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Original Article

Emerging Trends in Antimicrobial Resistance (AMR)

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ABSTRACT

Antimicrobial resistance (AMR) is a major global public health threat that reduces the effectiveness of antibiotics and endangers the treatment of infectious diseases. The misuse and overuse of antimicrobials in healthcare, agriculture, and the environment, along with bacterial mutation and gene transfer, are key drivers of AMR. This review examines global trends, surveillance systems, and the socioeconomic impact of AMR, particularly in low- and middle-income countries. It highlights the importance of international initiatives such as the WHO Global Action Plan, the One Health approach, and the UN Sustainable Development Goal 3 (Good Health and Well-being). The study also explores novel strategies, including antimicrobial stewardship, public awareness, and emerging therapeutic options like bacteriophages, peptides, and nanotechnology-based solutions. Addressing AMR requires coordinated global efforts, innovation, and multisectoral collaboration to preserve the effectiveness of current and future antimicrobials.

Keywords: AMR (Antimicrobial Resistance),BSI (Bloodstream Infections),Carbapenem resistance, Indicator antibiotics, Surveillance systems, Resistance drivers ,Low- and middle-income countries (LMICs), Cost implications, One Health approach, SDG 3 (Good Health and Well-being),Novel therapeutics, Infectious diseases, Control strategies, Global health

INTRODUCTION

When microorganisms like bacteria, fungi, viruses, and parasites develop the ability to resist drugs that once killed them. This makes infections harder to treat and increases the risk of disease spread, severe illness, and death. The main cause of AMR is the misuse and overuse of antibiotics in humans, animals, and agriculture. Poor hygiene, lack of new medicines, and weak infection control also worsen the problem. AMR is often called the “Silent Pandemic” and is a major global health threat. It is estimated to cause 1.2 million deaths each year, which could rise to 10 million by 2050 if not controlled. To fight AMR, organizations like WHO, FAO, and OIE promote the “One Health Approach”, encouraging cooperation between human, animal, and environmental health sectors. WHO also started programs like GAP-AMR and GLASS to monitor and manage resistance. Increasing public awareness, rational antibiotic use, and strong infection control are key to preventing AMR and protecting global health.

Global Epidemiological Trends:

Rising Global Burden:

AMR causes millions of infections and over 1.3 million deaths annually worldwide.

Regional Variations:

Low- and Middle-Income Countries (LMICs): Highest AMR rates due to misuse of antibiotics, poor sanitation, and lack of regulation.

High-Income Countries: Better surveillance and stewardship, but rising resistance in hospital settings.

Key Resistant Pathogens (WHO Priority List):

E. coli, Klebsiella pneumoniae – resistant to third-generation cephalosporin and carbapenems.

Staphylococcus aureus (MRSA) – methicillin-resistant.

Pseudomonas aeruginosa, Acinetobacter baumannii – multidrug-resistant.

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Neisseria gonorrhoeae, Salmonella, Mycobacterium tuberculosis – emerging resistance.

Drivers of Resistance:

Overuse in humans, livestock, and agriculture. Poor infection control and sanitation. Global travel and trade accelerating spread.

Surveillance Insights:

Systems like WHO GLASS, ECDC EARS-Net, and CDC NARMS show increasing trends of resistance to carbapenems and fluoroquinolones globally.

Emerging Concerns:

Resistance genes (e.g., NDM-1, mcr-1) spreading between species. Environmental contamination with antibiotic residues.

