Spring 2025, Volume 10, Issue 37 (20- 30) DOI: 10.22034/pmj.2025.2058093.1057

Personalized & Precision Medicine Journal

Homepage: www.pmjournal.ir

Emerging Threats: Multidrug Resistance and Clinical Challenges of Acinetobacter spp. in Modern Healthcare

Azadeh Taftian[1,*], Neda Abedi[2], Ali Zolfi Gol[3]

[1]Department of Obstetrics and Gynecology, Kamali Hospital, Alborz University of Medical Sciences, Karaj, Iran.
[2]Department of Microbiology, North Branch of Azad University, Tehran, Iran.
[3]Department of Pediatrics, School of Medicine, Urmia University of Medical Sciences, Urmia, Iran.

ARTICLE INFO

Paper Type: Review Article

Submitted: 2025-02-11
Accepted: 2025-05-25

Keywords:
MDR Acinetobacter baumannii
Multidrug resistance
Middle East
Carbapenem resistance
Novel therapeutics

Corresponding author:
Azadeh Taftian, Department of Obstetrics and Gynecology, Kamali Hospital, Alborz University of Medical Sciences, Karaj, Iran. Email: Azadehtaftian64@gmail.com.

ABSTRACT

Multidrug-resistant (MDR) bacteria, including *Acinetobacter baumannii*, have increased in healthcare systems, particularly in the Middle East. This bacterium is notoriously resistant to various medications, complicating disease therapy. The proliferation of XDR bacteria and the decline of effective antibiotics threaten patient safety and healthcare efficiency.

This study addresses the issues associated with MDR *Acinetobacter baumannii* in hospitals, especially in the Middle East. It examines the bacterium's epidemiology, molecular resistance mechanisms, clinical problems, and innovative treatment approaches.

We conducted a comprehensive study by searching PubMed, Scopus, and Web of Science for research published from 2010 to 2024. The investigation identified Middle Eastern research regarding the prevalence, resistance mechanisms, clinical care, and patient outcomes of MDR Acinetobacter baumannii. This study offers a comprehensive perspective on the escalating threat posed by this disease and its ramifications for regional healthcare professionals through the integration of qualitative and quantitative data.

Carbapenem-resistant *Acinetobacter baumannii* is common in 60–70% of Middle Eastern intensive care units and kills 40–50%. OXA-type carbapenemases, ESBLs, MBLs, efflux pump overexpression, target site changes, and biofilm formation make the bacterium resistant. We also found novel resistance determinants including bla_OXA-235 and regulatory gene alterations like adeRS. Overcrowded hospitals, long stays, antibiotic overuse, and poor infection control aggravate this issue. However, these issues are being fixed. Modern molecular diagnosis, ultraviolet disinfection, and genetic surveillance reduce these diseases. Increasing MDR *Acinetobacter baumannii* prevalence in the Middle East presents a difficult challenge that requires a coordinated, multidisciplinary approach. This pathogen's hazards can be reduced by improved antimicrobial stewardship, infection control, regional surveillance, and therapeutic development.

How to Cite this Article:
A. Taftian, N. Abedi, A. Zolfi Gol. "EEmerging Threats: Multidrug Resistance and Clinical Challenges of Acinetobacter spp. in Modern Healthcare" Personalized & Precision Medicine Journal, Vol. 10, no. 37, pp. 20- 30.

INTRODUCTION

Background and Clinical Significance

Acinetobacter species are a diverse group of Gram-negative bacteria that thrive in oxygen-rich environments and do not ferment sugars. These bacteria are found almost everywhere in nature soils, water, and even on plant surfaces. Their ability to survive in both natural and man-made environments makes them incredibly resilient and adaptable. Among this group, *Acinetobacter baumannii* stands out as particularly important in the medical field (1).

What makes *A. baumannii* so concerning is its ability to survive on a wide range of surfaces, including those found in hospitals. It can withstand drying out and resist many disinfectants, which allow it to form colonies that are difficult to eliminate (2). This makes it a serious threat in healthcare settings, as the bacteria can contaminate various objects, such

as hospital equipment, ventilators, and even the hands and clothing of healthcare workers. As a result, *A. baumannii* can spread easily and become a dangerous hospital-acquired infection (3).

A. baumannii is associated with several serious illnesses. It is one of the leading causes of ventilator-associated pneumonia (VAP), and it is also frequently found in bloodstream infections (BSIs), urinary tract infections (UTIs), meningitis, and wound infections (4). This bacterium is especially dangerous for critically ill patients, particularly those who have undergone invasive procedures or have weakened immune systems. The growing number of multidrug-resistant (MDR) and extensively drug-resistant (XDR) strains of A. baumannii over the past few decades has made treatment more complicated, and the outcomes less predictable (2).

The World Health Organization (WHO) has recognized *A. baumannii* as a priority pathogen due to the rising threat posed by these resistant strains. This designation highlights the urgent need for new treatments and more effective infection control strategies in hospitals to combat the increasing prevalence of this dangerous bacterium (5).

Focus on the Middle East

The genus Acinetobacter includes a diverse range of Gram-negative bacteria that are strictly aerobic and do not ferment sugars. These bacteria can be found all around us, in places like soil, water, and on plant surfaces. Thanks to their impressive resilience, they can thrive in both natural and man-made environments, making them highly adaptable to various conditions. Among the Acinetobacter species, Acinetobacter baumannii is particularly concerning in the medical field (6).

What makes *A. baumannii* so problematic is its ability to survive on a wide range of surfaces, including those commonly found in hospitals. It has an extraordinary ability to resist drying out and can withstand many disinfectants, which allows it to form colonies that are tough to eliminate. This makes it easy for the bacterium to spread through contaminated hospital equipment, ventilators, and even the hands and clothing of healthcare workers, turning it into a dangerous hospital-acquired infection (7).

