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Antimicrobial Resistance in Pathogenic Bacteria: Mechanisms, Global Trends, and Control Strategies – A Review

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Abstract
Antimicrobial resistance (AMR) has emerged as one of the most critical global health challenges of the 21st century, significantly undermining the efficacy of antibiotics and contributing to increased morbidity, mortality, and healthcare costs worldwide. The rapid emergence and dissemination of resistant bacterial strains are largely driven by the misuse and overuse of antimicrobial agents in human medicine, agriculture, and animal husbandry. This review provides a comprehensive analysis of the key mechanisms underlying antimicrobial resistance in pathogenic bacteria, including enzymatic drug inactivation, target site modification, overexpression of efflux pumps, and decreased membrane permeability. Furthermore, this study highlights the most clinically significant multidrug-resistant (MDR) pathogens, with particular emphasis on both Gram-positive and Gram-negative bacteria that pose substantial therapeutic challenges. Recent global epidemiological trends are examined to illustrate the rising prevalence and widespread distribution of resistant infections. In addition, current diagnostic approaches—ranging from conventional phenotypic methods to advanced molecular techniques—are critically evaluated in terms of their accuracy, speed, and clinical applicability. The review also discusses existing and emerging strategies to combat AMR, including antimicrobial stewardship programs, the development of novel antibiotics, combination therapies, bacteriophage-based treatments, and alternative approaches such as antimicrobial peptides. Despite these advancements, significant challenges persist, particularly in drug discovery, regulatory frameworks, and the need for coordinated global action.

Keywords:
Antimicrobial Resistance (AMR), Multidrug-Resistant Bacteria (MDR), Bacterial Pathogens, Antibiotic Resistance Mechanisms, Efflux Pumps, Drug Inactivation.

1. Introduction

Antimicrobial resistance (AMR) has become a significant health crisis in the world, becoming a threat to the effective treatment and prevention of infectious diseases. The extensive and unsuitable application of antibiotics in human medicine, veterinary care, agriculture and aquaculture has increased the rate of development of the resistant strains of bacteria, making most of the traditional therapies less effective. This has increased the difficulty with which previously easy to treat infections can be treated, resulting in increased morbidity, mortality, and a rising healthcare bill. The global health authorities suggest that AMR is expected to kill millions of people every year unless effective interventions are taken and this is why there are dire needs to develop comprehensive measures to deal with this increasing problem [1, 2].

Bacterial pathogens have evolved extensive resistance mechanisms, which make them survive when exposed to antimicrobials. Such mechanisms involve enzyme degradation or modification of antibiotics, changes in target sites to lower the drug binding affinity, active efflux of antimicrobial agents by membrane transport systems, and reduced permeability of bacterial cell envelope. The multicomponent nature and intricacy of these processes, coupled with the capacity of bacteria to obtain resistance genes via horizontal gene transfer, have played a major role in the quick spread of multidrug-resistant (MDR) strains across various settings and geographic areas [1, 3].

Over the past few years, a number of clinically significant pathogens (also known as priority or high-risk organisms) have shown disturbing degrees of resistance to various groups of antibiotics. Gram-positive bacteria, including methicillin-resistant Staphylococcus aureus (MRSA) and Gram-negative bacteria, including Escherichia coli, Klebsiella pneumoniae, and Pseudomonas aeruginosa have been linked to severe infections which are becoming more difficult to treat. The worldwide distribution of these pathogens highlights the importance of increased surveillance mechanisms and a better comprehension of the resistance patterns [4].

Diagnosis is essential in the management of AMR as a timely and accurate diagnosis will allow the selection of the correct antimicrobials and decrease improper use of antibiotics. Conventional phenotypic approaches though valid are usually time consuming compared to the new molecular and genomic approaches which have fast and accurate methods of detecting resistance determinants. Nonetheless, issues pertaining to cost, availability, and adoption are still present, especially in the low- and middle-income nations [5-7].

A complex strategy is needed to reduce the effects of AMR. The most important of them are the introduction of antimicrobial stewardship programs to streamline the use of the antibiotics, the creation of new antimicrobial agents, the combination therapy, and the investigation of other treatment options, like bacteriophage therapy and antimicrobial peptides. Moreover, international cooperation, policy formulation, and sensitization of the people are also critical elements in fighting the resistance [9, 10].

This review will offer a broad general account of the issue of antimicrobial resistance in pathogenic bacteria by outlining the mechanisms underlying the resistance, examining the recent trends in the issue in the world, critically analyzing the current diagnostic methods, and discussing the current and emerging methods of controlling and managing AMR.

