morbidity and mortality because they don't respond well to treatment. Superbug infections increase healthcare expenses, lengthen hospital stays, and restrict clinicians' options for therapy. These resistant bacteria have occasionally also developed increased transmissibility and pathogenicity [9]. There are few or no treatments available for superbugs, which are bacteria and fungi that are no longer successfully destroyed by medications intended to treat them. Drug resistant strains of *Pseudomonas aeruginosa* and *Acinetobacter*, ESBL producing Enterobacterales, Vancomycin Resistant Enterococci (VRE), Carbapenem Resistant Enterobacterales (CRE), Carbapenem Resistant *Klebsiella pneumoniae* (CRKP), and Methicillin Resistant *Staphylococcus aureus* (MRSA) are some of the most alarming challenges of our time.

The widespread and extended usage of antibiotics usually led to the emergence of multidrug resistant microorganisms. For instance, Multidrug Resistant Tuberculosis (MDR-TB), a significant superbug that is currently common in poor and impoverished nations, emerged because of decades of antitubercular medication. *Salmonella*, *Serratia*, *Campylobacter jejuni*, *Citrobacter freundii*, *Enterobacter*, *Haemophilus influenzae*, *Proteus mirabilis*, *Staphylococcus epidermidis*, *Clostridium difficile*, *Streptococcus pneumoniae*, *Burkholderia cepacia*, and *Stenotrophomonas maltophilia* are some more prominent superbugs [10].

SOURCES AND ROUTES OF TRANSMISSION OF AMR

Human-to-human interaction, both within and outside of healthcare institutions, is the main way that antimicrobial resistance (AMR) is acquired and spread. Resistance genes spread across and within reservoirs, which include humans, animals, water, and the environment. Different bacterial species and resistance factors have different modes of transmission. The human reservoir is a major source of *E. coli*, and intimate contact has been found to be a high-risk mode of transmission. Nearly half of household members obtained genetically similar strains of *E. coli*, according to genetic study. There are also significant concerns of animal to human and animal to environment transmission, particularly from poultry. Another significant risk factor for acquiring *E. coli* is visiting Asia [11]. Antimicrobial resistant bacteria may spread in both ways due to the ongoing interaction between human and cattle activities. Direct contact, contaminated food, water, biowaste, transportation of animal products, soil, manure, wastewater, and vectors, such as insects, wild animals, and sewage, are some of the ways that antimicrobial resistance (AMR) spreads [12].

MECHANISMS OF DRUG RESISTANCE

Because bacteria and antibiotics share an ecological niche, bacteria have evolved defensive mechanisms against antibiotics. The cell wall, cell membrane, machinery involved in protein synthesis, and nucleic acid synthesis are the four main components of bacterial cells that antibiotics usually target. By reducing drug absorption, changing drug targets, inactivating medicines, and enhancing drug efflux, bacteria are able to withstand these medications. Target modification, drug inactivation, and efflux are frequently involved in acquired resistance, whereas reduced uptake, inactivation, and efflux are the causes of intrinsic resistance. Gram-positive and gram-negative bacteria are physically different; since gram-positive bacteria do not have an outer membrane made of lipopolysaccharides, they are less likely to exhibit reduced uptake and efflux-based resistance to some medications (Figure 1) [13].