Clinically, *A. baumannii* is linked to a variety of serious health conditions. It's often found in bloodstream infections (BSIs), urinary tract infections (UTIs), meningitis, and wound infections. One of its most concerning roles is as a major cause of ventilator-associated pneumonia (VAP), especially in critically ill patients who are intubated in intensive care units (ICUs). People in these vulnerable states especially those who've had invasive surgeries or have weakened immune systems are at high risk of infection, making *A. baumannii* a significant public health threat (4, 8).

Over the past few decades, the rise of multidrug-resistant (MDR) and extensively drug-resistant (XDR) strains of *A. baumannii* has made treatment options more limited and clinical outcomes more unpredictable. The World Health Organization (WHO) has designated *A. baumannii* as a priority pathogen due to the growing danger posed by these resistant strains. This classification highlights the urgent need for new treatment strategies and stronger infection control practices in healthcare settings to prevent the spread of this dangerous bacterium (9).

Epidemiology of MDR *A. baumannii* in the Middle East

Overview and Regional Trends

Recent studies across several countries in the Middle East namely Iran, Saudi Arabia, Egypt, and Lebanon have consistently shown that multidrug-resistant (MDR) Acinetobacter baumannii is a growing concern in hospitals. In intensive care units (ICUs), carbapenem resistance in *A. baumannii* strains has been found in 60% to 70% of cases, limiting treatment options and leading to poorer outcomes for patients. A study published in 2023 revealed that the overall hospital death rate for patients infected with MDR A. baumannii is around 45%, which is notably higher than for patients infected with strains that are susceptible to antibiotics (10).

In Iran, hospitals, especially tertiary care centers, have reported that up to 40% of ICU samples show resistance to multiple drugs. These outbreaks not only highlight the bacteria's ability to rapidly develop resistance but also point to gaps in infection control and antibiotic use. The situation in Iran makes it clear that there is an urgent need for faster diagnostic tools and targeted treatments to help prevent the continued spread of these resistant strains (11).

In Saudi Arabia, the problem is equally concerning, with some hospitals reporting resistance rates exceeding 70% in their ICUs. The situation is worsened by high mortality rates sometimes above 50%. Overcrowding, the overuse of broad-spectrum antibiotics and weaknesses in infection control practices are all contributing factors to the rise in resistance and the grim outlook for patients (12).

Egypt faces particular challenges, especially when it comes to ventilator-associated pneumonia (VAP). Many studies have shown that VAP, which is common in critically ill patients requiring mechanical ventilation, is often caused by MDR *A. baumannii* (13). This not only increases the risk of serious complications for patients but also puts additional strain on the healthcare system due to longer hospital stays and higher resource demands. The data from Egypt underscores the need for stronger infection control measures—such as improved

hand hygiene, better sterilization practices, and more effective antibiotic management.

Together, these findings paint a worrying picture of a public health crisis in the Middle East. The widespread presence of MDR *A. baumannii* in intensive care units, along with the growing number of patient deaths, calls for immediate action. It's clear that improving infection control, optimizing antibiotic use, and strengthening surveillance systems must be a priority to curb the spread of this dangerous pathogen and improve patient outcomes in the region. Only through collective, coordinated efforts can healthcare systems hope to control *A. baumannii* and protect public health (14).

Contributing Factors

Several interconnected factors contribute to the rise and rapid spread of MDR *Acinetobacter baumannii* in the Middle East, creating complex challenges for healthcare systems in the region. Here's a closer look at the key issues:

Overcrowded Hospitals and Limited Resources: In many Middle Eastern hospitals, especially those in densely populated urban areas, overcrowding is a major issue. Intensive care units (ICUs), in particular, struggle with a high patient-to-bed ratio. This congestion makes it difficult for healthcare workers to provide the necessary time and attention for effective infection control. Research from hospitals in Egypt, for example, shows that up to 75% of ventilator-associated pneumonia (VAP) cases are linked to MDR *A. baumannii*, a situation that's worsened by overcrowding and understaffing. On top of that, limited funding means that essential equipment like sterilization machines and rapid diagnostic tools are often outdated or unavailable, making it even harder to control infections effectively (15).

Prolonged Hospital Stays and Invasive Procedures: Patients with severe illnesses frequently endure prolonged hospital stays, during which they may require invasive interventions, such as mechanical ventilation or urine catheterization (16). Regrettably, these medical gadgets may serve as conduits for bacteria, such as A. baumannii, to infiltrate the body. The duration of a patient's hospital stay correlates positively with the likelihood of acquiring a nosocomial infection. Epidemiological data highlight the prevalence of infectious and febrile diseases, leading to frequent healthcare visits (17). Inadequate infection control methods during invasive procedures might undermine natural defenses, facilitating bacterial colonization and infection in patients (18, 19).

Unrestricted Use of Antibiotics: The extensive and frequently improper utilization of antibiotics significantly contributes to the emergence of antibiotic-resistant microorganisms. Numerous hospitals in the Middle East provide antibiotics without sufficient testing or microbiological investigation, hence fostering optimal circumstances for the proliferation of resistant bacteria. The situation is exacerbated by the accessibility of over-the-counter antibiotics and the prevalent habit of self-medication. The excessive or extended administration of antibiotics in patients elevates the risk of acquiring and disseminating *MDR A. baumannii* (20).

Inefficient Infection Control Measures: Efficient infection management is essential for averting the dissemination of resistant germs; yet, numerous hospitals in the region have difficulties in this domain. Factors contributing to the issue include substandard hand hygiene, irregular cleaning of hospital settings, and insufficient sterilization of medical instruments. Although several hospitals have commenced the utilization of advanced technology such as UV light disinfection, which has demonstrated a 30% reduction in environmental contamination, these practices remain inadequately adopted. The disparity between existing procedures and optimal criteria for infection control facilitates the ongoing proliferation of resistant pathogens (21).

