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Review Article

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Multidrug-Resistant Bacterial Infections: A Mini-Review

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ABSTRACT

Multidrug-resistant (MDR) bacterial infections are a major global public-health and sustainable-development challenge. MDR bacteria are generally defined as organisms that are non-susceptible to at least one antimicrobial agent in three or more antimicrobial categories, although definitions may vary by organism and clinical context [1]. Resistance compromises the treatment of common infections, increases mortality and hospitalisation, raises healthcare costs, and threatens procedures such as transplantation, cancer chemotherapy, intensive care, and major surgery. The Global Burden of Disease study estimated that bacterial antimicrobial resistance (AMR) was associated with 4.71 million deaths in 2021, including 1.14 million deaths directly attributable to resistance, and projected a substantial future burden if effective action is not sustained [2]. The World Health Organization's 2024 Bacterial Priority Pathogens List identifies 24 priority pathogens across 15 families, with carbapenem-resistant Acinetobacter baumannii, carbapenem-resistant Enterobacterales, third-generation-cephalosporin-resistant Enterobacterales, and rifampicin-resistant Mycobacterium tuberculosis classified as critical priorities [3]. This mini-review discusses the epidemiology, major MDR pathogens, molecular mechanisms, drivers, clinical and environmental consequences, diagnostic approaches, and prevention strategies. It emphasises that MDR infections require coordinated One Health action involving antimicrobial stewardship, infection prevention, vaccination, improved laboratory capacity, responsible agricultural antibiotic use, wastewater management, surveillance, and development of new therapeutic and preventive technologies.

Keywords: Antimicrobial Resistance, Multidrug-Resistant Bacteria, ESKAPE Pathogens, Antibiotic Stewardship, One Health, Infection Prevention, Bacterial Infections

Introduction

Antibiotics have transformed medicine by making bacterial infections treatable and enabling modern surgery, transplantation, cancer chemotherapy, neonatal care, and intensive-care medicine. However, the effectiveness of these medicines is increasingly undermined by antimicrobial resistance. AMR occurs when microorganisms survive exposure to medicines that would normally inhibit or kill them. Multidrug resistance is a particularly serious form of AMR because it reduces the effectiveness of several unrelated antimicrobial classes and leaves clinicians with fewer reliable treatment options.

MDR bacteria are not confined to hospitals. They circulate through communities, healthcare facilities, food-producing animals, wastewater, soil, surface water, wildlife, and international travel. Resistance therefore represents a connected biological, environmental, and socioeconomic problem. Inadequate infection prevention, inappropriate prescribing, self-medication, poor sanitation, incomplete treatment, antibiotic use in livestock, pharmaceutical pollution, and insufficient microbiological surveillance all contribute to the emergence and dissemination of MDR organisms.

The WHO 2024 Bacterial Priority Pathogens List identifies 24 antibiotic-resistant pathogens or pathogen groups in critical, high, and medium priority categories. The list includes resistant Gram-negative organisms, resistant M. tuberculosis, MRSA, vancomycin-resistant Enterococcus faecium, drug-resistant Neisseria gonorrhoeae, and resistant enteric pathogens [4]. The list is intended to guide research and development, surveillance, infection prevention, and public-health action rather than to replace national treatment guidelines.

The global burden is substantial. The GBD 2021 analysis estimated 4.71 million deaths associated with bacterial AMR in 2021, including 1.14 million deaths attributable directly to resistance [2]. The same analysis projected that AMR-related deaths could rise markedly by 2050 without effective interventions.

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In October 2025, WHO reported that approximately one in six laboratory-confirmed bacterial infections associated with common infections in 2023 was resistant to antibiotic treatment, although the report also emphasised important limitations in global surveillance coverage [5].

Definition and Classification

The term MDR is generally applied to bacteria that are non-susceptible to at least one agent in three or more antimicrobial categories. XDR describes non-susceptibility to at least one agent in nearly all categories, while PDR refers to non-susceptibility to all agents in all relevant categories [1]. These definitions are laboratory-based and should not be confused with treatment failure, which may also result from delayed diagnosis, inadequate dosing, poor tissue penetration, drug interactions, non-adherence, or an inappropriate duration of therapy.