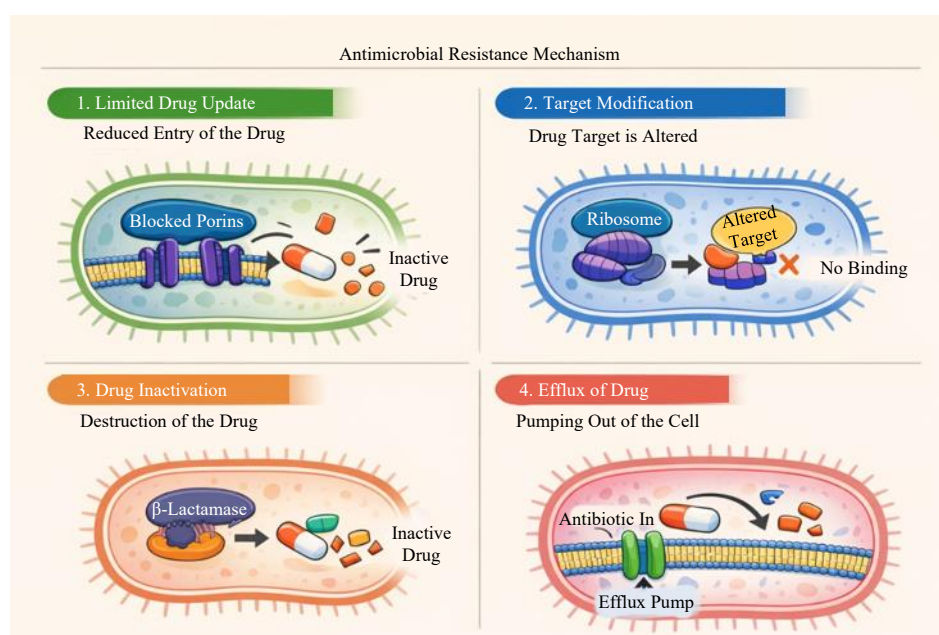


Figure 1. Mechanisms of drug resistance.

Limiting Drug Uptake

Gram-negative bacteria have an outer membrane made of lipopolysaccharide, a highly acylated glycolipid that serves as an antibiotic barrier. This reduced permeability and alterations in porin proteins, which control the entrance of hydrophilic antibiotics, such as tetracyclines, fluoroquinolones, and β -lactams, influence bacterial susceptibility and lead to resistance [14]. Mutations that affect the production or function of porins can lead to acquired antibiotic resistance, particularly when paired with mechanisms like enzymatic degradation or efflux pumps. Furthermore, bacteria including *Staphylococcus aureus*, *Pseudomonas aeruginosa*, and *Escherichia coli* that build biofilms improve resistance. Biofilms encourage tolerance and persistence by blocking the entry of antibiotics and preventing bactericidal concentrations from reaching all bacterial cells [15].

Modification of Targets for Drug

By altering genes that encode drug target proteins, bacteria become resistant to drugs and decrease their ability to attach to them. For instance, both gram-positive and gram-negative bacteria develop fluoroquinolone resistance because of mutations in the DNA gyrase quinolone resistance-determining region (QRDR) [16]. Methylation based target alteration is a very powerful resistance mechanism. *Erm* methylases provide resistance to streptogramin B, lincosamides, and macrolides. Similarly, in *Proteus*, *Staphylococcus*, *Enterococcus*, *Bacillus*, and *E. coli*, methylation of the chloramphenicol florfenicol resistance gene fosters resistance. *Staphylococcus* also decreases β -lactam affinity through different penicillin binding proteins that are encoded by *mecA* and *mecC* [17].

Inactivation of Drug

If bacteria inactivate antibiotics by chemical group transfers or degradation, drug resistance may result. The β -lactam ring of penicillins and cephalosporins is hydrolyzed by β -lactamases, which are produced by Enterobacterales and other bacteria like *Staphylococcus aureus* and *Enterococcus* species. This stops the antibiotics from binding to penicillin binding proteins. Horizontal gene transfer is frequently used to propagate these β -lactamase genes. Likewise, an enzyme that hydrolyzes tetracycline is encoded by the *tetX* gene. Chemical changes are also a part of drug inactivation: acetylation targets aminoglycosides, chloramphenicol, streptogramins, and fluoroquinolones, whereas phosphorylation and adenylation mostly affect aminoglycosides [18].

Efflux of Drug

To maintain internal balance, bacteria expel metabolites, signaling chemicals, and antibiotics using energy dependent efflux pumps in the cytoplasmic membrane. Tetracycline was ejected by the first plasmid encoded efflux pump, which was found in *E. coli* in 1980. Numerous gram-positive and gram-negative bacteria have since demonstrated multidrug efflux systems, which are usually chromosomally encoded for intrinsic resistance [19]. Mobile genetic elements frequently contain genes for substrate specific efflux pumps, including those for macrolides, tetracycline, and chloramphenicol. ATP binding cassette (ABC), major facilitator superfamily (MFS), multidrug and toxic compound extrusion (MATE), small multidrug resistance (SMR), resistance nodulation division (RND), and drug metabolite transporter (DMT) are the six families into which efflux pumps are divided. Gram-negative bacteria primarily rely on clinically significant RND systems made up of a cytoplasmic pump, periplasmic protein, and outer membrane channel, whereas gram-positive bacteria are dominated by the ABC and MFS families [20].