Vulnerable Patient Populations: The Middle East exhibits a significant prevalence of chronic health disorders such as diabetes, cancer, and chronic kidney disease. Individuals with these conditions frequently possess compromised immune systems, rendering them more vulnerable to infections. In hospital environments, these susceptible patients face an elevated risk of acquiring MDR *A. baumannii*, potentially resulting in severe consequences and heightened mortality rates. The interplay of preexisting health conditions and exposure to intrusive interventions establishes a perilous loop, wherein infection and resistance perpetually escalate.

Collectively, these characteristics establish an environment conducive to the proliferation and persistence of MDR *A. baumannii*. A comprehensive approach is required to tackle this escalating issue, encompassing enhancements to hospital infrastructure, fortification of infection control protocols, enforcement of rigorous antibiotic stewardship programs, and prioritization of targeted treatments to safeguard the most at-risk patients (22).

Outbreaks and Surveillance

Multidrug-resistant *A. baumannii* has significantly affected the region, as evidenced by numerous epidemiological investigations. A recent epidemic in a prominent hospital in Tehran revealed that around 40% of ICU isolates exhibited resistance to various drugs. Subsequent analysis verified that these strains proliferated through clonal expansion, with certain strains harboring OXA-23 and OXA-51-like enzymes, which enhance their resistance. Comparable epidemics have been noted in Saudi Arabia, where patients frequently endure extended

hospitalizations—occasionally an extra 10 to 15 days attributable to infections induced by MDR *A. baumannii*. Regrettably, these prolonged durations are associated with elevated mortality rates, exacerbating the overall burden. Notwithstanding these concerning tendencies, a deficiency in cooperation persists regarding regional surveillance. Despite advancements in real-time genetic surveillance, the lack of defined standards throughout the region complicates consistent and effective problem resolution (23) (Table 1) .

Mechanisms Underpinning Multidrug Resistance

Acquisition of Resistance Genes

MDR Acinetobacter baumannii exhibits remarkable adaptability and can rapidly acquire antibiotic resistance due to its capacity for horizontal gene transfer with other bacteria. This mechanism, termed horizontal gene transfer (HGT), enables bacteria to exchange DNA, encompassing genes that confer antibiotic resistance. This exchange occurs through three primary methods:

Conjugation: This resembles a bacterial "handshake" between two bacteria. One bacteria can transfer a tiny segment of DNA, known as a plasmid, to another using a specialized structure called a conjugative pilus. These plasmids frequently possess antibiotic resistance genes. The bla_OXA-235 gene, which confers resistance to Carbapenem drugs in *A. baumannii*, can be transferred between bacteria via conjugation. The capacity to disseminate resistance genes enables *A. baumannii* to endure in antibiotic-laden environments, such as hospitals (29).

Transformation: In this process, *A. baumannii* acquires free DNA fragments from its environment, typically originating from deceased bacteria. By integrating these DNA fragments, the bacteria acquire novel resistance characteristics, complicating treatment efforts. *A. baumannii's* inherent capacity to assimilate exogenous DNA is crucial to the development of resistance to many antibiotics (30).

•**Transduction**: This technique resembles a virus functioning as a genetic delivery system. During transduction, a bacteriophage may inadvertently acquire DNA from its bacterial host, encompassing genes associated with antibiotic resistance. The virus subsequently introduces this DNA into a novel bacterium, disseminating resistance. Although less prevalent in *A. baumannii* compared to certain other bacteria, transduction remains a viable mechanism for the dissemination of resistance genes among bacterial populations (31). Collectively, these pathways render MDR A. baumannii a formidable pathogen in healthcare settings. Comprehending the mechanisms by which it disseminates its resistance genes is essential for devising strategies to halt the proliferation of antibiotic resistance and effectively address this escalating issue (32).

Together, these mechanisms make MDR *A. baumannii* a dangerous pathogen in hospitals. Understanding how it shares and spreads its resistance genes is crucial in finding ways to stop the spread of antibiotic resistance and better tackle this growing problem (33).

Intrinsic Resistance Mechanisms

β-Lactamase Production

Multidrug-resistant (MDR) Acinetobacter baumannii can evade many antibiotics, especially β-lactam antibiotics, by producing β-lactamases. These are special enzymes that break down and deactivate the antibiotics, such as penicillins, cephalosporins, and Carbapenems, which are usually essential for treating bacterial infections. By producing these enzymes, *A. baumannii* can survive even in the presence of antibiotics that would normally kill it (34). The main types of β-lactamases that help A. baumannii resist treatment are:

OXA-Type Carbapenemases: OXA-type carbapenemases are some of the most important β-lactamases in A. baumannii, especially because they make the bacteria resistant to Carbapenems antibiotics that are often used as a last line of defense against serious infections. There are a few main types of these enzymes, including:

Table 1. Summary of Epidemiology and Resistance Characteristics of MDR A. *baumannii* in the Middle East

Country	Carbapenem Resistance Rate	Mortality Rate (%)	Notable Resistance Mechanisms	Key Contributing Factors	Ref
Iran	~65%	~45%	OXA-23, OXA-51-like enzymes, ESBLs, MBLs	Overcrowded ICUs, prolonged hospital stays, invasive procedures	(21,22)
Saudi Arabia	~70%	>50%	OXA-23, overexpressed efflux pumps, mutations (e.g., adeRS)	High ICU occupancy, indiscriminate antibiotic use, suboptimal infection control	(23)
Egypt	~60%	~40–50%	OXA-type carbapenemases, robust biofilm formation	Overcrowded facilities, limited healthcare resources, high VAP rates	(24)
Lebanon	~55%	~45%	Emerging determinants (e.g., bla_OXA-235), OXA-23, genomic variants	Variable surveillance, suboptimal infection control, inconsistent antibiotic stewardship	(25)

•OXA-23, OXA-24/40, and OXA-58: These acquired carbapenemases are found in many multidrug-resistant *A. baumannii* strains and are primarily responsible for resistance to imipenem, meropenem, and doripenem, which are all powerful Carbapenems antibiotics.
•OXA-51-like Variants: These enzymes are a bit different because they are part of *A. baumannii*'s natural DNA, not something it has acquired. Although they don't have strong Carbapenems resistance on their own, they can become much more active when certain genetic elements, like ISAba1, are added. These elements act like "boosters," making the enzymes more powerful and helping the bacteria resist treatment (35).