MDR classification is organism-specific. Antimicrobial categories relevant to Enterobacterales differ from those relevant to P. aeruginosa, A. baumannii, S. aureus, or M. tuberculosis. Therefore, authors and clinicians should specify the organism, antimicrobial categories tested, laboratory standards used, and the exact definition applied.

Clinically important MDR groups include:

- Methicillin-resistant Staphylococcus aureus (MRSA).
- Vancomycin-resistant Enterococcus faecium (VRE).
- Extended-spectrum-β-lactamase-producing Enterobacterales.
- Carbapenem-resistant Enterobacterales (CRE).
- Carbapenem-resistant Acinetobacter baumannii.
- Carbapenem-resistant Pseudomonas aeruginosa.
- Multidrug-resistant and rifampicin-resistant Mycobacterium tuberculosis.
- Drug-resistant Neisseria gonorrhoeae.
- Fluoroquinolone-resistant Salmonella Typhi and Shigella species.

Many of these organisms are included among the ESKAPE pathogens: Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa, and Enterobacter species. Their clinical importance arises from their capacity to cause severe disease, survive in healthcare environments, form biofilms, acquire mobile resistance genes, and evade several antimicrobial classes.

Global Epidemiological Burden

MDR infections increase the risk of treatment failure, sepsis, prolonged hospitalisation, disability, and death. They also increase healthcare expenditure through longer admissions, additional diagnostic testing, intensive-care support, use of expensive reserve antibiotics, infection-control interventions, and management of complications.

The GBD 2021 analysis identified major regional and age-related differences in bacterial AMR mortality. AMR-related deaths among children under five years have declined in several settings, partly because of improvements in vaccination, neonatal care, and infection management. However, the burden among older adults has increased, reflecting population ageing, chronic disease, repeated healthcare exposure, immunosenescence, and increased use of invasive medical devices [2].

South Asia remains particularly vulnerable because of high population density, variable access to quality healthcare, inappropriate antibiotic use, limited diagnostic facilities, inadequate sanitation, and uneven implementation of infection-prevention programmes. However, available figures may underestimate the true burden because many countries lack comprehensive laboratory surveillance and reliable cause-of-death registration.

WHO's 2025 global surveillance report analysed more than 23 million bacteriologically confirmed infections and provided estimates for 93 pathogen–infection–antibiotic combinations in 2023 [6]. The report provides important evidence of global resistance patterns but also demonstrates the continuing need to strengthen laboratory coverage, data quality, representativeness, and standardisation.

MDR infections also threaten sustainable development. They undermine universal health coverage, maternal and child health, poverty reduction, food security, and pandemic preparedness. Effective treatment of an apparently minor infection may become impossible when diagnostic services are delayed or last-line antibiotics are unavailable.

Major MDR Pathogens

Methicillin-Resistant Staphylococcus Aureus

MRSA is resistant to methicillin, oxacillin, and most β-lactam antibiotics. It causes skin and soft-tissue infections, pneumonia, bloodstream infections, osteomyelitis, endocarditis, and surgical-site infections. Healthcare-associated MRSA is strongly associated with hospitalisation, surgery, intensive-care treatment, invasive devices, and previous antibiotic exposure. Community-associated MRSA may infect healthy individuals and spread through close contact, shared equipment, crowding, and poor wound hygiene.

Treatment depends on infection severity, anatomical site, local resistance patterns, and susceptibility results. Vancomycin, linezolid, daptomycin, ceftaroline, and other agents may be used in appropriate clinical circumstances. Prevention requires hand hygiene, environmental cleaning, contact precautions, wound care, appropriate device management, and antimicrobial stewardship. MRSA should not automatically be treated with broad-spectrum antibiotics without microbiological justification.

Vancomycin-Resistant Enterococcus faecium

VRE can cause urinary tract infections, bacteraemia, intra-abdominal infections, wound infections, and endocarditis. It is especially problematic in intensive-care and haematology units, where patients often receive broad-spectrum antibiotics and undergo invasive procedures. The vanA and vanB resistance determinants alter the bacterial cell-wall target and reduce glycopeptide activity.