DRIVERS TO AMR

Antimicrobial resistance is caused by several causes such as abuse of antibiotics, inadequate sanitation, fake medications, and restricted access to healthcare, inadequate lab equipment, poverty, illiteracy, and pervasive antibiotic use myths [21].

Misuse and Overuse of Antibiotics

Although it occurs naturally, antibiotic abuse in both people and animals has advanced antibiotic resistance. Overuse and resistance are clearly linked, according to epidemiological research. Around

the world, 40–80% of animal and 20–50% of human antibiotic use is needless. The effectiveness of controlling the use of antibiotics was demonstrated by Denmark's ban on avoparcin, which dramatically decreased vancomycin resistant infections [22]. Particularly in intensive care units, where overuse of antibiotics leads to resistance, doctors are complicit in antibiotic misuse. Prescriptions that are inappropriate are prevalent in both wealthy and underdeveloped nations. In the latter, a lack of laboratory access results in empirical therapies, which encourage misuse and the rise of microorganisms resistant to antibiotics [23].

Increase in Gross Domestic Product (GDP)

Growing GDP, especially in emerging nations, is largely to blame for the rise in antibiotic use worldwide. Higher antibiotic use is associated with improved living conditions in low and middle income (LMIC) nations. The use of antibiotics increased by 65% between 2000 and 2015 (Klein et al.). Increased consumption of animal protein also has a role in the spread of AMR from animal sources [24].

Inappropriate Prescribing Pattern

Antimicrobial resistance (AMR) is largely caused by inappropriate antibiotic prescribing, which includes overuse, incorrect selection, dosage, and duration [25]. Fifty percent of hospital patients received at least one antibiotic without a good reason, according to research. Prescriptions should ideally be written after testing for bacterial isolation and susceptibility. But according to the CDC (2017), one third did not have the appropriate testing. Seventy five percent of nursing home medications were unsuitable, involving the wrong antibiotics, dosages, or durations [26].

Paucity in Futuristic Antibiotic

Pharmaceutical companies must work quickly to develop innovative antibiotics in response to the growing issue of antibiotic resistance. However, little progress has been made despite many WHO calls. Only eight of the 51 newly created antibiotics are genuinely novel; the majority are reformulated versions of earlier medications that could soon become resistant. Vulnerable people are now at higher risk because of the treatment of drug-resistant TB, pneumonia, urinary tract infections, and other gram-negative infections being compromised by this lack of alternatives. 18 large firms stopped producing antibiotics due to regulatory barriers and expensive prices, which discouraged innovation. Instead, they shifted their focus to more lucrative therapies for chronic diseases [27].

Agricultural Use of Antibiotics

Several of the main causes of antimicrobial resistance (AMR) is the non-human usage of antibiotics, particularly in agriculture and animal husbandry. Animals that get antibiotics for treatment, prophylaxis, or growth promotion develop resistant germs that can infect humans through contaminated food, direct contact, or the environment. Because of the selective pressure that this extensive use puts on resistant strains, it is imperative that these industries adopt sustainable and responsible antibiotic practices to successfully combat AMR [28].

Non-Human Use of Antimicrobials

One of the main causes of antimicrobial resistance (AMR) is the non-human usage of antibiotics, particularly in agriculture and animal husbandry. Animals are frequently given antibiotics for therapy, disease prevention, and growth promotion. Because of this approach, animals develop resistant bacteria that can infect humans through food, the environment, or direct contact. Combating such use necessitates responsible farming practices, which are essential in the fight against AMR. There is evidence that the public and healthcare professionals lack enough awareness about antibiotic use and resistance. Although effective surveillance is crucial, there is still a dearth of worldwide data on antibiotic usage and AMR [29].

Knowledge Gap

The public and healthcare professionals' ignorance about antibiotic use and resistance is well documented. Global statistics on antibiotic usage and AMR in agriculture and health are still

insufficient, despite the fact that surveillance is essential for measuring AMR and developing therapies [30].