Global Action:

Focus on One Health approach, antimicrobial stewardship, rapid diagnostics, and global data sharing to control AMR trends. [1]

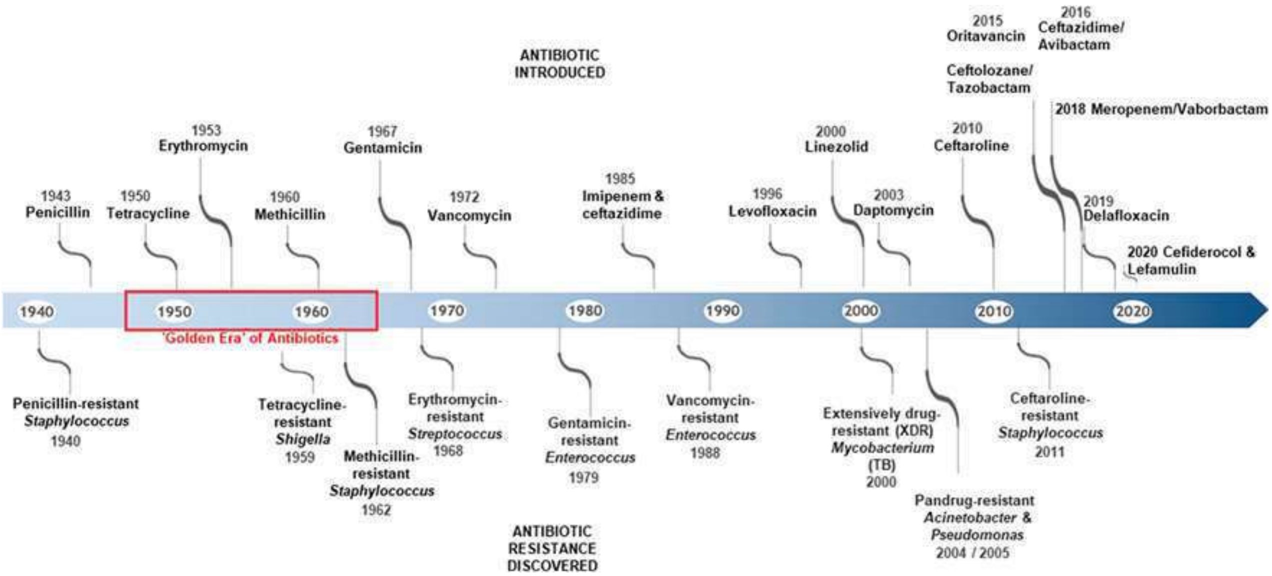

Fig 1: Timeline showing some of the key antibiotic discoveries and report of the emergence of antibiotic resistance strains

Molecular and Genetic Insights in Antimicrobial Resistance (AMR):

1. Genetic Basis of AMR:

Resistance can occur through two major genetic routes:

a. Mutation (De novo mutagenesis):

Spontaneous mutations occur in bacterial chromosomal genes. These mutations alter target sites or metabolic pathway

Example: rpoB gene mutation → resistance to Rifampicin.

gyrA/gyrB mutation → resistance to Fluoroquinolones.

b. Horizontal Gene Transfer (HGT):

Microbes acquire resistance genes from other organisms via:

Conjugation – transfer of plasmids carrying resistance genes. [5,6,7]

Transformation – uptake of free DNA from the environment.

Transduction – bacteriophage-mediated gene transfer.

2. Mobile Genetic Elements (MGEs):

Plasmids, transposons, and integrons carry and spread antibiotic resistance genes (ARGs) among bacteria.

3. Molecular Mechanisms of AMR:

a. Genetic Mutations:

Mutations in 23S rRNA (A2058G, A2059G, A2064G) cause macrolide resistance by altering ribosomal binding sites. Mutations in gyrA (Ser83Leu) and parC (Ser80Tyr) genes lead to fluoroquinolone resistance by modifying topoisomerase enzymes.

b. Efflux Pumps:

Overexpression of efflux transporter genes (ABC, MATE, MFS families) actively removes antibiotics from the cell, lowering drug concentration.

c. Biofilm Formation:

M. hyopneumoniae forms biofilms that protect cells from antibiotics and immune attacks. Biofilms limit drug penetration and promote horizontal gene transfer.

d. Other Mechanisms:

Methylation of ribosomal RNA by methyltransferase enzymes (e.g., ErmB, CFR) reduces antibiotic binding. Structural protein changes (like L22) alter ribosomal conformation and affect drug efficiency.

