



The spread of antibiotic resistance in Iran: A review of multidrug-resistant pathogens, resistance mechanisms, and national challenges

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Abstract

Background: Antimicrobial resistance (AMR) represents one of the most significant global health threats of the 21st century and undermines advances in modern medicine. As a geographically and demographically strategic nation, Iran faces a severe and escalating AMR crisis. This review synthesizes current evidence on the epidemiology, molecular mechanisms, and systemic drivers of AMR in Iran while outlining priorities for an effective national response.

Methods: A structured review was conducted of studies published between January 2015 and November 2024 in PubMed, Scopus, and Web of Science, supplemented by searches of national and Persian-language databases. Eligible studies investigated the prevalence, molecular characteristics, and clinical outcomes of antibiotic-resistant bacteria in Iran. Data were extracted and narratively synthesized.

Results: Iran faces an alarming burden of multidrug-resistant and extensively drug-resistant Gram-negative pathogens, notably *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and carbapenem-resistant *Enterobacteriaceae*, with carbapenem resistance rates exceeding 80-90%. Widespread dissemination of key carbapenemase genes (*blaNDM*, *blaOXA-48*, *blaVIM*) has been documented. Gram-positive pathogens, including methicillin-resistant *Staphylococcus aureus* and vancomycin-resistant enterococci, also remain highly prevalent. The crisis is driven by unregulated and excessive antibiotic use, weak infection prevention and control measures, fragmented surveillance, and limited diagnostic capacity.

Conclusion: AMR in Iran has reached critical levels and constitutes a national public health emergency. Urgent, coordinated reforms involving integrated surveillance, mandatory antimicrobial stewardship, strengthened infection prevention and control, One Health integration, expanded research, and public engagement are required. Without decisive national action, Iran risks entering a post-antibiotic era in which routine infections and medical procedures become life-threatening.

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Introduction

The discovery of antibiotics transformed medicine and dramatically reduced infectious disease mortality worldwide. However, this achievement is now being reversed by the relentless spread of antimicrobial resistance (AMR), a phenomenon that endangers all aspects of modern health care (1). By 2050, it is estimated that AMR could cause up to 10 million deaths annually and impose economic losses exceeding USD 100 trillion if left unchecked (2). In 2019 alone, AMR was directly responsible for an estimated 1.27 million deaths globally and was associated with nearly 5 million additional deaths, exceeding the burden of many major diseases (3). The crisis disproportionately affects low- and middle-income countries (LMICs) because of weak regulatory systems, limited diagnostic capacity, and infrastructural constraints (4). Iran occupies a pivotal position in this global context. It is the second most populous nation in the Middle East, shares borders with seven countries, and serves as a regional hub for medical tourism and labor migration. Its complex healthcare network, ranging from tertiary medical centers to rural clinics, faces challenges related to drug regulation, hospital infection control, and antibiotic governance (5). The unregulated sale and use of antibiotics, combined with systemic deficiencies in national surveillance and public awareness, have accelerated the emergence and dissemination of resistant pathogens. Iran's AMR burden is exacerbated by its location in the Middle East, a region with some of the highest reported rates of multidrug-resistant pathogens globally because of ongoing conflicts, population displacement, cross-border movement, and inconsistent AMR control measures in neighboring countries (6). Although Iran adopted a National Action Plan on Antimicrobial Resistance in 2016-2017 in alignment with the WHO Global Action Plan on AMR, its implementation has been limited by challenges in interministerial coordination, resource allocation, and enforcement of regulations

governing antibiotic sales and agricultural use. This review synthesizes the available evidence on AMR in Iran by systematically addressing four core dimensions: the epidemiological trends of key resistant pathogens; the molecular and genetic mechanisms that drive the acquisition and dissemination of resistance; the systemic and behavioral determinants—including prescribing practices, healthcare infrastructure, and public awareness—that shape the AMR burden; and the strategic imperatives for implementing effective control measures. By integrating these interrelated components within a "One Health" framework that recognizes the interconnectedness of human, animal, and environmental health, this review aims to provide a comprehensive overview of the current AMR landscape in Iran and identify priority areas for policy development, strengthened surveillance, and targeted interventions to mitigate the growing threat of resistance in the country.