GLOBAL BURDEN OF AMR

AMR poses a serious threat to public health since it has an impact on the environment, animal health, and human health globally. While the EU reports more than 670,000 cases every year, AMR infections in the UK increased from 61,946 in 2018 to 65,162 in 2019. In 2019, 4.95 million deaths worldwide were attributed to bacterial AMR, of which 1.27 million were directly caused. AMR's concerning impact is highlighted by projections that suggest it could result in 10 million deaths annually by 2050 [31].

Human Health Impact

Rising mortality rates are one of the main ways that the worldwide burden of AMR negatively affects healthcare and society [32]. Infections that were once curable, such as pneumonia and urinary tract infections, are now potentially fatal. Because of hospital stays, operations, and the need for costly last resort antibiotics, AMR lengthens sickness, increases patient suffering, and drives up healthcare costs. These elements increase financial expenses, put a strain on healthcare systems, and make treatment more difficult. The combined impacts make it clear that comprehensive policies are desperately needed to solve this escalating global health catastrophe [33].

Economic Impact

The costs of antibiotic-resistant infections to already overburdened healthcare systems are substantial and preventable. Compared to infections that are easily treated, they frequently necessitate longer, more expensive treatments, longer hospital stays, and additional medical care, which increases disability and mortality. About 2.5 million hospital days, 25,000 fatalities, and €1.5 billion in economic costs are attributed to resistance in the EU each year. About 23,000 people die from AMR in the US each year, and the economic impacts include \$20 billion in direct medical costs and \$35 billion in lost productivity. All things considered, AMR raises healthcare expenses, puts a strain on budgets, and has a significant negative impact on people, healthcare systems, and societies everywhere [34].

Healthcare System Impact

According to the rise in hospital admissions, the need for isolation protocols, and the need for specific therapies, antimicrobial resistance (AMR) puts a significant burden on healthcare systems and depletes available resources [35]. It decreases the effectiveness of surgery, chemotherapy, and organ transplants, as antibiotics become less reliable in preventing infections, leaving patients more exposed. Additionally, resistant microorganisms proliferate readily in hospitals, making infection control more difficult and requiring more resources. All things considered, AMR compromises patient safety, erodes the effectiveness of medical therapies, and jeopardizes the provision of healthcare, necessitating immediate action to safeguard patients and maintain quality treatment [36].

Global Health Security

The ability to control infectious illnesses and pandemics is weakened by antimicrobial resistance (AMR), which is a serious danger to the security of global health. Cross border resistant infections increase disease and mortality while decreasing the effectiveness of therapies. Control is made more difficult by AMR in illnesses like malaria, HIV, and tuberculosis. International cooperation, surveillance, ethical antibiotic use, and innovative treatments to combat infectious threats are all necessary to strengthen global health security [37].

Environmental Impact

Beyond the medical field, antimicrobial resistance (AMR) affects the environment through over usage and inappropriate antibiotic disposal in wastewater, aquaculture, and agriculture. As a result, environmental reservoirs develop resistant germs that infect humans and animals. To limit AMR and safeguard the health of people and the environment, reasonable procedures are needed to address this interrelated issue [38].

Loss of Treatment Options

Since there are fewer effective medicines available, the emergence and quick spread of antimicrobial resistance (AMR) pose a threat to world health. Once-treatable infections may suddenly become incurable, necessitating the use of toxic and ineffective last resort medications that expose patients to serious adverse effects and a poor prognosis [39]. This unchecked trend necessitates immediate action because it threatens our capacity to control infectious illnesses. Governments, healthcare institutions, pharmaceutical companies, agribusiness, veterinarians, and the public must all work together to combat AMR. To safeguard public health and security, important tactics include appropriate use of antibiotics in human and animal health, novel drug development, improved surveillance, and antibiotic stewardship [40].

CLINICAL IMPLICATIONS OF AMR [41]

The following points highlight key concerns associated with “antimicrobial resistance and its clinical implications.”

- Treatment of viral, bacterial, and fungal diseases is hampered by AMR.
- Resistant strains result in disability or death from common ailments like flu, typhoid, respiratory infections, and UTIs.
- Without new medications, it poses a threat to simple dental procedures, cancer treatment, and potentially transplants.
- Longer treatments, more expenses, and the usage of pricey substitutes are all consequences of AMR.

CURRENT AMR DETECTION METHODS

To detect and track AMR, direct therapy, aid in infection management, and understand resistance processes, traditional microbiological and molecular methods are essential.