4. Genetic Regulation of Resistance:

Two-component regulatory systems (TCRS): Sense environmental stress and activate resistance genes (e.g., VanS/VanR in vancomycin resistance).

Global transcriptional regulators: Control multiple resistance pathways simultaneously.

Mobile genetic elements (MGEs): Integrons, transposons, and plasmids serve as vehicles for spreading resistance genes.

5. Molecular Diagnostics and Genomic Insights:

Modern molecular tools help detect and track AMR genes:

PCR and qPCR: Identify specific resistance genes (e.g., bla, mecA, vanA).

Whole-Genome Sequencing (WGS): Reveals complete resistome of an organism.

CRISPR-Cas-based detection: Emerging rapid diagnostics for AMR gene identification. [4,5]

Novel Antimicrobial Strategies:

The fast rise of antimicrobial resistance (AMR) has made many common antibiotics useless, creating a serious global health problem. Since developing new drugs takes a long time and is expensive, there is an urgent need for new and smart antimicrobial strategies that can overcome resistance, target germs more precisely, and reduce the chances of resistance developing further. [8,9,10]

1. Alternative and Novel Strategies:

a. Antimicrobial Peptides (AMPs):

Mechanism: AMPs are small, naturally occurring molecules that disrupt bacterial membranes, leading to cell death.

Examples: Defensins, cathelicidins, and synthetic peptides like pexiganan.

Advantages: Broad-spectrum activity and low likelihood of resistance development.

b. Bacteriophage Therapy:

Mechanism: Uses viruses (phages) that specifically infect and lyse bacterial cells.

Example: Phage cocktails used against multidrug-resistant Pseudomonas aeruginosa and Acinetobacter baumannii.

Advantages: High specificity, self-replication at infection sites, minimal harm to normal flora.

Current Status: Under clinical trials and compassionate-use cases.

c. CRISPR-Cas–Based Antimicrobial Systems:

Mechanism: Gene-editing tools (e.g., CRISPR-Cas9) can be programmed to specifically target and cleave resistance genes in bacteria.

Advantages: High precision; can remove plasmid-borne resistance genes without affecting normal flora.

Application: CRISPR-loaded phages to target blaNDM-1 and mecA genes.

d. Nanoparticle-Based Antimicrobials:

Mechanism: Metal nanoparticles (Ag, ZnO, CuO) damage bacterial membranes, generate reactive oxygen species, and disrupt DNA/protein synthesis.

Example: Silver nanoparticles incorporated in wound dressings and coatings.

Advantages: Broad antimicrobial activity and potential for drug delivery.

e. Anti-Quorum Sensing Agents:

Mechanism: Inhibit bacterial cell-to-cell communication (quorum sensing), which regulates virulence and biofilm formation.

Examples: Furanones, azithromycin (at sub-MIC), and plant-derived compounds like curcumin.

Benefit: Reduces pathogenicity without applying selective pressure for resistance.

f. Biofilm Disruption Strategies:

Approaches:

Use of enzymes (e.g., DNase, dispersin B) to break down the biofilm matrix. Nanocarriers or AMPs that penetrate biofilms. Combination therapy (antibiotic + biofilm disruptor).

g. Host-Directed Therapies:

Mechanism: Boosting the host's immune system to clear infections rather than directly killing bacteria.

Examples: Immunomodulators (e.g., interferons, cytokines)

Vaccines against resistant bacteria (e.g., MRSA vaccines under development).

h. Combination and Hybrid Therapies:

Approach: Using two or more drugs with different mechanisms of action to prevent resistance development.

Example: β-lactam + β-lactamase inhibitor (e.g., amoxicillin–clavulanate)

Polymyxin + rifampicin for Gram-negative infections.

i. Antisense and RNA-Based Therapies:

Mechanism: Small oligonucleotides bind to bacterial mRNA, preventing translation of resistance genes.

Example: Peptide nucleic acids (PNAs) targeting essential bacterial genes.