2. Related Work

The problem of antimicrobial resistance (AMR) has been the focus of long-term research due to its growing clinical, epidemiological, and socioeconomic consequences [11-13]. Recent large-scale reviews have taken AMR in broad public-health and mechanistic viewpoints, highlighting that resistance is caused by a combination of factors that include improper use of antibiotics, selective pressure in healthcare and agriculture, and the rapid exchange of resistance genes between bacterial groups. These researches have consistently shown that enzymatic inactivation of antibiotics, alteration of targets, efflux expression, and minimization of permeability are the fundamental biological biases of bacterial resistance. A number of key articles have enhanced the evidence base on the burden and rank of priority of resistant pathogens in the world. The 2022 Lancet systematic analysis of the global burden of AMR recognized resistant bacterial infections as a primary cause of mortality on the global stage, along with making AMR a projected threat become a quantitatively reported current crisis. The most recent global prioritization of bacteria by the WHO 2024 Bacterial Priority Pathogens List was published in 2024, and it lists 24 pathogens in 15 families of bacteria, with the continued dominance of high-risk Gram-negative organisms, and major community and hospital pathogens being listed, including Pseudomonas aeruginosa, Staphylococcus The second significant body of literature has been on the clinically important multidrug-resistant bacteria and new resistance trends. Published in 2023-2025, reviews have been especially keen on Gram-positive and Gram-negative priority organisms, such as methicillin-resistant Staphylococcus aureus (MRSA), carbapenem-resistant Acinetobacter baumannii, resistant Klebsiella pneumoniae, and other ESKAPE-related pathogens. The studies have enhanced the comprehension of pathogen-specific resistance architecture, although most are structured around a single taxa or resistance category as opposed to providing a synthesis across mechanisms, surveillance patterns, diagnosis, and interventions [14-16].

There has also been a rapid growth in diagnostic research. Most recent reviews have contrasted traditional methods of phenotypic antimicrobial susceptibility testing with molecular and genotypic platforms, such as PCR-based platforms, resistance-gene panels, sequencing-based platforms and more recent detection platforms aimed at reducing turnaround time. This literature demonstrates that state-of-the-art diagnostics can enhance timely decision making in therapy and stewardship, yet it also reveals unresolved issues surrounding the cost, infrastructure needs, gene-phenotype mismatch, and lack of access in low-resource environments. Parallel to this, other sets of studies have assessed response measures to AMR. Systematic reviews on antimicrobial stewardship have demonstrated that systematic prescribing supervision, monitoring, education, and policy-driven initiatives have the capability to decrease improper antibiotic prescribing and aid in limiting the selection of resistance. Alternatives and adjuncts to conventional antibiotics have been discussed in recent literature at the therapeutic frontier, including bacteriophage therapy and phage-enabled strategies of multidrug-resistant infections. These works are hopeful, but they also mention that there are still unresolved concerns in the field of standardization, regulation pathways, safety testing, the development of resistance to phages, and the requirement to provide more solid evidence of clinical trials [17].

Although recent AMR scholarship is rich, there is a gap that needs to be filled. Most of the reviews available focus on a single aspect of the issue, e.g. molecular mechanisms, diagnostics, stewardship, or alternative therapies. Others give general summaries and fail to adequately relate pathogen prioritization, global epidemiology, diagnostic potential, and intervention measures into one analysis framework [17].

As such, there is still a need to have a thorough-going review that incorporates mechanisms of resistance, primary multidrug-resistant pathogens, global trends, diagnostic methods, and existing and emerging control strategies to give a more consistent and practically valuable insight on AMR in pathogenic bacteria.

3. Mechanisms of Antimicrobial Resistance

The mechanisms involved in antimicrobial resistance (AMR) in pathogenic bacteria are various and diverse in nature such that they allow microorganisms to survive the effects of antimicrobial agents. Such mechanisms can be inherent or acquired and are frequently facilitated by genetic mutation or horizontal gene transfer via plasmids, transposons and integron. These processes are critical in understanding how to develop effective therapeutic interventions and in reducing transmission of resistant strains [5, 18]. The major mechanisms of antimicrobial resistance are illustrated in figure 1. The key processes of antimicrobial resistance are as follows.