Classical Microbiological Techniques

Culture and Susceptibility Testing

Isolating and cultivating bacteria from environmental or clinical samples is the initial stage. The antibiotic response to Enterobacteriaceae in human and animal samples is determined by susceptibility testing such as Kirby Bauer or broth microdilution [42].

Phenotypic Confirmatory Test

Resistance mechanisms are confirmed by additional phenotypic testing. For example, ESBL detection in *E. coli* and Enterobacteriaceae uses double disk synergy with clavulanic acid, whereas the D zone test finds inducible clindamycin resistance in staphylococci [43]. A center disk containing amoxicillin clavulanic acid is encircled by disks containing cephalosporins. Zone extension following incubation signifies positive. This method identified ESBL producing *E. coli* in humans, pets, and wild animals [44].

Agar Dilution and Broth Dilution

To find the least inhibitory concentration (MIC), a bacterial isolate can be tested against a range of antibiotic concentrations. Minimum inhibitory concentration is the lowest antibiotic concentration at which bacterial growth is inhibited. This information aids in assessing the bacteria's degree of resistance [45].

Molecular Techniques

Polymerase Chain Reaction (PCR)

The prominent molecular method for identifying certain genes linked to antimicrobial resistance (AMR) is polymerase chain reaction, or PCR. Using particular primers and DNA polymerase, it amplifies target DNA sequences. Resistance genes, like blaCTX-M in Enterobacteriaceae that produce ESBL and mecA in MRSA, can be found by PCR [46].

DNA Sequencing

Antimicrobial resistance (AMR) related mutations or genetic variants are found using DNA sequencing, which includes techniques like Sanger sequencing and next-generation sequencing (NGS). It facilitates thorough examination of bacterial genomes, providing information on resistance mechanisms and contributing to the comprehension of the emergence and transmission of AMR [47].

Hybridization Technique

To identify resistance genes or mutations in numerous bacterial isolates at once, hybridization techniques, like DNA microarrays and hybridization probes, are employed. Multiple antimicrobial resistance determinants in bacterial genomes can be quickly screened thanks to the binding of tagged DNA probes to target sequences [48].

Whole Genome Sequencing (WGS)

An efficient technique for monitoring microorganisms that are resistant to antibiotics is whole genome sequencing (WGS). Researchers can detect resistance genes, mutations, and mobile genetic elements in bacteria and track their spread across farms, regions, or nations by sequencing complete bacterial genomes. Resistome databases facilitate efficient containment tactics and enhance data access. Additionally, WGS allows for more accurate strain identification than conventional techniques. This predicts the spread of AMR between species and improves phylogenetic modeling. WGS has been used on animals in Portugal and children with UTIs in France that have ESBL producing Enterobacteriaceae [49].

Machine Learning

Machine learning (ML) has emerged as a useful tool in the study of antimicrobial resistance (AMR) in recent years. Large AMR datasets may be analyzed by ML algorithms, which can also spot trends and forecast resistant infection outbreaks. AMR transmission channels can be identified by combining phylogenetics, machine learning, and artificial intelligence (AI), according to a study by Ali et al. Furthermore, AI facilitates useful diagnosis and therapy, and machine learning techniques have been used to detect AMR and identify livestock [50].

Wearable Technology

Real time animal health monitoring is made possible by wearable technology, such as biosensors and smart tags, which can identify early infection symptoms and quickly combat germs resistant to antibiotics. By incorporating these techniques into AMR surveillance, farms can better respond to outbreaks, safeguarding public health and encouraging sustainable farming practices. While Lee and Seo point out that these devices precisely track cattle activities including eating, ruminating, reclining, and standing times, Zhang et al. emphasize the relevance of Wireless Internet of Things (W-IoT) in precision livestock production [51].