VRE can colonise the gastrointestinal tract and persist on hospital surfaces. Management may involve linezolid, daptomycin, or other susceptibility-guided agents. Prevention depends on early recognition, contact precautions, environmental

decontamination, prudent glycopeptide use, and careful management of high-risk patients.

ESBL-Producing Enterobacterales

ESBL-producing Escherichia coli and Klebsiella pneumoniae hydrolyse many penicillins and cephalosporins. They cause urinary tract infections, bloodstream infections, intra-abdominal infections, pneumonia, and wound infections in both hospitals and communities.

ESBL genes are frequently carried on plasmids, which facilitate transfer between bacterial species. Carbapenems may be effective in severe infections, but indiscriminate carbapenem use can select for CRE. Treatment should be guided by infection site, clinical severity, susceptibility results, patient-specific factors, and local guidelines.

Carbapenem-Resistant Enterobacterales

CRE are among the most important MDR pathogens because carbapenems are often reserved for serious infections caused by ESBL-producing or otherwise resistant Gram-negative bacteria. Carbapenem resistance may be caused by KPC, NDM, VIM, IMP, and OXA-48-like carbapenemases, combined in some isolates with porin loss or enhanced efflux.

CRE can cause pneumonia, bloodstream infections, urinary tract infections, intra-abdominal infections, and postoperative infections. Mortality may be high in patients with sepsis, immunosuppression, organ failure, or delayed effective treatment. New β-lactam/β-lactamase inhibitor combinations have improved treatment options for selected resistance mechanisms, but access is unequal and resistance may emerge during treatment. Rapid laboratory identification of carbapenemase type is therefore clinically important.

Carbapenem-Resistant Acinetobacter baumannii

Carbapenem-resistant A. baumannii is classified by WHO as a critical-priority pathogen. It causes ventilator-associated pneumonia, bloodstream infections, wound infections, meningitis, and infections in critically ill or traumatised patients. The organism can survive for extended periods on dry surfaces and spread through contaminated equipment and healthcare environments.

Resistance involves OXA-type carbapenemases, metallo-β-lactamases, reduced permeability, efflux pumps, and biofilm formation. Treatment is difficult and may include sulbactam-containing regimens, cefiderocol, polymyxins, or other agents, depending on susceptibility results and clinical circumstances. Prevention requires strict hand hygiene, contact precautions, environmental cleaning, equipment decontamination, and outbreak surveillance.

Carbapenem-Resistant Pseudomonas aeruginosa

P. aeruginosa causes pneumonia, bloodstream infections, urinary tract infections, burn-wound infections, otitis, keratitis, and chronic respiratory infections. It has intrinsic resistance to several antimicrobial classes and can acquire further resistance through mutations, efflux pumps, porin changes, β-lactamases, and biofilm formation.

MDR and carbapenem-resistant strains occur particularly among patients receiving prolonged hospital care, mechanical ventilation, repeated antibiotic treatment, or care for severe burns. Therapy must be based on reliable susceptibility testing. In selected severe infections, combination treatment may be considered, but unnecessary combination therapy can increase toxicity and selection pressure.

Drug-Resistant Mycobacterium Tuberculosis

Rifampicin-resistant M. tuberculosis is a critical-priority pathogen in the WHO 2024 list. MDR tuberculosis is resistant to at least rifampicin and isoniazid, the two most important first-line drugs. Additional resistance may result in pre-XDR or XDR tuberculosis.

Resistance arises through chromosomal mutations and is amplified by delayed diagnosis, poor adherence, inadequate treatment regimens, drug shortages, and transmission of resistant strains. Rapid molecular testing, contact tracing, airborne infection control, adherence support, and access to effective all-oral regimens are essential. Because tuberculosis spreads through the air and requires prolonged therapy, MDR-TB control must combine clinical, social, and public-health measures.

Molecular Mechanisms

Enzymatic Inactivation

Bacteria produce enzymes that destroy or chemically modify antibiotics. β-lactamases hydrolyse β-lactam antibiotics, while aminoglycoside-modifying enzymes chemically alter aminoglycosides. Carbapenemases are especially concerning because they inactivate carbapenems and are often carried on mobile genetic elements.