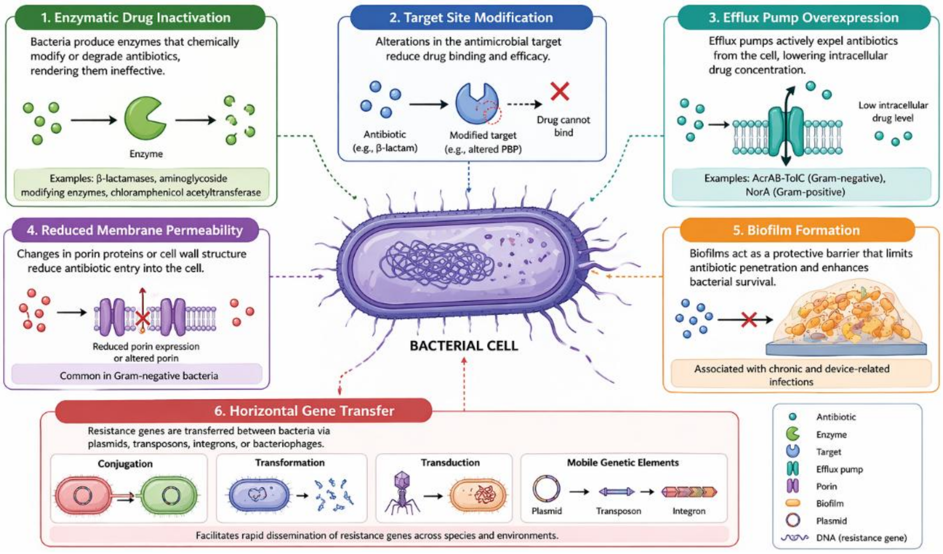

Figure 1. Major mechanisms of antimicrobial resistance in pathogenic bacteria

3.1 Enzymatic Drug Inactivation

Production of enzymes that chemically inactivate the antibiotics before they reach their target sites is one of the most prevalent mechanisms of resistance. One of such classic examples is the synthesis of beta-lactamases which cleave the beta-lactam ring in antibiotics like penicillins, cephalosporins and carbapenems, making them useless [19].

The presence of extended-spectrum β-lactamases (ESBLs) and carbapenemases has been especially worrying because they enable them to cause resistance to a wide spectrum of β-lactam antibiotics. Along with β-lactamases, other modifying enzymes can be produced by bacteria, including aminoglycoside-modifying enzymes (AMEs), which modify the structure of antibiotics by acetylating, phosphorylating, or adenylating. These enzymatic reactions greatly decrease the binding affinity of antibiotics towards their targets and hence the antimicrobial activity of the antibiotics is inhibited [20].

3.2 Target Site Modification

The other highly important resistance mechanism is structural changes in the target site of the antibiotic that diminish or abolish the drug binding. These changes can either be genetic mutations or can be as a result of acquiring resistance genes which encode different proteins. Staphylococcus aureus (MRSA) resistance to methicillin is an example of this: the gene mediates this resistance by encoding a low-affinity penicillin-binding protein (PBP2a).

Equally, DNA gyrase and topoisomerase IV gene mutations can make them resistance to fluoroquinolones whereas mutations in ribosomal subunits are linked to resistance to macrolides, tetracyclines, and aminoglycosides. Target modification is especially problematic due to the fact that it frequently results in high-level resistance and may influence a variety of antibiotics of the same group [21].

3.3 Efflux Pump Overexpression

Efflux pumps are a group of membrane-related transport proteins that actively pump out antibiotics and other toxic substances of bacterial cells. The overexpression of these pumps causes the intracellular concentration of antimicrobial agents to decrease below the therapeutic level, thus allowing bacteria to survive.

The efflux systems are categorized into a number of families such as the major facilitator superfamily (MFS), resistance-nodulation-division (RND) family, ATP-binding cassette (ABC) transporters and multidrug and toxic compound extrusion (MATE) family. Most prominently of these are RND-type efflux pumps, which play a role in Gram-negative bacteria in multidrug resistance through the export of a broad spectrum of structurally unrelated antibiotics. Efflux pumps can significantly contribute to multidrug resistance (MDR) because of their broad substrate specificity, and they can synergize with other resistance mechanisms [22].

3.4 Reduced Membrane Permeability

Reduced cell envelope permeability can also cause bacterial resistance, by restricting the entry of antibiotics into the cell. It occurs particularly in Gram-negative bacteria where the outer membrane is a selective barrier.

Alterations of porin proteins, which permit the passive diffusion across small molecules, can greatly decrease the uptake of antibiotics. An example of such loss or alteration of porins which can reduce the susceptibility to β-lactams and carbapenems includes the loss or loss or mutation of porins in Escherichia coli (OmpF, OmpC) or Pseudomonas aeruginosa (OprD). Reduced permeability can be used together with efflux systems to provide a two-barrier effect that further increases resistance [23].

3.5 Biofilm Formation

Biofilm formation is a significant form of phenotypic resistance whereby the bacterial communities stick to the surfaces and become entrenched within a self-produced extracellular polymeric matrix.

Bacteria in biofilms are much more antibiotic and host immune resilient. The biofilm matrix limits the penetration of the antibiotics and the availability of the slow-growing or dormant cells inhibits the efficacy of the antibiotics, which targets the active cellular functions. Moreover, biofilms help in horizontal gene transfer and therefore propagating resistance genes across bacterial populations. Biofilm-associated infections are especially hard to treat and are usually linked with medical equipment and chronic infections [23].

3.6 Horizontal Gene Transfer

The concept of horizontal gene transfer (HGT) is key to the fast spread of antimicrobial resistance among bacteria. The most common ways of transferring resistance genes are transformation (free DNA uptake), transduction (transfer via bacteriophages), and conjugation (transfer via plasmids between bacteria). The mobile genetic factors like plasmids, integrons and transposons tend to carry more than one resistance gene and can contribute to acquisition of resistance to multiple antibiotics at the same time. This plays a large role in the development of multidrug resistant (MDR) and extensively drug resistant (XDR) strains [24].