The widespread spread of OXA-type carbapenemases has seriously limited the effectiveness of carbapenem drugs against *A. baumannii* infections, making these enzymes a significant contributor to the growing problem of antimicrobial resistance (36).

Extended-Spectrum β-Lactamases (ESBLs)

Extended-spectrum β-lactamases (ESBLs) are another major class of β-lactamases found in MDR *A. baumannii*. These enzymes provide resistance to third- and fourth-generation Cephalosporins, hence diminishing the efficacy of medications such as cefotaxime, ceftazidime, and Cefepime (37). The predominant ESBL families found in *A. baumannii* encompass:
• TEM-type (Temoneira) β-lactamases
• SHV-type (Sulfhydryl Variable) β-lactamases
•CTX-M-type (Cefotaximase) β-lactamases
β-lactamases
In contrast to carbapenemases, ESBL-producing *A. baumannii* strains may retain susceptibility to Carbapenems; nonetheless, their capacity to hydrolyze Cephalosporins considerably restricts treatment alternatives. The introduction of ESBLs, in conjunction with additional resistance mechanisms such as porin loss or efflux pump overexpression, complicates treatment further (37).

Metallo-β-Lactamases (MBLs)

Metallo-β-lactamases (MBLs) represent a significant threat among carbapenemases due to their ability to hydrolyze practically all β-lactam antibiotics, encompassing carbapenems, cephalosporins, and penicillins, except for monobactams such as aztreonam. These enzymes contrast with OXA-type carbapenemases as they necessitate divalent metal ions, such as zinc (Zn^{2+}), for their enzymatic function (38). The most clinically relevant MBLs in *A. baumannii* comprise:

•**NDM (New Delhi Metallo-β-lactamase)**: A formidable Carbapenemase that has been extensively spread in healthcare settings.

•**VIM (Verona Integron-encoded Metallo-β-lactamase)**: Commonly linked to integrons that enable the horizontal transmission of resistance genes.

•**IMP (Imipenemase-type Metallo-β-lactamase)**:

One of the first identified metallo-β-lactamases, responsible for imipenem resistance. Given that MBLs are not susceptible to inhibition by clavulanic acid or Sulbactam, conventional β-lactamase inhibitors are ineffectual against them. Nevertheless, they are vulnerable to zinc chelators (such as EDTA), which inhibit enzyme activity by removing vital metal ions (39).

CLINICAL IMPLICATIONS

The presence of many β-lactamase enzymes in a single strain of *A. baumannii* complicates treatment significantly, as these bacteria may demonstrate resistance to almost all β-lactam medicines. The extensive prevalence of OXA-type carbapenemases, ESBLs, and MBLs has resulted in the recurrent ineffectiveness of empirical antibiotic therapy, requiring the implementation of alternative or combination treatments such as:
• Polymyxins (Colistin and Polymyxin B)
•Tigecycline
•Combinations based on Sulbactam
Comprehending the function of β-lactamases in *A. baumannii* resistance is essential for informing antibiotic choice and formulating new β-lactamase inhibitors that can reinstate the efficacy of current β-lactam antibiotics (40).

Efflux Pump Overexpression

Efflux pumps actively expel antibiotics, reducing intracellular concentrations. The key systems are:

•**AdeABC System:** Composed of AdeA, AdeB, and AdeC, and is regulated by the AdeRS two-component system. Mutations in regulatory genes can lead to up to a fivefold increase in pump expression (41).

•**AdeIJK System:**Although constitutively expressed, this system is inducible under antibiotic stress and is crucial for intrinsic resistance (42).

Target Site Modifications

Mutations in target proteins decrease antibiotic binding:
•**Penicillin-Binding Proteins (PBPs):** Alterations reduce susceptibility to β-lactams (43).
•**DNA Gyrase and Topoisomerase IV:** Mutations in gyrA and parC confer resistance to fluoroquinolones (44).
•**Ribosomal Alterations:** Structural changes diminish aminoglycoside binding (45).

Reduced Membrane Permeability

Downregulation or modification of outer membrane proteins (e.g., CarO and OmpA) limits drug uptake, working in tandem with efflux mechanisms (46).

Biofilm Formation

Biofilms act as a physical and metabolic barrier, protecting bacterial communities from antibiotics and immune responses. Advanced imaging studies have detailed the structure of *A. baumannii* biofilms and the role of extracellular polymeric substances (EPS) in impeding drug penetration (47).

Detailed Analysis of Resistance Mechanisms

β-Lactamase Production

Recent research employing genomic and proteomic studies has found new variants of OXA-type carbapenemases, including OXA-235. These changes, together with insertion sequences such as ISAba1, markedly augment resistance. The simultaneous occurrence of ESBLs and MBLs restricts therapeutic options by inactivating a wide range of β-lactams (48).

Mechanisms of Efflux Pumps

The overexpression of efflux pumps is a crucial element in the emergence of multidrug resistance. A quantitative study showed that mutations in the AdeRS regulation system lead to substantial enhancements in efflux pump activity, hence decreasing the intracellular concentration of pharmaceuticals. Recent studies on efflux pump inhibitors (EPIs) indicate that preclinical results may show possible reductions in minimum inhibitory concentrations (MICs) when these inhibitors are used in conjunction with traditional therapies (49).