Target Modification

Bacteria may alter the target to which an antibiotic binds. Examples include modified penicillin-binding proteins in MRSA, mutations in DNA gyrase and topoisomerase genes, ribosomal target alteration, and modification of cell-wall precursors in VRE.

Reduced Permeability

Gram-negative bacteria can reduce antibiotic entry by modifying or losing outer-membrane porins. This mechanism often acts synergistically with β-lactamase production and contributes to carbapenem resistance.

Efflux Pumps

Efflux pumps remove antibiotics from bacterial cells. Because some efflux systems transport structurally unrelated drugs, they may contribute to multidrug rather than single-drug resistance. Efflux mechanisms are important in P. aeruginosa, A. baumannii, Enterobacterales, and other organisms.

Biofilms

Biofilms are structured microbial communities enclosed in extracellular polymeric substances. Bacteria within biofilms may be protected from antibiotics, host immune responses, disinfectants, and environmental stress. Biofilms contribute to catheter-associated infections, prosthetic-device infections, chronic wounds, dental disease, and chronic pulmonary infections.

Horizontal Gene Transfer

Resistance genes can spread by conjugation, transformation, and transduction. Plasmids, integrons, transposons, and insertion sequences facilitate movement of resistance determinants between bacterial species and ecological compartments. Hospitals, wastewater systems, livestock facilities, aquaculture operations, and pharmaceutical manufacturing sites may act as important interfaces for horizontal gene transfer.

Drivers of MDR Infections

Inappropriate Antibiotic Use

Important prescribing problems include unnecessary treatment of viral infections, incorrect antibiotic selection, excessive duration, inappropriate dosing, lack of de-escalation, and use without microbiological support. Self-medication, incomplete courses, informal drug markets, and non-prescription access may further promote resistance.

Healthcare Transmission

MDR transmission is facilitated by inadequate hand hygiene, overcrowding, poor ventilation, contaminated equipment, inadequate isolation capacity, and insufficient environmental cleaning. Invasive devices, prolonged hospitalisation, and intensive-care treatment increase risk.

Agriculture and Food Production

Antibiotics are used in livestock, poultry, aquaculture, and sometimes crop production. Resistant bacteria and genes may spread through food, direct animal contact, manure, soil, wastewater, irrigation water, and the food chain. Antibiotics important for human medicine should not be used routinely for growth promotion or unnecessary disease prevention.

Environmental Dissemination

Hospital wastewater, pharmaceutical effluent, municipal sewage, livestock waste, and agricultural runoff may contain antibiotics, resistant bacteria, and resistance genes. Conventional wastewater treatment may reduce microbial loads but does not always eliminate resistant organisms or genetic determinants. Rivers, sediments, soils, groundwater, and irrigation systems may therefore act as environmental reservoirs and pathways of dissemination.

Social and Health-System Inequality

Limited access to qualified healthcare, diagnostic testing, quality medicines, sanitation, vaccination, and infection prevention can lead to delayed diagnosis, inappropriate antibiotic use, and treatment failure. Shortages of effective medicines create an additional problem in which some populations experience overuse while others cannot obtain appropriate treatment.

Clinical and Environmental Consequences

MDR infections may cause delayed effective therapy, prolonged illness, sepsis, organ damage, disability, and death. They increase dependence on expensive or toxic drugs and may require prolonged intravenous treatment. The risks of cancer chemotherapy, transplantation, dialysis, intensive care, and major surgery increase when reliable antibiotics are unavailable.

Environmental consequences are also important. Antibiotic residues and resistant organisms in wastewater can alter microbial communities and select for resistance in environmental bacteria. Resistance genes may persist in sediments and biofilms and move among environmental, animal, and human-associated microorganisms. Environmental surveillance should therefore complement hospital and community surveillance within a One Health framework.

Diagnosis and Surveillance

Rapid diagnosis is essential for selecting effective treatment and reducing unnecessary antibiotic exposure. Culture and susceptibility testing remain central but may require 24–72 hours or longer. Molecular tests can detect resistance genes rapidly, although gene detection does not always predict phenotypic resistance and may miss mechanisms not included in the assay.