3.7 Combined and Synergistic Mechanisms

In most instances, bacteria use a combination of several resistance mechanisms at a time, leading to a higher survival rate and increased levels of resistance. As an example, a bacterium can integrate decreased permeability and overexpression of efflux pumps and enzymatic inactivation of drugs and produce a very robust system of defense. This kind of synergistic interaction makes treatment regimens challenging and necessitates combination therapy and new antimicrobial strategies to overcome resistance [25].

4. Major Multidrug-Resistant (MDR) Pathogens

Multidrug-resistant (MDR) bacteria pose a significant challenge to the global population health because of the capacity to resist various classes of antimicrobial agents and thus restrict the treatment options and consequently elevate the rate of morbidity and mortality. Of these, a subset of clinically important pathogenic organisms has received special focus due to their capacity to circumvent the action of widely-used antibiotics, known as the ESKAPE pathogens. A high percentage of hospital-acquired infections is caused by these organisms and they are often linked to serious clinical outcomes [26].

4.1 ESKAPE Pathogens

The ESKAPE group includes Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa, and Enterobacter species. These pathogens exhibit high levels of resistance through diverse mechanisms such as β-lactamase production, efflux pump activity, and genetic adaptability. Their prevalence in healthcare settings, combined with their resistance profiles, makes them a primary focus of antimicrobial research and infection control strategies [27].

- Enterococcus faecium: Vancomycin-resistant E. faecium (VRE) commonly due to van genes that modify cell wall targets.
- Staphylococcus aureus: Methicillin-resistant S. aureus (MRSA) continues to be a major pathogen in hospital and community settings.
- Klebsiella pneumoniae: Produces many carbapenemases (e.g., KPC, NDM) and is therefore a common cause of carbapenem-resistant klebsiella pneumoniae (CRKP).
- Acinetobacter baumannii: Has extensive drug-resistant (XDR) and environmental persistence in hospitals.
- Pseudomonas aeruginosa: Intrinsic resistance and effective efflux pumps.
- Enterobacter spp.: Inducible β-lactamases and rising resistance.

4.2 Gram-Positive MDR Pathogens

Gram-positive bacteria remain an important cause of MDR infections, especially in the community and hospital [28].

- Methicillin-resistant Staphylococcus aureus (MRSA): β-lactam antibiotic resistant due to mutated penicillin-binding proteins. It causes skin infections, pneumonia and bloodstream infections.
- Vancomycin-resistant Enterococci (VRE): Enterococcus faecium and Enterococcus faecalis, resistant to glycopeptides antibiotics and are often associated with urinary tract and bloodstream infections.
- Resistant Streptococcus pneumoniae: Resistant to penicillin and macrolides and can be difficult to treat in respiratory tract infections.

4.3 Gram-Negative MDR Pathogens

Gram-negative bacteria are more difficult to treat because they have more complicated cell envelope and can acquire multiple resistance mechanisms [29].

- Carbapenem resistant Klebsiella pneumoniae (CRKP): One of the most feared MDR pathogens due to its lack of effective therapies.
- Multidrug-resistant Escherichia coli: A common cause of urinary tract infections and capable of producing extended-spectrum β-lactamases (ESBLs). • Acinetobacter baumannii: Frequently resistant to most antibiotics, commonly found in ICU.
- Pseudomonas aeruginosa: Intrinsically resistant, forms biofilms, and acquires mutations.
- Neisseria gonorrhoeae: A new MDR pathogen resistant to several antibiotics, making it difficult to treat sexually transmitted infections.

4.4 Clinical Impact and Global Distribution

The spread of MDR pathogens in the world has been growing exponentially in the last decade due to international travels, transmission in hospitals, and poor infection control measures. Limited diagnostic infrastructure and regulatory oversight largely affect low- and middle-income countries. MDR infections are linked to a longer hospitalization period, high costs of treatments, and mortality rates. Moreover, the development of extensively drug-resistant (XDR) and pan-drug-resistant (PDR) strains has cast some grave doubts regarding the possibility of untreatable infections. Surveillance initiatives like the one spearheaded by the World Health Organization (WHO) are important in the tracking of resistance patterns and the strategy to respond to them in the whole world [30].