Amendments Concerning the Membrane and the Designated Location

A correlation exists between mutations in penicillin-binding proteins (PBPs), DNA gyrase, and topoisomerase IV, and elevated minimum inhibitory concentrations (MICs) for certain pharmaceuticals. Moreover, proteomic analyses have demonstrated that resistant strains often have diminished levels of outer membrane proteins, such as CarO and OmpA, thereby limiting the quantity of medication that can be assimilated by the organism (50).

The Mechanisms of Biofilm Development

The formation of biofilm complicates treatment by establishing antibiotic gradients and promoting bacterial persistence. Recent studies employing confocal microscopy have elucidated the three-dimensional structure of *A. baumannii* biofilms, underscoring the significance of extracellular polymeric substances (EPS) in conferring antibiotic resistance to bacteria. In clinical environments, infections linked to biofilms are associated with extended treatment periods and increased chances of relapse (51).

Clinical Implications and Therapeutic Challenges

Colistin: Efficacy and Limitations

Colistin (polymyxin E) is among the limited therapeutic alternatives available for the treatment of extensively drug-resistant (XDR) *Acinetobacter baumannii* infections. This cationic polypeptide antibiotic destabilizes the bacterial outer membrane by engaging with lipopolysaccharides (LPS), resulting in cell lysis (52). Although colistin is effective against multidrug-resistant bacteria, its usage is considerably limited by certain clinical challenges:

• Narrow Therapeutic Window: Colistin demonstrates a precarious equilibrium between efficacy and toxicity, necessitating meticulous dosing to prevent inadequate treatment or significant adverse effects (53).

• Nephrotoxicity and Neurotoxicity: A significant issue associated with colistin therapy is dose-dependent renal impairment, with documented acute kidney injury (AKI) rates above 50% in critically ill patients. Neurological side effects, including dizziness, paresthesia, and neuromuscular blocking, have also been noted (54).

• Emerging Resistance: The rising resistance to colistin significantly jeopardizes its therapeutic efficacy. Resistance mechanisms encompass alterations in lipid A of LPS (regulated by genes such as pmrAB and lpxACD) and plasmid-mediated resistance genes (e.g., mcr-1 to mcr-10). Documented resistance rates of 20–30% in critical care units (ICUs) further diminish its efficacy as a monotherapy (55). Considering these constraints, combination therapy and alternative treatment options are being rigorously investigated to enhance outcomes and reduce the development of resistance.

Combination Therapies

To enhance the efficacy of colistin and minimize resistance emergence, combination therapy with other antimicrobial agents has been extensively studied. These combinations work through synergistic mechanisms, often targeting different bacterial pathways to enhance bactericidal effects (56).

Promising Combination Regimens:With the increasing prevalence of multidrug-resistant (MDR) and extensively drug-resistant (XDR) Acinetobacter baumannii, monotherapy with colistin has shown limited efficacy due to high nephrotoxicity, poor tissue penetration, and the rapid emergence of resistance. To overcome these limitations, combination therapy has been proposed as an effective strategy to enhance bacterial clearance, delay resistance development, and improve patient outcomes (57).

Mechanism of Synergy in Combination Therapy:

Combination therapies work through synergistic mechanisms, where different antimicrobial agents target distinct bacterial pathways to increase bactericidal effects (58). This approach not only improves drug efficacy but also reduces the likelihood of resistance emergence. Key mechanisms include:

•**Membrane Disruption & Protein Synthesis Inhibition:** Colistin disrupts the bacterial outer membrane, allowing better penetration of intracellularly acting antibiotics (59).

•**Inhibition of Bacterial RNA Polymerase:** Some antibiotics enhance the susceptibility of A. baumannii by interfering with RNA transcription and gene expression (60).

•**β-Lactamase Inhibition:** Novel β-lactamase inhibitors restore the activity of β-lactam antibiotics against resistant strains (61).

Emerging Therapeutic Strategies

With the rising prevalence of pan-drug-resistant (PDR) A. baumannii strains, novel therapeutic approaches are being developed to overcome resistance mechanisms and provide alternative treatment options beyond conventional antibiotics (62).

Novel β-Lactamase Inhibitors

Next-generation β-lactamase inhibitors are under development to target both serine β-lactamases (OXA-type, ESBLs) and metallo-β-lactamases (MBLs). These inhibitors, when used in combination with existing β-lactam antibiotics, have shown promising reductions in minimum inhibitory concentrations (MICs) for resistant A. baumannii strains (63).

Key β-Lactamase Inhibitors in Development:

•**Vaborbactam**: Primarily targets class A carbapenemases, but is less effective against OXA-type enzymes (64).

•**Relebactam**: Demonstrates synergy with imipenem against MDR *A. baumannii* (65).

Taniborbactam: Exhibits efficacy against both serine β-lactamases and metallo-β-lactamases, positioning it as a formidable option for combating resistance (36).

•As these inhibitors progress through clinical trials, they may offer viable treatment alternatives for carbapenem-resistant infections.

Infection Control and Antimicrobial Stewardship

Enhanced Monitoring and Swift Diagnostics

The use of whole-genome sequencing (WGS) and fast PCR diagnostics into standard surveillance have markedly enhanced outbreak detection and management. Hospitals utilizing these technologies have documented a 30–40% decrease in outbreak durations (66).

Enhancing Environmental and Clinical Controls

Improved infection control protocols—such as ultraviolet light disinfection and antimicrobial surface treatments—have been linked to a reduction in environmental contamination of up to 30%. These techniques are essential for preventing the dissemination of MDR infections when used alongside rigorous hand hygiene and patient isolation policies (67).

Antimicrobial Stewardship Initiatives

Effective stewardship systems are crucial for mitigating the misuse of broad-spectrum antibiotics. Numerous hospitals in the Middle East have seen a 20–25% reduction in antibiotic prescriptions after the introduction of stewardship initiatives (68).