Methods

A structured narrative review was conducted. Literature published from January 2015 to November 2024 was searched in international databases (PubMed, Scopus, Web of Science) and national Persian-language databases (Scientific Information Database (SID), MagIran). The search terms combined keywords related to antimicrobial resistance (e.g., antimicrobial resistance, antibiotic resistance, multidrug-resistant, MDR, extensively drug-resistant, XDR, carbapenem-resistant, ESBL, carbapenemase, MRSA, VRE) with Iran-specific terms (Iran, Iranian). No language restrictions were applied. The reference lists of included studies were hand-searched for additional relevant articles.

Inclusion and Exclusion Criteria: Studies were included if they focused on bacterial pathogens in Iran with defined resistance profiles, provided laboratory-confirmed molecular data (e.g., gene identification, typing), or reported surveillance findings or outbreaks. Reviews without primary data, studies limited to fungal or viral resistance, and studies lacking clear microbiological confirmation were excluded.

Data Extraction and Quality Assessment: Data were extracted thematically and synthesized narratively, with the findings categorized according to epidemiological trends, molecular mechanisms, and systemic determinants of resistance.

The methodological quality of the included studies (Primarily cross-sectional prevalence studies) was assessed using the Joanna Briggs Institute (JBI) Critical Appraisal Checklist for Studies Reporting Prevalence Data. Studies were classified as being of high, moderate, or low quality; no studies were excluded solely on the basis of quality.

Results

The epidemiological landscape of AMR in Iran

Gram-negative pathogens

- ***Acinetobacter baumannii*:** *Acinetobacter baumannii* remains a leading cause of hospital-acquired infections in Iranian intensive care units (ICUs), notably ventilator-associated pneumonia, bloodstream infections, and sepsis (7). Carbapenem resistance frequently exceeds 90% nationwide, with most isolates classified as extensively drug-resistant (XDR) or pan-drug-resistant (PDR) (8). The predominant resistance mechanisms include OXA-type carbapenemases (blaOXA-23, blaOXA-24, blaOXA-58) and, increasingly, metallo- β -lactamases such as blaNDM (9). Clonal complex 92 (International clone II) predominates, indicating both local expansion and the importation of high-risk global lineages. Alarming, colistin resistance mediated by the plasmid-borne mcrI gene has recently been reported in Tehran and Isfahan, threatening the efficacy of this last-resort therapy (10). Recent *in vitro* studies have explored the potential of novel 1,3,4-oxadiazole derivatives as alternative therapeutic agents against *A. baumannii*, demonstrating promising antimicrobial properties and highlighting the continuing need for new drug discovery (11). Furthermore, these compounds have been evaluated for their ability to inhibit biofilm formation, a key virulence factor, by targeting bap gene expression in *A. baumannii*, demonstrating a potential strategy for combating persistent infections (12).
- ***Pseudomonas aeruginosa*:** *P. aeruginosa* exhibits broad-spectrum resistance through multiple coordinated mechanisms: efflux pumps (MexAB-OprM), porin mutations (OprD loss), β -lactamases (PER, VEB, GES), and biofilm-associated tolerance (13). Carbapenem resistance rates typically range from 60-80% nationwide, with ST235, ST111, and ST357 identified as the predominant clones (14). Reduced susceptibility to colistin and aminoglycosides has also emerged, complicating combination therapy strategies.
- **Carbapenem-Resistant Enterobacteriaceae (CRE):** The expansion of carbapenem-resistant *Klebsiella pneumoniae* and *Escherichia coli* represents a growing health emergency. Between 2018 and 2024, the prevalence of CRE increased more than twofold in tertiary hospitals (15). The main carbapenemase genes, blaNDM-1, blaOXA-48, and, occasionally, blaKPC, have been confirmed through molecular typing (16). Many strains concurrently carry extended-spectrum β -lactamase (ESBL) genes, such as blaCTX-M-15, conferring near-pan-resistance. Clinical outcomes are poor, with mortality rates exceeding 40% during ICU outbreaks (17).
- **National Trends from Meta-Analyses:** Pooled estimates suggest an MDR prevalence of >85% among Gram-negative isolates from ICUs. Resistance to ciprofloxacin (~50%), co-trimoxazole (~60%), and third-generation cephalosporins (~70%) remains high across provinces, including Tehran, Isfahan, Shiraz, and Mashhad (18).