Table 1. Major Multidrug-Resistant Pathogens and Their Characteristics

Pathogen	Type	Key Resistance Mechanism	Associated Infections
***Staphylococcus aureus* (MRSA)**	Gram-positive	Altered PBP (mecA gene)	Skin, bloodstream, pneumonia
***Enterococcus faecium* (VRE)**	Gram-positive	Cell wall modification (van genes)	UTI, bloodstream
Streptococcus pneumoniae	Gram-positive	Target modification	Respiratory infections
***Klebsiella pneumoniae* (CRKP)**	Gram-negative	Carbapenemase production	Pneumonia, sepsis
***Escherichia coli* (ESBL)**	Gram-negative	β-lactamase production	UTI, sepsis
Acinetobacter baumannii	Gram-negative	Efflux pumps, enzyme production	ICU infections
Pseudomonas aeruginosa	Gram-negative	Efflux pumps, low permeability	Respiratory, wound
Neisseria gonorrhoeae	Gram-negative	Target mutation, efflux	Sexually transmitted infections

5. Global Trends of Antimicrobial Resistance

Antimicrobial resistance (AMR) has become a rapidly growing global health threat, with marked differences in rates, scale and consequences in different geographical areas. The latest surveillance reports and global progress reports on AMR reveal a global problem that is no longer confined to developing nations but is spreading in industrialised nations. The growth in resistant infections is a result of a mix of biological, environmental and socio-economic conditions driving the emergence and spread of resistant pathogens [31].

5.1 Increasing Global Prevalence of AMR

The latest global surveillance reports show a dramatic increase in the resistance of many bacterial species to a range of antibiotics. The World Health Organization (WHO) reports that one-sixth of all bacterial infections globally in 2023 were resistant to frequently used antibiotics, highlighting the extent of the problem . Moreover, the number of resistant pathogens and antibiotics increased in over 40% of pathogen-antibiotic pairs from 2018 to 2023, with an average yearly growth of 5-15% . Moreover, new research estimates a 43% rise in multidrug-resistant infections, especially in hospital infections, suggesting hospitals continue to be a significant source of resistant infections . These reports underline the rapid pace of AMR and its consequences for health [31].

5.2 Regional Distribution and Disparities

AMR prevalence differs by region. Antimicrobial resistance (AMR) is more prevalent in low- and middle-income countries (LMICs) as a result of poor access to diagnostic tools, weak infection control and inappropriate antibiotic consumption. Recent reports from the World Health Organization (WHO) show resistance is highest in areas like South Asia, the Middle East and sub-Saharan Africa, where in some instances resistance to first-line antibiotics for certain infections is greater than 70% . By comparison, higher-income countries tend to have lower resistance rates because of better access to health care and the implementation of antimicrobial stewardship policies; even so, AMR remains a significant problem in these countries. The growing global surveillance networks, including the World Health Organization (WHO) Global Antimicrobial Resistance and Use Surveillance System (GLASS), now include more than 100 countries, providing a better understanding of regional variations and trends [31].

5.3 Trends in Antibiotic Consumption

Antibiotic use is a key driver of the rise in antimicrobial resistance. There has been a substantial increase in the use of antibiotics globally, with one study reporting a 16.3% growth in the total antibiotic consumption from 2016 to 2023, especially in the developing world.

This growth is driven by a rising demand for medical care, increasing population density, and often misuse and overuse of antibiotics. Antibiotic overuse in livestock farming also plays a role in the rise of AMR by providing more opportunities for bacterial adaptation. The interdependence of human, animal and environmental health - known as the "One Health" concept - underlines the challenges of AMR control worldwide [31, 32].

5.4 Emergence of High-Risk Resistant Pathogens

The latest global data show worrying levels of increasing resistance in Gram-negative bacteria, including Klebsiella pneumoniae, Escherichia coli and Acinetobacter baumannii. Data indicate that almost half of Klebsiella pneumoniae bloodstream infections are resistant to third-generation cephalosporins, and the use of "last line" antibiotics such as carbapenems has subsequently increased. Unfortunately, resistance to these antibiotics is also on the rise, leaving few options. The swift rise of carbapenem-resistant and extensively drug-resistant (XDR) strains is a major threat to healthcare in critical care and vulnerable patient populations [31].

5.5 Mortality and Future Projections

AMR has a significant and increasing global health burden. In 2019, it is estimated that antimicrobial resistance was directly responsible for around 1.27 million deaths globally and accounted for almost 5 million deaths in total.

The outlook is even more dire. Estimates predict that, by 2050, up to 1.9 million people per year could die from AMR, leading to tens of millions of deaths worldwide as a result of AMR. This underscores the need for global action to mitigate a looming post-antibiotic world where infections will be untreatable [31, 32].

5.6 Impact of COVID-19 and Recent Developments

AMR trends have also been affected by the COVID-19 pandemic. The pandemic has led to greater antibiotic use, often for COVID-19, driving resistance in some areas. Moreover, pandemic-related disruptions in health care and infection prevention have led to the spread of resistant infections, especially in hospitals. Recent studies have reported an increase in resistant infections, particularly with Gram-negative bacteria, post-2020 in health-care facilities, highlighting the need for improved infection prevention and antibiotic stewardship measures [33].