Case Analyses and Regional Insights

Investigation of the Tehran Outbreak

An exhaustive outbreak investigation at a tertiary care hospital in Tehran indicated that approximately 40% of ICU isolates were multidrug-resistant, with molecular typing verifying clonal proliferation of bacteria harboring OXA-23 and OXA-51-like enzymes. The outbreak led to elevated mortality rates, prolonged hospitalizations (averaging 10–15 days), and increased healthcare expenditures. These findings highlight the necessity for immediate intervention and comprehensive genetic surveillance (69).

Multicenter Investigation in Saudi Arabia

A multicenter study done in various Saudi Arabian hospitals found that MDR *A. baumannii* infections were associated with extended hospital stays and fatality rates of over 50% in severe instances. The adoption of combination medicines and improved surveillance techniques resulted in better clinical results, underscoring the efficacy of integrated infection control strategies (70).

National Surveillance Programs in Lebanon

Lebanese hospitals have recently established a statewide surveillance program that integrates whole genome sequencing and quick diagnostic techniques. This endeavor has disclosed elevated resistance rates to Carbapenems, Cephalosporins, and Colistin, along with the emergence of resistance determinants. The statistics have guided policy modifications and emphasized the necessity for coordinated regional efforts to address MDR *A. baumannii* (71).

Prospective Directions and Research Priorities

Progressing Molecular Research

Continued research utilizing next-generation sequencing (21) and proteomics is crucial for elucidating emerging resistance mechanisms and pinpointing new treatment targets. Research on new plasmids and point mutations will enhance tailored treatment techniques (72).

Advancement of Innovative Therapeutics

Expedited investigation into innovative antimicrobials such as next-generation β-lactamase inhibitors, bacteriophage therapy, immunomodulators, and nanoparticle-based therapies is essential. Cooperative initiatives involving academic institutions, industry, and global health organizations are essential to translate these advances into clinical practice (73).

Enhancing Regional Surveillance

Standardizing laboratory techniques and creating real-time genomic surveillance networks throughout the Middle East will enhance the identification of developing resistance trends and inform targeted public health responses (74).

Improving Infection Control Protocols

Future infection control should utilize both conventional approaches and advanced technologies (e.g., automated UV disinfection systems, and antimicrobial coatings) to mitigate nosocomial spread. Training and continuous oversight of healthcare staff are critical elements (75).

Policy and Regulatory Measures

Enhanced limits on antibiotic prescriptions and over-the-counter sales, along with comprehensive antimicrobial stewardship programs, are essential for mitigating the selective pressure that fosters resistance. Policymakers must endorse these programs through sufficient funding and incorporation into national public health plans (76).

Interdisciplinary Collaborations

A collaborative, interdisciplinary strategy involving clinicians, microbiologists, public health specialists, and policymakers is essential. Forming regional consortia for research and data sharing would expedite the dissemination of best practices and the execution of innovative solutions (77).

CONCLUSION

Acquired resistance genes and intrinsic mechanisms contribute to the rapid proliferation of multidrug-resistant *Acinetobacter baumannii* in healthcare environments in the Middle East. These methods encompass the synthesis of β-lactamase, the overexpression of efflux pumps, modifications to target sites, and the development of biofilms. The treatment efforts are further complicated by recently identified determinants such as bla_OXA-235. The threat presented by MDR *A. baumannii* is undeniable, as its prevalence in intensive care units (ICUs) exceeds 70 percent, with fatality rates surpassing 50 percent in specific nations. An urgent need exists for a comprehensive and multidisciplinary strategy. This plan must encompass enhanced antibiotic stewardship, stringent infection control, advanced molecular diagnostics, and the creation of novel therapeutics. To safeguard patient care in the Middle East, forthcoming studies must enhance our comprehension of resistance mechanisms and translate these findings into effective clinical therapies.

Author's Contribution

Azadeh Taftian, Neda Abedi and Ali Zolfi Gol were involved in the conceptualization, design and writing of the manuscript draft. The authors read and confirmed the final manuscript.

Funding

This study is the outcome of self-directed research carried out without any financial assistance.

Ethics approval and consent to participate

Not applicable.

Conflict of Interest

The authors declared no conflict of interest.

Consent for publication

Not Applicable

REFERENCES

1.Howard A, O'Donoghue M, Feeney A, Sleator RD. Acinetobacter baumannii: an emerging opportunistic pathogen. Virulence. 2012;3(3):243-50.
2.Ayoub Moubareck C, Hammoudi Halat D. Insights into Acinetobacter baumannii: A Review of Microbiological, Virulence, and Resistance Traits in a Threatening Nosocomial Pathogen. Antibiotics (Basel). 2020;9(3).
3.Gedefie A, Demsis W, Ashagrie M, Kassa Y, Tesfaye M, Tilahun M, et al. Acinetobacter baumannii Biofilm Formation and Its Role in Disease Pathogenesis: A Review. Infect Drug Resist. 2021;14:3711-9.
4.Mukhopadhyay H, Bairagi A, Mukherjee A, Prasad AK, Roy AD, Nayak A. Multidrug resistant Acinetobacter baumannii: A study on its pathogenesis and therapeutics. Current Research in Microbial Sciences. 2025;8:100331.
5.Męcik M, Stefaniak K, Harnisz M, Korzeniewska E. Hospital and municipal wastewater as a source of carbapenem-resistant Acinetobacter baumannii and Pseudomonas aeruginosa in the environment: a review. Environmental Science and Pollution Research. 2024;31(36):48813-38.
6.Nguyen M, Joshi SG. Carbapenem resistance in Acinetobacter baumannii, and their importance in hospital-acquired infections: a scientific review. Journal of Applied Microbiology. 2021;131(6):2715-