Gram-positive pathogens

- **Methicillin-Resistant *Staphylococcus aureus* (MRSA):** MRSA remains endemic in both hospital-associated (HA-MRSA) and community-associated (CA-MRSA) settings. The average hospital prevalence is 35-45% of *Staphylococcus aureus* (*S. aureus*) isolates, although substantial regional variation exists (19). Nasal carriage among healthcare workers reaches 25-30%, facilitating nosocomial transmission. Molecular studies identify the ST239 and ST22 (EMRSA-15) clones as predominant, with the occasional detection of PVL-positive strains. Reduced susceptibility and intermediate resistance to vancomycin (VISA, hVISA) have also been reported (20).

- **Vancomycin-Resistant Enterococci (VRE):** VRE, predominantly *E. faecium*, causes bloodstream and urinary tract infections in immunocompromised patients and transplant recipients. Both vanA and vanB genotypes circulate in Iranian hospitals, with resistance rates of up to 35% among bloodstream isolates (21). The potential for horizontal transfer of van genes increases the regional risk of gene exchange with *S. aureus*.
- **Other Relevant Pathogens:** Increasing reports of nonsusceptible *Streptococcus pneumoniae* (20-25% penicillin resistance) and multidrug-resistant *Enterococcus faecalis* highlight the community-level implications of antibiotic misuse (22). The treatment of *E. faecalis* infections is further complicated by its robust biofilm-forming capacity, which contributes to antibiotic tolerance. Novel therapeutic approaches are being investigated, including the evaluation of new oxadiazole compounds that have demonstrated efficacy in inhibiting *esp* gene expression, a critical determinant of biofilm formation and virulence in *E. faecalis* (23). Such research is essential for developing targeted strategies against biofilm-associated infections that are often refractory to conventional antibiotics.

The key epidemiological features, resistance rates, and predominant molecular mechanisms of the major Gram-negative and Gram-positive pathogens described in Result Section are systematically summarized in the upper sections of Table 1.

Molecular and systemic drivers of resistance

Genetic architecture of resistance

The AMR crisis in Iran is underpinned by efficient horizontal gene transfer (HGT) mediated by mobile genetic elements (MGEs), plasmids, transposons, and integrons (24). Class 1 integrons carrying gene cassettes for aminoglycoside-modifying enzymes and ESBLs are prevalent among hospital isolates. The CTX-M lineage, particularly blaCTX-M-15, predominates in β -lactam resistance among community strains of *E. coli* and *K. pneumoniae* (25). The co-occurrence of qnr (Quinolone resistance), mphA (Macrolide resistance), and armA (Aminoglycoside methyltransferase) genes on the same plasmids reflects the linked selection of multidrug resistance (26). Whole-genome sequencing (WGS) studies conducted in Tehran and Shiraz between 2021 and 2024 confirm plasmid convergence between clinical and environmental reservoirs, supporting the presence of a broader resistome across ecosystems (27).

Systemic and behavioral catalysts

- **Inappropriate Antimicrobial Use:** Nonprescription access to antibiotics persists despite existing regulations. Surveys indicate that 40-60% of Iranian adults practiced self-medication with antibiotics during the preceding year, often for viral infections (28). Pharmacists frequently dispense antimicrobials without a prescription because of economic or social pressures. In hospitals, empirical therapy is often guided by limited diagnostic data, thereby increasing selection pressure (29).
- **Weak Infection Prevention and Control (IPC):** Hospital overcrowding, insufficient staff-to-patient ratios, poor adherence to hand hygiene, and inadequate environmental decontamination are widespread problems (30). Surveillance of healthcare-associated infections (HAIs) remains fragmented and is often limited to major university hospitals.
- **Agricultural and Environmental Contributions:** Antibiotics are used extensively in the livestock industry for prophylaxis and growth promotion. Studies have reported substantial levels of antibiotic residues and resistance genes on poultry and cattle farms (31). Untreated hospital effluent in urban wastewater contributes to environmental contamination with ESBL- and carbapenemase-producing bacteria (32).
- **Deficient National Surveillance:** Iran's participation in the WHO Global Antimicrobial Resistance Surveillance System (GLASS) remains incomplete. Data collection is sporadic and regionally fragmented. Currently, no centralized genomic or phenotypic AMR database exists, which impedes national and international comparability (33).