Advantages: Highly specific and reversible action.

J. Microbiome Modulation and Probiotics:

Mechanism: Restoring or protecting the natural gut microbiota to suppress pathogenic bacteria.

Example: Lactobacillus and Bifidobacterium strains prevent colonization by resistant pathogens.

Emerging Concept: "Bacteriotherapy" – using beneficial bacteria to outcompete resistant strains.

2. Computational and AI-Driven Drug Discovery:

Use of AI and machine learning to identify new antimicrobial compounds, optimize drug structures, and predict resistance evolution.

Example: Discovery of halicin, a novel antibiotic found using AI screening.

3. Vaccination and Preventive Strategies:

Preventing infections reduces the need for antibiotics and hence the spread of resistance.

Examples: Pneumococcal and influenza vaccines reduce secondary bacterial infections.

Diagnostics and surveillance Innovations:

1. **Rapid Diagnostic Tests (RDTs) and Point-of-Care AMR Detection:**

These are tests that give results very quickly (minutes to hours) instead of waiting 2–3 days for culture reports.

Why important?

- Helps doctors choose the right antibiotic.
- Reduces overuse of broad-spectrum antibiotics.
- Identifies resistant bacteria at the patient's bedside (point-of-care).

Examples:

PCR-based rapid tests (e.g., MRSA PCR)
Lateral-flow immunoassays
Cartridge-based tests (e.g., GeneXpert)

2.Artificial Intelligence (AI) and Machine Learning in Resistance Prediction:

Computer algorithms analyse huge biological datasets to predict antibiotic resistance patterns.

How it helps:

- Predicts which bacteria are likely to be resistant
- Helps design better treatment guidelines
- Improves surveillance by analysing millions of genome sequences

Example:

AI models can examine bacterial DNA sequences and identify mutation patterns that cause resistance (e.g., fluoroquinolone resistance in E. coli).

3. Big Data and Bioinformatics Platforms for AMR Tracking:

These platforms collect and analyse large global datasets on resistant bacteria.

Uses:

- Track spread of AMR in different regions
- Identify new resistance genes
- Help governments plan AMR control programs

Examples:

WHO GLASS (Global Antimicrobial Resistance Surveillance System)
NCBI Pathogen Detection database
Bioinformatics tools for genome analysis (e.g., ResFinder, CARD)

One Health Approches:

The One Health approach recognizes that human health, animal health, and environmental health are interconnected. AMR does not arise or spread in isolation; resistant bacteria and resistance genes circulate between people, animals, and the environment. Therefore, controlling AMR requires coordinated actions across all three sectors.

1. **Interconnection of Human–Animal–Environment:**

AMR spreads through multiple pathways:

Human → Environment

Hospitals, households, and healthcare facilities release resistant bacteria through untreated sewage. Pharmaceutical waste adds antibiotic residues to water sources.

Animal → Environment

Livestock (cattle, poultry, pigs) treated with antibiotics release resistant bacteria through manure. Animal waste contaminates soil, crops, and water bodies.

Environment → Humans & Animals

Contaminated water, food crops, and aquaculture products carry resistant organisms back to humans and animals. Resistant bacteria survive long periods in water, soil, and sediments.

Food Chain Transmission

Meat, milk, eggs, and fish can introduce resistant bacteria into the human gut.

2. **Antibiotic Use in Agriculture and Aquaculture:**

Antibiotics are used as growth promoters, disease prevention, and mass treatment in farms. Aquaculture often uses antibiotics directly in water, accelerating resistance. These practices lead to the development of resistant bacteria in animals, which spread to the environment and humans.

3. Environmental Contamination:

The environment acts as a large reservoir of resistance:

Hospital wastewater
Pharmaceutical effluents
Municipal sewage
Agricultural runoff
Contaminated rivers, lakes, and soil

These areas accumulate:

Antibiotic residues
Resistant bacteria
Resistance genes (ARGs)
Horizontal gene transfer in the environment leads to the emergence of new resistant strains.