38.
7.Ibrahim S, Al-Saryi N, Al-Kadmy IMS, Aziz SN. Multidrug-resistant Acinetobacter baumannii as an emerging concern in hospitals. Mol Biol Rep. 2021;48(10):6987-98.
8.Piperaki ET, Tzouvelekis LS, Miriagou V, Daikos GL. Carbapenem-resistant Acinetobacter baumannii: in pursuit of an effective treatment. Clinical Microbiology and Infection. 2019;25(8):951-7.
9.Tamburro M, Lombardi A, Sammarco ML, Ripabelli G. Molecular Epidemiology Revealed Distinct Patterns Among Multidrug Resistant Clinical Acinetobacter baumannii Strains in Different Periods in the Main Hospital in Molise Region, Central Italy. 2025;5(1):9.
10.Elbehiry A, Marzouk E, Moussa I, Mushayt Y, Algarni AA, Alrashed OA, et al. The Prevalence of Multidrug-Resistant Acinetobacter baumannii and Its Vaccination Status among Healthcare Providers. Vaccines (Basel). 2023;11(7).
11.Salarvan S, Abdollahi A, Afarinesh Khaki P, Norouzi Shadehi M, Beigh Mohammadi MT, Miratashi Yazdi SA, et al. Antibiotic Resistance Pattern in Intensive Care Units in a Large Referral Hospital in Iran. Iran J Pathol. 2023;18(4):433-8.
12.Almakrami M, Salmen M, Aldashel YA, Alyami MH, Alquraishah N, AlZureea M, et al. Prevalence of multidrug-, extensively drug-, and pandrug-resistant bacteria in clinical isolates from King Khaled Hospital, Najran, Saudi Arabia. Discover Medicine. 2024;1(1):108.
13.Elsheikh M, Kuriyama A, Goto Y, Takahashi Y, Toyama M, Nishikawa Y, et al. Incidence and predictors of ventilator-associated pneumonia using a competing risk analysis: a single-center prospective cohort study in Egypt. BMC Infect Dis. 2024;24(1):1007.
14.Kruk ME, Gage AD, Arsenault C, Jordan K, Leslie HH, Roder-DeWan S, et al. High-quality health systems in the Sustainable Development Goals era: time for a revolution. Lancet Glob Health. 2018;6(11):e1196-e252.
15.Du X, Du Y, Zhang Y, Zhu Y, Yang Y. Urban and rural disparities in general hospital accessibility within a Chinese metropolis. Scientific Reports. 2024;14(1):23359.
16.Jafari N, Shahabi Rabori V, Zolfi Gol A, Saberiyan M. Crosstalk of NLRP3 inflammasome and noncoding RNAs in cardiomyopathies. Cell biochemistry and function. 2023;41(8):1060-75.
17.Roosta Y, Abedi N. The Evolving Landscape of Drug Resistance: From Mechanisms to Therapeutic Strategies %J Personalized Medicine Journal. 2025;10(36):1-11.
18.Zhang T, Xu X, Xu C-F, Bilya SR, Xu W. Mechanical ventilation-associated pneumonia caused by Acinetobacter baumannii in Northeast China region: analysis of genotype and drug resistance of bacteria and patients' clinical features over 7 years. Antimicrobial Resistance & Infection Control. 2021;10(1):135.
19.Zolfigol A, Pirhadi M. Phytotherapy in Children's Colds %J Plant Biotechnology Persa. 2025;7(1):96-100.
20.Endale H, Mathewos M, Abdeta D. Potential Causes of Spread of Antimicrobial Resistance and Preventive Measures in One Health Perspective-A Review. Infect Drug Resist. 2023;16:7515-45.
21.Tartari E, Weterings V, Gastmeier P, Rodríguez Baño J, Widmer A, Kluytmans J, et al. Patient engagement with surgical site infection prevention: an expert panel perspective. Antimicrob Resist Infect Control. 2017;6:45.
22.Gupta A, Marzook H, Ahmad F. Comorbidities and clinical complications associated with SARS-CoV-2 infection: an overview. Clinical and Experimental Medicine. 2023;23(2):313-31.
23.Azimzadeh M, Bahador A, Shiralizadeh S, Mahshouri P, Akbari L, Makari S, et al. A single-center analysis of clonal transmission of carbapenem-resistant Acinetobacter baumannii among intensive care unit patients during the COVID-19 pandemic. Scientific Reports. 2024;14(1):25897.
24.Bialvaei AZ, Kouhsari E, Salehi-Abargouei A, Amirmozafari N, Ramazanzadeh R, Ghadimi-Daresajini A, et al. Epidemiology of multidrug-resistant Acinetobacter baumannii strains in Iran: a systematic review and meta-analysis. J Chemother. 2017;29(6):327-37.
25.Jasemi S, Douraghi M, Adibhesami H, Zeraati H, Rahbar M, Boroumand MA, et al. Trend of extensively drug-resistant Acinetobacter baumannii and the remaining therapeutic options: a multicenter study in Tehran, Iran over a 3-year period. Lett Appl Microbiol. 2016;63(6):466-72.
26.Ibrahim ME. Prevalence of Acinetobacter baumannii in Saudi Arabia: risk factors, antimicrobial resistance patterns and mechanisms of carbapenem resistance. Ann Clin Microbiol Antimicrob. 2019;18(1):1.
27.Thomsen J, Abdulrazzaq NM, AlRand H, Everett DB, Senok A, Menezes GA, et al. Epidemiology and antimicrobial resistance trends of Acinetobacter species in the United Arab Emirates: a retrospective analysis of 12 years of national AMR surveillance data. Front Public Health. 2023;11:1245131.
28.Al-Orphaly M, Hadi HA, Eltayeb FK, Al-Hail H, Samuel BG, Sultan AA, et al. Epidemiology of Multidrug-Resistant Pseudomonas aeruginosa in the Middle East and North Africa Region. mSphere. 2021;6(3).
29.Zong G, Zhong C, Fu J, Zhang Y, Zhang P, Zhang W,