Economic and social impact

The economic burden of AMR in Iran is substantial, although it remains insufficiently quantified. Hospital-associated AMR increases the average length of stay by 7-10 days and treatment costs by an estimated 15-25% (34). Some projections indicate that indirect costs, lost productivity, and resource diversion exceed USD 400 million annually. Social determinants, including socioeconomic disparities, inequities in

healthcare access, and limited public perception of risk, further exacerbate the problem (35). Collectively, the molecular genetic architecture, systemic and behavioral catalysts, environmental contributions, and socioeconomic effects are integrated with the pathogen data in Table 1, providing a comprehensive, at-a-glance summary of the epidemiology, mechanisms, and drivers of AMR in Iran from 2015 to 2024.

Table 1. Comprehensive summary of the epidemiology, mechanisms, and drivers of antimicrobial resistance in Iran (2015-2024)

Dimension	Pathogen / Key aspect	Epidemiological features and resistance rates	Dominant molecular mechanisms	Clinical impact / Threat
Critical gram-negative pathogens	<i>Acinetobacter baumannii</i>	Leading cause of HAIs in ICUs (VAP, BSI, sepsis). Carbapenem resistance: >90%. High prevalence of XDR/PDR isolates.	OXA-type carbapenemases (e.g., blaOXA-23, -24, -58). Emerging metallo-β-lactamases (e.g., blaNDM).	Emergence of plasmid-borne *mcr-1*-mediated colistin resistance, threatening last-resort therapy.
	<i>Pseudomonas aeruginosa</i>	Carbapenem resistance rates: 60-80% nationally.	Coordinated mechanisms: efflux pumps (MexAB-OprM), porin loss (OprD), ESBLs (PER, VEB, GES).	Reduced susceptibility to colistin and aminoglycosides, complicating combination therapy.
	Carbapenem-Resistant Enterobacteriaceae (CRE)	Prevalence increased more than twofold in tertiary hospitals (2018-2024).	Carbapenemases: blaNDM-1, blaOXA-48 (Occasionally blaKPC). Frequent co-carriage of ESBLs (e.g., blaCTX-M-15).	High mortality rates (>40%) in ICU outbreaks. A growing public health emergency.
Critical gram-positive pathogens	Methicillin-Resistant <i>Staphylococcus aureus</i> (MRSA)	Hospital prevalence: 35-45%. Nasal carriage in HCWs: 25-30%. Endemic in HA and CA settings.	Presence of <i>mecA</i> gene. Reduced susceptibility to vancomycin (VISA/hVISA) reported.	Sustained endemicity with reservoir in HCWs. Threat of vancomycin susceptibility loss.
	Vancomycin-Resistant Enterococci (VRE)	Resistance in <i>E. faecium</i> BSI isolates up to 35%. Causes infections in immunocompromised hosts.	Presence of <i>vanA</i> and <i>vanB</i> gene clusters.	Risk of horizontal transfer of <i>van</i> genes to other Gram-positives like <i>S. aureus</i> .
Key drivers of resistance	Genetic Architecture	Widespread, facilitated by mobile genetic elements (Plasmids, transposons, integrons).	High prevalence of Class 1 integrons and CTX-M-15. Co-localization of resistance genes (<i>qnr</i> , <i>mphA</i> , <i>armA</i>) on same plasmids.	Fuels rapid dissemination of multi-drug resistance and creates a broad environmental "resistome."
	Inappropriate Antimicrobial Use	40-60% of adults report self-medication with antibiotics (Often for viral URIs). Non-prescription dispensing is common. Empirical therapy often lacks microbiological guidance.	Creates direct selection pressure, favoring the survival and spread of resistant clones.	A primary driver of resistance selection in both community and hospital settings.
	Weak Infection Prevention and Control (IPC)	Hospital overcrowding, low staff-to-patient ratios, and suboptimal hand hygiene compliance. HAI surveillance is fragmented.	Facilitates cross-transmission of resistant organisms within healthcare facilities.	Turns hospitals into epicenters for amplifying and disseminating resistant infections.
	Environmental and Agricultural Pressure	Extensive use of antibiotics in livestock. Significant levels of antibiotic residues and resistance genes in farm environments.	Direct contamination of ecosystems with resistant bacteria and genes (e.g., from untreated hospital effluents).	Creates external reservoirs that re-seed healthcare and community settings, enabling a One Health crisis.
Impact	Economic and Social	Increases hospital LOS by 7-10 days and direct treatment costs by 15-25%. Projected annual indirect costs > USD 400 million.	Linked to socioeconomic disparities, inequitable healthcare access, and low public risk perception.	Imposes a substantial, under-quantified burden on the health system and economy, exacerbating health inequities.