Priority surveillance activities include:

- Routine antimicrobial susceptibility testing.
- Laboratory-based reporting of priority pathogens.
- Detection of clusters and outbreaks.
- Whole-genome sequencing and genomic epidemiology.
- Monitoring antimicrobial consumption.
- Integrated human, animal, food, and environmental surveillance.
- Monitoring of antibiotic residues and resistance genes in wastewater.
- Standardised laboratory quality assurance.

WHO's GLASS programme supports international AMR and antimicrobial-use surveillance. The enhanced GLASS dashboard introduced in 2025 provides updated information for common bacterial pathogens and infection types [7]. However, major data gaps remain, especially in low-resource settings. Improved laboratory infrastructure, sample representativeness, testing quality, and data sharing are essential.

Prevention and Control

Infection Prevention and Control

Essential interventions include hand hygiene, appropriate personal protective equipment, contact precautions, environmental cleaning, sterilisation, safe injection practices, isolation or cohorting, safe management of invasive devices, and appropriate ventilation. Screening may be useful for selected high-risk populations and outbreak situations.

Antimicrobial Stewardship

Stewardship aims to ensure the correct antibiotic, dose, route, duration, and indication. Effective programmes include prescribing guidelines, audit and feedback, antimicrobial time-outs, pharmacy-led review, formulary control, rapid diagnostics, education, and de-escalation after laboratory results become available.

Stewardship does not mean simply reducing antibiotic use. Its objective is to optimise treatment, prevent unnecessary exposure, reduce adverse effects, and preserve antimicrobial effectiveness.

Vaccination, Sanitation, and Hygiene

Vaccination reduces bacterial infections and therefore reduces antibiotic use and selection pressure. Vaccines against pneumococcal disease, Haemophilus influenzae type b, meningococcal disease, typhoid, and other infections contribute to AMR control.

Water, sanitation, and hygiene interventions reduce transmission and the need for antibiotics. Safe water, sanitation, handwashing, food hygiene, wastewater treatment, and environmental cleaning should be integrated into AMR programmes.

One Health Governance

AMR control requires collaboration among human health, veterinary medicine, agriculture, food systems, environmental agencies, universities, and communities. Key priorities include integrated surveillance, responsible antibiotic sales, veterinary stewardship, pharmaceutical-waste controls, improved infection prevention, environmental monitoring, public education, and research into transmission pathways.

Therapeutic and Research Priorities

The antibiotic development pipeline remains inadequate relative to the pace and diversity of resistance. Priority areas include new antibiotics for resistant Gram-negative bacteria, β-lactamase inhibitors, phage therapy, antimicrobial peptides, anti-virulence agents, monoclonal antibodies, microbiome-based therapies, CRISPR-based antimicrobials, nanotechnology, improved vaccines, host-directed therapies, and rapid point-of-care diagnostics.

New interventions should be evaluated for efficacy, safety, affordability, resistance potential, scalability, and suitability for low-resource settings. Drug discovery alone will not solve AMR. Prevention, stewardship, vaccination, sanitation, surveillance, and equitable access remain equally important [8].

Conclusion

MDR bacterial infections are driven by the interaction of microbial evolution, antibiotic selection pressure, healthcare transmission, environmental contamination, agricultural practices, and social inequality. Major threats include MRSA, VRE, ESBL-producing Enterobacterales, CRE, carbapenem-resistant A. baumannii, carbapenem-resistant P. aeruginosa, drug-resistant M. tuberculosis, and resistant enteric and sexually transmitted pathogens.

The global burden is already considerable, with millions of deaths associated with bacterial AMR each year. Recent WHO surveillance indicates widespread resistance to commonly used antibiotics, while the WHO 2024 priority list highlights pathogens for which research, surveillance, and public-health interventions are most urgent. MDR infections threaten not only clinical medicine but also sustainable development, food systems, environmental health, and health security.

Effective control requires a coordinated One Health response. Infection prevention, antimicrobial stewardship, vaccination, improved water and sanitation, responsible use of antibiotics in animals, environmental management, laboratory strengthening, rapid diagnostics, genomic surveillance, equitable access to treatment, and development of new therapies must be implemented together. Protecting the effectiveness of existing antimicrobials is a shared responsibility across healthcare systems, governments, universities, agriculture, industry, and communities.

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