HOW TO COMBAT AMR

A major problem that impacts people, animals, plants, and the environment is antimicrobial resistance (AMR). Multidrug resistant (MDR) bacteria can be transferred from animals to people through contact or animal products. AMR cannot be addressed by a single government or group; coordinated cooperation between national and international non-governmental organizations (NGOs), healthcare, agriculture, finance, trade, and education is needed. Both vertical (across levels) and horizontal (across sectors) collaboration are possible. Antimicrobial use in animals and the over prescription of broad-spectrum antibiotics need to be restricted. The main goals of the fight against AMR include patient education, adherence, and judicious use of antibiotics, restricted prophylactics, and stewardship of hospital hygiene. Antimicrobial profiling and quicker diagnosis are crucial. Raising awareness, enhancing surveillance, enhancing cleanliness, maximizing the use of antibiotics, and investing in innovative medications and diagnostics are the five tactics recommended by the World Health Assembly [52].

International Measures

AMR is acknowledged as a worldwide problem. WHO emphasized it as a major theme in 2011 and called for global cooperation to combat and lower antimicrobial resistance [53].

- Promote collaboration between international agencies, experts, NGOs, and governments.
- Create and assist with AMR containment initiatives.
- Create networks to monitor antimicrobial use and AMR.
- Encourage global efforts to combat fake antibiotics.
- Encourage the study and creation of novel medications and vaccines.

National Strategies

A condensed and updated version of the national measures in bullet points is provided below [54]:

- Establish a policy for the responsible use of antibiotics in agriculture and health.
- Integrate the veterinary and public health sectors to improve national surveillance.
- Create point-of-care diagnostics to track resistance and identify pathogens.
- Invest in the development of novel vaccinations and antibiotics.
- Increase international cooperation on AMR and build capabilities.
- Adopt antimicrobial stewardship in hospital settings by using an essential drug list.

Rational Use of Antibiotics

Administering antibiotics appropriately based on clinical needs, the right dosage, duration, and cost is one example of an international metric. Reducing drug toxicity, pathogen selection, and the emergence of resistance is necessary for effective infection treatment. Globally, Antibiotic Stewardship Programs (ASPs) in healthcare settings are essential to guaranteeing the prudent use of antibiotics [41].

Ban on Over-the-Counter (OTC) Antibiotics

The over-the-counter selling of injectable and oral antibiotics, which are still widely used in many underdeveloped nations, needs to be strictly regulated. Only legitimate prescriptions should be used to distribute antibiotics. It is crucial to have ongoing awareness campaigns and to regularly reassess antibiotic regulations considering local AMR data [55].

Infection Prevention and Control (IPC)

A crucial, evidence-based strategy for shielding patients and medical staff from preventable illnesses, such as those caused by drug resistant microorganisms, is infection prevention and control, or IPC. It is essential for lowering AMR in medical environments. In this endeavor, doctors, nurses, pharmacists, and other healthcare professionals play a critical role. To reduce antimicrobial resistance, they must promote treatment compliance, educate patients and employees about AMR and aseptic procedures, and follow infection control guidelines.

The points have been condensed and updated as follows [56]:

- Establish an Infection Prevention and Control (IPC) committee.
- Make sure you wash your hands properly.
- Encourage precise diagnosis and efficient care.
- Antimicrobials should be used carefully.
- Conduct continual surveillance of antibiotic use and resistance.
- Preserve a high-quality supply chain for antimicrobials.
- Observe appropriate microbiological laboratory procedures.

Antimicrobial Stewardship Program (ASP)

A concerted effort to promote appropriate antimicrobial selection, dosage, and duration to enhance patient outcomes and lower resistance is known as antimicrobial stewardship. Its objectives are to minimize resistance, avoid overuse or misuse, and ensure appropriate prescribing. Optimizing patient outcomes and guaranteeing sustainable access are two important strategies. The CDC unveiled “Core Elements” for stewardship in 2014, which may be applied to any hospital, even smaller ones [57].

Use of Antibiotics in Animals

To combat antibiotic resistance, the WHO calls for stronger regulations on medically necessary antibiotics in animals. It proposes for lowering and banning use for growth promotion or routine prevention, allowing preventive use only after identified infections. Probiotics, better diet, vaccinations, better husbandry techniques, and better hygiene are alternatives [58].

Development of New Drugs and Vaccines

The need for integrated measures, including vaccines and newer antibiotics, is highlighted by the quick rise in resistance and the scarcity of new medications. Collaboration between academia and industry is necessary to invest in research and innovation to combat AMR. Long used for preventive, vaccines lower the demand for antibiotics without causing resistance. It is essential to develop vaccinations against resistant organisms such as *Acinetobacter baumannii* and carbapenem-resistant Enterobacterales [59].