6. Diagnostic Approaches for AMR Detection

The timely and accurate identification of antimicrobial resistance (AMR) in patients is critical for optimal patient care, antibiotic prescribing, and implementation of infection control measures. AMR diagnostic methods can be broadly divided into phenotypic methods, which monitor bacterial growth in the presence of antibiotics, and genotypic methods, which detect the presence of resistance genes or mutations [34].

The use of new technologies has enhanced the accuracy and timeliness of AMR detection, but there are still several issues with cost, access and interpretation.

6.1 Phenotypic Methods

Conventional, or "phenotypic" methods are the most common methods used to determine bacterial susceptibility to antibiotics (AST). These assess the real-life interaction of bacteria with antimicrobials in the laboratory. Common techniques include[34]:

- Disk diffusion (Kirby–Bauer method): Assesses the diameter of the inhibition zone around antibiotics disks on agar.
- Broth dilution: Measures the minimum inhibitory concentration (MIC) of antibiotics.
- Automated methods: Like VITEK and BD Phoenix, for quicker results with uniform procedures.

Phenotypic methods are the "gold standard" as they directly determine bacterial susceptibility. But they take time (24-72 hours), which can impact on treatment decisions in urgent situations.

6.2 Molecular (Genotypic) Methods

Molecular methods detect the presence of resistance genes or mutations that cause AMR. These are highly sensitive and fast, and are increasingly being implemented in clinical labs. Key techniques include[34]:

- Polymerase Chain Reaction (PCR): Targets resistance genes like mecA, blaKPC and vanA.
- Real-time PCR (qPCR): Allows for real-time detection and quantification of resistance genes.
- DNA microarrays: Simultaneously detect several resistance genes.
- Whole genome sequencing (WGS): Offers detailed information about resistance genes, mutations and strain types.

While molecular techniques are quicker (usually hours), they can be misleading as they may not correlate with resistance due to gene expression. Moreover, they need sophisticated equipment and skills.

6.3 Emerging and Rapid Diagnostic Technologies

The past few years have seen the emergence of new technologies to shorten the time to diagnosis and increase accuracy [35].

- Matrix-Assisted Laser Desorption/Ionization Time-of-Flight (MALDI-TOF) Mass Spectrometry: Mainly used to rapidly identify bacteria, but also being used for resistance detection.
- CRISPR-based technologies: New technologies for specific detection of resistance genes.
- Biosensors and microfluidics: Allow for real-time detection with little sample processing.

- Nanotechnology-based methods: Improve sensitivity and allow detection of very low levels of bacteria.

Such innovations could be valuable tools for real-time diagnosis, particularly in intensive care units, but are still experimental or in early clinical development.

6.4 Challenges in AMR Diagnostics

While there has been tremendous advances, there are still a number of challenges [34, 35]:

- Time-consuming in conventional methods
- Cost and infrastructure needs for new technologies
- Lack of congruence in molecular diagnostics
- Access issues in resource limited settings
- Standardisation and validation of new technologies

Overcoming these barriers will help in the uptake and optimal use of AMR diagnostic tools.

Table 2. Comparison of Diagnostic Methods for AMR Detection

Method Type	Technique	Advantages	Limitations	Time Required
Phenotypic	Disk Diffusion	Simple, low cost	Less precise, slower	24–48 h
Phenotypic	Broth Dilution (MIC)	Accurate, quantitative	Time-consuming	24–72 h
Phenotypic	Automated Systems	Standardized, faster	Expensive	8–24 h
Molecular	PCR/qPCR	Rapid, highly sensitive	Detects only known genes	2–6 h
Molecular	DNA Microarray	Multiplex detection	High cost	6–12 h
Molecular	Whole Genome Sequencing	Comprehensive analysis	Expensive, complex	24–48 h
Emerging	MALDI-TOF	Rapid identification	Limited resistance detection	Minutes–hours
Emerging	Biosensors	Point-of-care potential	Limited clinical validation	Minutes
Emerging	CRISPR-based	High specificity	Early-stage technology	<1–2 h

7. Strategies to Combat Antimicrobial Resistance

The growing problem of antimicrobial resistance (AMR) is an issue that calls for a multi-faceted approach in clinical, technological and policy measures. The main strategies of curbing AMR are to optimize the existing therapeutic agents, develop new therapeutic agents and global measures to control the spread of resistant pathogens. This paragraph discusses the major current and emerging measures to deal with AMR [36]. The most important steps to prevent antimicrobial resistance are summarised in Figure 2.