4. Wastewater-Based Surveillance:

Detects emerging resistant strains early
Monitors resistance trends in communities
Tracks the spread of resistance genes
Helps policymakers design targeted interventions
Cost-effective method for population-level surveillance

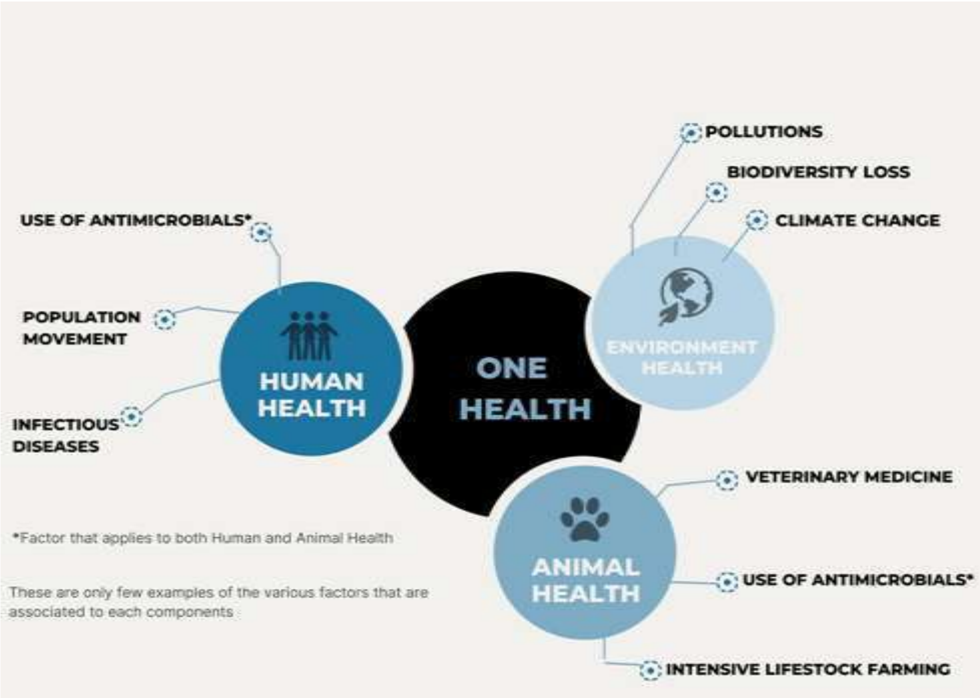

Fig 2: Illustration representing the concept of one health approach.

Stewardship and Policy Interventions in AMR:

Antimicrobial Resistance (AMR) is a major global health threat.

1. Antimicrobial Stewardship (AMS):

Antimicrobial Stewardship means using antibiotics responsibly and optimally to improve patient outcomes and reduce resistance.

Key Components of Stewardship:

a. Rational Antibiotic Use:

Right drug, right dose, right duration, right route. Avoid unnecessary broad-spectrum antibiotics.

b. Diagnostic Stewardship:

Use culture, sensitivity testing, rapid diagnostics. Ensures antibiotics are given only when needed.

c. Infection Prevention and Control (IPC):

Hand hygiene, sterilization, vaccination, isolation practices.

Prevents infections → reduces antibiotic use.

d. Monitoring and Surveillance:

Track antibiotic consumption and resistance trends in hospitals and communities.

e. Education and Awareness:

Training of doctors, pharmacists, nurses, and veterinarians. Public education to stop misuse (self-medication, incomplete courses).

f. Stewardship in Veterinary/Agriculture Sectors:

Avoid antibiotics as growth promoters. Use antibiotics only through veterinary prescription. Improve animal housing, vaccination, and hygiene to reduce disease burden.