Discussion

The evidence reveals a systemic and entrenched AMR crisis in Iran. MDR and XDR pathogens have become endemic across tertiary care centers, leaving clinicians with few therapeutic options. Reliance on legacy drugs such as colistin poses risks of toxicity and resistance. Empirical prescribing practices persist in the absence of robust diagnostic infrastructure and stewardship oversight. Although substantial data describe prevalence, most studies remain cross-sectional and descriptive; few have investigated transmission dynamics through genomic analysis or longitudinal surveillance (36). Implementing whole-genome sequencing and molecular typing across sentinel hospitals would facilitate the detection of high-risk clones and plasmid migration and strengthen outbreak control. From a One Health perspective, the epidemiology of AMR in Iran cannot be confined to hospitals. Substantial environmental overlap exists among clinical, agricultural, and waterborne determinants of resistance. National policies have insufficiently integrated the human, veterinary, and environmental health sectors, although momentum has grown following Iran's 2019 National Action Plan for AMR (37). Coordination with food safety authorities and environmental ministries is essential for effective monitoring. Public education and behavioral interventions are equally critical. Studies demonstrate that improved awareness and stewardship training among clinicians, combined with public campaigns discouraging self-medication, can substantially reduce inappropriate antibiotic consumption (38). Economic analyses emphasize that investment in surveillance and stewardship is not only medically essential but also cost-effective in the long term (39). Strengthened IPC infrastructure, enforcement of hand hygiene, screening of high-risk patients, and routine resistance audits must be institutionalized across all hospitals.

Conclusion

AMR in Iran is accelerating despite localized interventions. The nation stands at a pivotal juncture: it must either implement coordinated national countermeasures or face a return to a pre-antibiotic era. The following action pillars are recommended:

- Integrated National Surveillance System: Establish a centralized digital platform for real-time AMR data reporting that connects clinical, veterinary, and environmental laboratories. Integration with GLASS should be prioritized.
- Mandatory Antimicrobial Stewardship Programs (ASPs): Implement standardized ASPs across all healthcare facilities, with defined accountability, prescription auditing, and diagnostic stewardship components.
- Reinforced Infection Prevention and Control (IPC): Develop enforceable national IPC standards and ensure compliance through regular audits, transparent reporting, and investment in infrastructure.
- Operationalization of the One Health Framework: Coordinate policies across the ministries of health, agriculture, and the environment to regulate antibiotic use in animals, monitor environmental reservoirs, and align initiatives with WHO and FAO frameworks.
- Research and Capacity Building: Expand genomic surveillance capacity through national reference laboratories. Encourage funding for AMR-related economic and social science research to contextualize interventions.
- Public Engagement and Education: Launch national campaigns to raise awareness of AMR risks, focusing on the dangers of self-medication and the importance of completing prescribed courses.

The AMR crisis in Iran reflects broader global patterns but is intensified by regional and systemic vulnerabilities. Addressing it requires sustained political commitment, cross-sectoral coordination, and scientific innovation. Through strategic reforms grounded in surveillance, stewardship, and prevention, Iran can reposition itself as a regional leader in AMR containment. The need for decisive and coordinated national action is urgent.

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Ethical Statement

This article is a narrative review based on previously published literature and does not involve human participants, human data, or animal experiments.

Conflicts of Interest

The authors declare that they have no competing interests.

Author Contributions

Y.S. conceived and revised the manuscript; Y.S., B.O., S.Z., and Y.G. wrote the manuscript; Y.S. and B.O. edited and reviewed the manuscript; Y.S. analyzed the data and performed the statistical analysis; S.Z. and Y.G. acquired the data; and Y.S. prepared the tables.

Data Availability Statement

All data generated or analyzed during this review are derived from publicly available published sources. Data supporting the conclusions of this manuscript are included within the article. Further inquiries can be directed to the corresponding author.

Use of Artificial Intelligence

The authors confirm that this manuscript is their original work and has not been generated, written, or substantially assisted by artificial intelligence tools, including large language models or AI-based image generators.

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