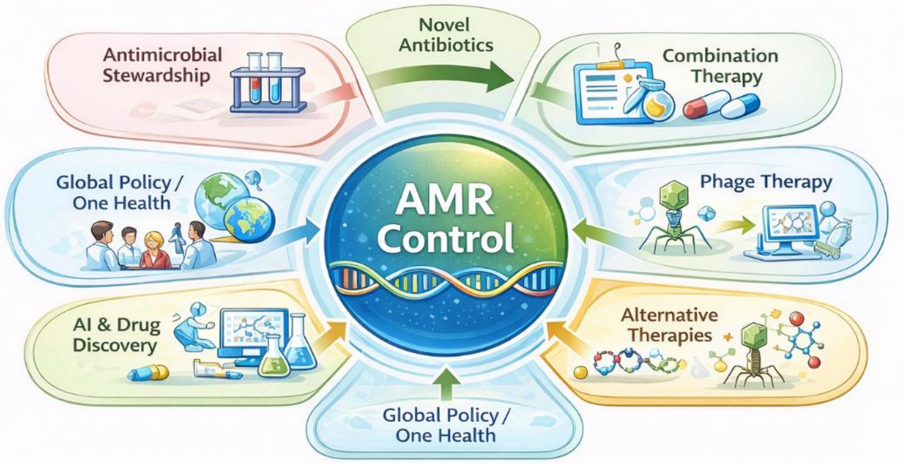

Figure 2. Strategies to combat antimicrobial resistance

7.1 Antimicrobial Stewardship Programs

One of the best approaches to decreasing the number of inappropriate antibiotic use and reduce the emergence of resistance is antimicrobial stewardship programs (ASPs). The goals of these programs are to have the right antibiotic, at the right dose, and at the right duration. Key components of ASPs include[36]:

- Evidence-based prescribing guidelines
- Surveillance of antibiotic use and resistance patterns
- Education and training of healthcare professionals
- De-escalation of therapy based on diagnostic results
- Restriction of broad-spectrum antibiotics

It has been shown that ASPs can lead to a substantial decrease in the use of antibiotics, reduce the patient outcomes, and decrease healthcare expenditure. They are especially important to be implemented in hospitals where the abuse of antibiotics is the most common.

7.2 Development of Novel Antibiotics

New antibiotics are urgently needed to combat the increasing resistance to current antibiotics. But progress in antibiotic development has been hampered by scientific, economic and regulatory factors. Recent efforts focus on [36]:

- Novel drug classes targeting previously unexplored bacterial pathways
- Antibiotics with enhanced stability against resistance mechanisms
- Synthetic and semi-synthetic compounds with improved efficacy

Despite these developments, the antibiotic pipeline is narrow and there is a pressing need for incentives that will motivate pharmaceutical companies to develop new antibiotics.

7.3 Combination Therapy

The use of more than one antimicrobial agent to increase the effectiveness of treatment and prevent the development of resistance is termed combination therapy. This approach can [36]:

- Improve bacterial killing through synergistic effects
- Prevent the emergence of resistant mutants
- Expand the spectrum of activity

For example, β-lactam antibiotics are often combined with β-lactamase inhibitors (e.g., clavulanic acid) to overcome enzymatic degradation. Combination therapy is widely used in the treatment of severe and multidrug-resistant infections.

7.4 Bacteriophage Therapy

Bacteriophage (phage) therapy represents a promising alternative to conventional antibiotics. Phages are viruses that specifically infect and lyse bacterial cells.

Advantages of phage therapy include:

- High specificity toward target bacteria
- Ability to replicate at the site of infection
- Effectiveness against antibiotic-resistant strains

However, challenges such as regulatory approval, standardization, and potential bacterial resistance to phages must be addressed before widespread clinical adoption[36].

7.5 Antimicrobial Peptides and Alternative Therapies

Antimicrobial peptides (AMPs) are naturally produced molecules that have broad-spectrum killing activity due to their ability to disrupt bacterial membranes. They have a number of benefits, such as speedy action and reduced risk of resistance. Other alternative approaches include[36]:

- Nanoparticle-based therapies
- Quorum sensing inhibitors (block bacterial signalling)
- Immunotherapy to boost the immune system

Such novel approaches are currently under investigation as a supplement to or replacement for antibiotics.

7.6 Vaccination and Infection Prevention

Vaccines are vital in preventing the spread of bacterial infections, thus reducing antibiotic use and minimising resistance. The impact of vaccines for Streptococcus pneumoniae and Haemophilus influenzae is substantial.

Furthermore, infection prevention and control strategies (such as hand hygiene, sterilisation, and health care-associated infection control) are critical to minimising the spread of resistant superbugs [37].

7.7 Artificial Intelligence and Drug Discovery

The use of artificial intelligence (AI) and machine learning technologies is growing to speed up the discovery of antibiotics and improve treatment approaches. AI-based models can [38]:

- Discover new antibiotics
- Predict resistance patterns
- Predict the effectiveness of drug combinations and doses

These tools have the potential to speed up and lower the cost of drug discovery, and enhance outcomes of treatment strategies.

7.8 Global Collaboration and Policy Interventions

To combat AMR, a global effort is needed from governments, health authorities and the international community. Key initiatives include [39]:

- National and global implementation of AMR plans
- Improving surveillance (e.g. WHO GLASS)
- Antibiotic use in agriculture and livestock
- Education campaigns on appropriate antibiotic use.