Introduction of Checkpoint

Self-medication and the selling of illegal antibiotics are still prevalent in many low-income nations where it is simple to obtain medications without a prescription. The misuse is exacerbated by patient driven prescribing. To effectively prevent antimicrobial resistance, minimize antibiotic overuse, and stop these detrimental activities, strict laws, delayed prescribing techniques, and appropriate enforcement are necessary [26].

Community Engagement

Community practices, like waste disposal, food manufacturing, cleanliness, and healthcare habits, are all associated with the development of AMR. Additionally, different communities have different perspectives on antibiotics and resistance. Treatments can be protected by involving communities to promote behavioral change. To convert people's experiences into workable AMR prevention solutions, more study is required [59].

Alternatives to Antibiotics

Although many are still untested, researchers are looking into natural resources as antibiotic substitutes. Plants provide intriguing substances such polyphenolics, alkaloids, and flavonoids. It might be difficult to apply findings from lab settings to clinical settings. Novel treatments are made possible by developments in synthetic chemistry, genetic engineering, and biotechnology. Using microbial "chemical warfare" to combat resistant diseases could result in the development of new antimicrobials [60].

Phage Therapy

Phage therapy fights infections by using bacteriophages, which are viruses that infect bacteria. Compared to antibiotics, phages have the following benefits: low toxicity, minimal resistance, availability, and specificity. There are still issues with host range, formulation, immunological responses, and clinical adoption, though. Phage treatment is effective against antibiotic resistant topical infections, although it is not a complete substitute [61].

Bacteriocins

Lactic bacteria, primarily *Lactococcus* species, create tiny antimicrobial peptides called bacteriocins, which have bacteriostatic or bactericidal effects on related strains. They must be combined with other substances to influence Gram-negative organisms, but they inhibit Gram-positive bacteria. Bacteriocins, which are thought to be harmless, are being investigated for food preservation and antibacterial treatment. A lantibiotic derived from *Lactococcus* and *Streptococcus*, nisin increases the shelf life of food and exhibits efficacy against a variety of infections, including resistant Gram-negative bacteria, MRSA, *Streptococcus pneumoniae*, *Enterococci*, and *C. difficile* [62].

One Health

The “One Health” framework is a cooperative, multisectoral, and Trans disciplinary method of tackling global health issues at the local, national, and worldwide levels. It was created in partnership with FAO and OIE. By combining policies, programs, and AMR surveillance, it seeks to attain the best possible health for people, animals, and the environment. AMR is a prime example of why this strategy is necessary because it impacts every industry. However, because of factors, like poverty, corruption, inadequate healthcare, poor sanitation, and restricted access to antibiotics, implementation is more challenging in LMICs than in HICs. Antibiotics are frequently the sole choice in LMIC farming due to a lack of adequate veterinary care and support networks [63].

Although resistant strains frequently spread in LMICs, AMR is mostly monitored in HICs. Three Cs form the foundation of the One Health approach: coordination, cooperation, and communication between environmental specialists, animals, and people. It encourages stewardship, advocacy, education, and awareness and is backed by the FAO, OIE, and WHO tripartite. Research on AMR is improved across sectors by sophisticated techniques like whole genome sequencing (WGS) and next generation sequencing (NGS) [64].

CONCLUSION

Antimicrobial resistance (AMR) is a rapidly evolving global health threat caused by chromosomal mutations and horizontal gene transfer in bacteria. Over the past two decades, it has severely limited treatment options, leading to multidrug-resistant (MDR) infections in diseases such as tuberculosis, urinary tract infections, and sexually transmitted infections. The slow pace of new antibiotic development since the 1980s has worsened the situation, increasing the risk of a post-antibiotic era. Addressing AMR requires strong political will and coordinated global action involving governments, healthcare professionals, researchers, and the public. Key strategies include antimicrobial stewardship, strict antibiotic policies, reduced over-the-counter antibiotic use, and limiting antibiotics in agriculture. Enhanced surveillance, diagnostics, and vaccination programs are also essential. Prevention and responsible antibiotic use remain the most effective approaches. Immediate investment in new antibiotics, alternative therapies, and advanced diagnostics is crucial to preserve modern medical practices and prevent severe health, social, and economic consequences.

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