2. Policy Interventions for AMR:

Policies ensure that stewardship practices are implemented effectively across all sectors.

a. Regulation of Antibiotic Use:

Prescription-only access to antibiotics. Ban non-therapeutic antibiotic use in agriculture and poultry farming. Regulate sales of over-the-counter antibiotics.

b. National AMR Action Plans:

Countries follow WHO's Global Action Plan. Focus on surveillance, rational use, IPC, awareness, and research.

c. Strengthening Surveillance Systems:

National monitoring of antibiotic use and resistance trends. Integration of data from humans, animals, food, and the environment.

d. Environmental and Wastewater Policies:

Regulations for effluent treatment in hospitals, pharma industries, and farms. Control antibiotic residues entering rivers, lakes, and soil.

e. Research and Innovation Policies:

Funding for developing new antibiotics, vaccines, and diagnostics. Encouraging public–private partnerships.

f. International Collaboration:

Cross-border data sharing and harmonized guidelines. Support from WHO, FAO, OIE under One Health approach.[11,12,13]

FUTURE PERSPECTIVES:

1. Development of New Antimicrobials:

Research into novel antibiotic classes with new mechanisms of action. Focus on pathogens listed under WHO priority list (e.g., E. coli, Klebsiella, Acinetobacter). Use of rational drug design, genomics, and structure-based drug discovery.

2. Alternatives to Antibiotics:

Future approaches focus on reducing antibiotic dependence:

a. Bacteriophage Therapy:

Viruses that kill bacteria. Especially promising for MDR infections.

b. Antimicrobial Peptides:

Natural immune molecules with broad action.

c. Probiotics & Microbiome Modulation:

Restoring healthy microbiota to reduce resistant pathogens.

d. Immunotherapy & Vaccines:

Vaccines for bacterial infections (e.g., TB, pneumococcus) to reduce antibiotic use.

3. Rapid and Advanced Diagnostics:

Point-of-care tests that detect pathogens in minutes. Molecular diagnostics (PCR, LAMP) for early detection. Whole-genome sequencing (WGS) for tracking resistance genes.AI-based platforms for predicting resistance patterns. These reduce unnecessary antibiotic use and guide targeted therapy.

4. Strengthening One Health Surveillance:

Integrated data from humans, animals, food, agriculture, and environment. Environmental monitoring of wastewater, rivers, soils for resistance genes (ARGs).Digital surveillance networks and global database systems

5. Antimicrobial Stewardship 2.0:

Future AMS programs will use: E-prescription with automatic checks.AI tools to guide clinicians on appropriate antibiotic choice. Real-time hospital dashboards showing resistance patterns.

6. Policy and Global Collaboration:

Stronger regulation on agricultural antibiotics. International funding for new drugs (e.g., global AMR innovation fund). Unified global standards under WHO–FAO–WOAH One Health platform. National Action Plans becoming mandatory for all countries.

7. Environmental Control Measures:

Advanced wastewater treatment technologies. Regulation of pharmaceutical effluent discharge. Monitoring resistance in rivers, lakes, aquaculture systems.

8. Personalized Medicine & Genomic Approaches:

Using patient-specific genetic and microbiome data to select precise antibiotics. CRISPR-based tools for targeted killing of resistant bacteria. Metagenomic sequencing for early outbreak detection.

9. Digital Health & Artificial Intelligence:

Predictive modelling of AMR outbreaks.AI-assisted antibiotic stewardship programs. Apps to identify early infection symptoms and guide appropriate care.[21,22,23]

CONCLUSION:

AMR is a rapidly growing global threat caused mainly by misuse of antibiotics in humans, animals, and the environment. Resistant infections are increasing worldwide, especially in LMICs, and involve major pathogens like E. Coli, Klebsiella, MRSA, and drug-resistant TB. Modern surveillance systems (WHO GLASS) show rising Carbapenem and fluoroquinolone resistance. Controlling AMR requires the One Health approach, antimicrobial stewardship, strict policies, better sanitation, and public awareness. New solutions such as bacteriophages, antimicrobial peptides, nanotechnology, and rapid molecular diagnostics offer promising alternatives. Strong global collaboration, innovation, and responsible antibiotic use are essential to protect the effectiveness of current and future antimicrobials.

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