The One Health approach, which recognises the interdependence of human, animal and environmental health, is crucial to addressing AMR globally.

8. Challenges and Future Directions

Although a lot of progress has been made towards the comprehension and management of antimicrobial resistance (AMR), a lot of challenges still persist to pose an obstacle in effective control and management of the global menace. The major issue is the fact that the rate of antibiotic discovery and development is decreasing, mainly because of the expensive research costs, low financial incentives, and the complicated regulatory regulations. Consequently, the existing pipeline of new antibiotics is not adequate to keep abreast with the emerging resistance pathogens [40]. The major challenges and future directions in combating antimicrobial resistance are illustrated in Figure 3.

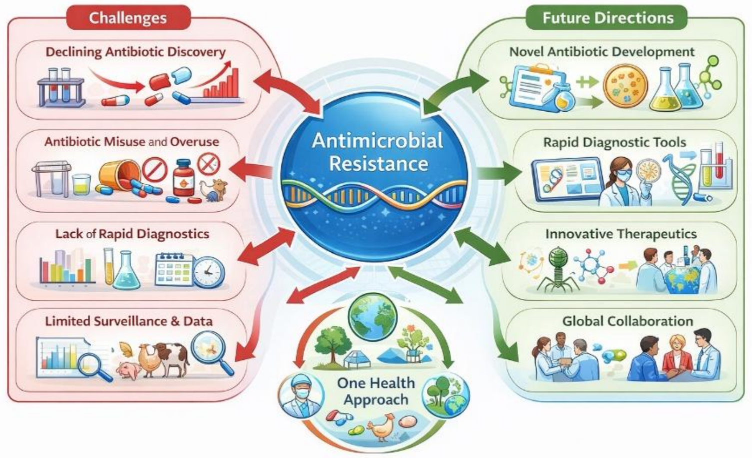

Figure 3. Challenges and Future Directions in Combating Antimicrobial Resistance

The universal overuse and abuse of antibiotics in human and veterinary medicine is another important problem. In most areas, antibiotics are over the counter, and are used improperly and with a greater selective pressure towards resistance development. Also, a high volume of antibiotic use in farms and cattle rearing is also a contributing factor to environmental reservoirs of resistance genes. The absence of quick, cheap and generally available diagnostic aids also increases the difficulties in AMR management especially in low and middle-income nations. Delays in diagnosing or diagnostic errors can lead to empirical and broad-spectrum antibiotic treatment that positively contributes to resistance. In addition, the lack of surveillance systems and irregularity in data reporting in different regions make it hard to track the trends of resistance and introduce specific interventions. Scientifically, the genetic malleability of bacteria and the effectiveness of horizontal gene transfer allow the rapid spread of resistance phenotypes between species and environments. The development of extensively drug-resistant (XDR) and pan-drug-resistant (PDR) isolates is causing alarm over the prospect of incurable infections in the near future.

In the future, there are a number of future directions that can be vital in fighting AMR. To begin with, it is necessary to rejuvenate antibiotic research and development by establishing public-corporate collaborations, funding, and expedited regulatory processes. Second, the development of the rapid diagnostics field, such as point-of-care and genomic solutions, should also be prioritized in order to make timely and accurate treatment decisions. In addition, novel therapeutic strategies, including bacteriophage therapy, antimicrobial peptides, and microbiome-based interventions have potential to serve as alternatives or complements to conventional antibiotics. Artificial intelligence and machine learning in drug discovery and predicting resistance are also set to have a transformative role in the next few years. Notably, the One Health approach that acknowledges the interrelationship between human, animal, and environmental health needs to be strengthened in order to combat AMR in an integrated way. The international cooperation, the implementation of the policy, the education of the population, and awareness will also be essential in maintaining the sustainable development. Unless the international community undertakes concerted action, the AMR burden is bound to keep increasing, with a critical impact on contemporary healthcare systems.

9. Conclusion

The problem of antimicrobial resistance (AMR) is a significant health challenge in the world, which compromises the success of antibiotics and decades of medical advances. This review looked at major resistance mechanisms in pathogenic bacteria such as inactivation of drugs, alteration of targets, efflux pumps, decreased permeability, biofilm formation, and horizontal gene transfer. It also emphasized key multidrug-resistant pathogens, especially the ESKAPE group, and discussed world trends indicating the growing prevalence of resistant infections. Detection is enhanced by advanced diagnostics (traditional phenotypic technologies to new molecular technologies) and the responses to this challenge include antimicrobial stewardship, new antibiotics, and alternative treatment approaches (e.g., bacteriophages and antimicrobial peptides). Nevertheless, there are still issues of less development of drugs, poor diagnostics, misuse of antibiotics, and poor international coordination. In sum, AMR must be tackled through integrated strategy that incorporates innovation, good policies and global partnerships to maintain sustainable efficacy of antimicrobials and alleviate post-antibiotic world.

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