et al. The carbapenem resistance gene bla(OXA-23) is disseminated by a conjugative plasmid containing the novel transposon Tn6681 in Acinetobacter johnsonii M19. Antimicrob Resist Infect Control. 2020;9(1):182.
30.Traglia GM, Pasteran F, Moheb S, Akhtar U, Gonzalez S, Maldonado C, et al. Insights into Acinetobacter baumannii AMA205's Unprecedented Antibiotic Resistance. International Journal of Molecular Sciences [Internet]. 2024; 25(21).
31.Pfeifer E, Bonnin RA, Rocha EPC. Phage-Plasmids Spread Antibiotic Resistance Genes through Infection and Lysogenic Conversion. mBio. 2022;13(5):e0185122.
32.Teng J, Imani S, Zhou A, Zhao Y, Du L, Deng S, et al. Combatting resistance: Understanding multi-drug resistant pathogens in intensive care units. Biomedicine & Pharmacotherapy. 2023;167:115564.
33.Gauba A, Rahman KM. Evaluation of Antibiotic Resistance Mechanisms in Gram-Negative Bacteria. Antibiotics [Internet]. 2023; 12(11).
34.Kyriakidis I, Vasileiou E, Pana ZD, Tragiannidis A. Acinetobacter baumannii Antibiotic Resistance Mechanisms. Pathogens. 2021;10(3).
35.Chan K-W, Liu C-Y, Wong H-Y, Chan W-C, Wong K-Y, Chen S. Specific Amino Acid Substitutions in OXA-51-Type β-Lactamase Enhance Catalytic Activity to a Level Comparable to Carbapenemase OXA-23 and OXA-24/40. International Journal of Molecular Sciences [Internet]. 2022; 23(9).
36.Liu B, Trout REL, Chu GH, McGarry D, Jackson RW, Hamrick JC, et al. Discovery of Taniborbactam (VNRX-5133): A Broad-Spectrum Serine- and Metallo-β-lactamase Inhibitor for Carbapenem-Resistant Bacterial Infections. J Med Chem. 2020;63(6):2789-801.
37.Castanheira M, Simner PJ, Bradford PA. Extended-spectrum β-lactamases: an update on their characteristics, epidemiology and detection. JAC Antimicrob Resist. 2021;3(3):dlab092.
38.Sakalauskienė GV, Malcienė L, Stankevičius E, Radzevičienė A. Unseen Enemy: Mechanisms of Multidrug Antimicrobial Resistance in Gram-Negative ESKAPE Pathogens. Antibiotics (Basel). 2025;14(1).
39.Huang Y-S, Zhou H. Breakthrough Advances in Beta-Lactamase Inhibitors: New Synthesized Compounds and Mechanisms of Action Against Drug-Resistant Bacteria. Pharmaceuticals [Internet]. 2025; 18(2).
40.Tooke CL, Hinchliffe P, Bragginton EC, Colenso CK, Hirvonen VHA, Takebayashi Y, et al. β-Lactamases and β-Lactamase Inhibitors in the 21st Century. J Mol Biol. 2019;431(18):3472-500.
41.Ranjbar R, Zayeri S, Afshar D. High Frequency of AdeA, AdeB and AdeC Genes among Acinetobacter baumannii Isolates. Iran J Public Health. 2020;49(8):1539-45.
42.Brand C, Newton-Foot M, Grobbelaar M, Whitelaw A. Antibiotic-induced stress responses in Gram-negative bacteria and their role in antibiotic resistance. Journal of Antimicrobial Chemotherapy. 2025.
43.Lunha K, Chumpol W, Jiemsup S, Samngamnim S, Assavacheep P, Yongkiettrakul S. Relationship between Penicillin-Binding Proteins Alterations and β-Lactams Non-Susceptibility of Diseased Pig-Isolated Streptococcus suis. Antibiotics (Basel). 2023;12(1).
44.Rezaei S, Tajbakhsh S, Naeimi B, Yousefi F. Investigation of gyrA and parC mutations and the prevalence of plasmid-mediated quinolone resistance genes in Klebsiella pneumoniae clinical isolates. BMC Microbiology. 2024;24(1):265.
45.O'Sullivan ME, Poitevin F, Sierra RG, Gati C, Dao EH, Rao Y, et al. Aminoglycoside ribosome interactions reveal novel conformational states at ambient temperature. Nucleic Acids Res. 2018;46(18):9793-804.
46.Uppalapati SR, Sett A, Pathania R. The Outer Membrane Proteins OmpA, CarO, and OprD of Acinetobacter baumannii Confer a Two-Pronged Defense in Facilitating Its Success as a Potent Human Pathogen. Front Microbiol. 2020;11:589234.
47.Shree P, Singh CK, Sodhi KK, Surya JN, Singh DK. Biofilms: Understanding the structure and contribution towards bacterial resistance in antibiotics. Medicine in Microecology. 2023;16:100084.
48.Hammoudi Halat D, Ayoub Moubareck C. The Current Burden of Carbapenemases: Review of Significant Properties and Dissemination among Gram-Negative Bacteria. Antibiotics [Internet]. 2020; 9(4).
49.Zhang S, Wang J, Ahn J. Advances in the Discovery of Efflux Pump Inhibitors as Novel Potentiators to Control Antimicrobial-Resistant Pathogens. Antibiotics [Internet]. 2023; 12(9).
50.Gauba A, Rahman KM. Evaluation of Antibiotic Resistance Mechanisms in Gram-Negative Bacteria. Antibiotics (Basel). 2023;12(11).
51.Roy S, Chowdhury G, Mukhopadhyay AK, Dutta S, Basu S. Convergence of Biofilm Formation and Antibiotic Resistance in Acinetobacter baumannii Infection. Front Med (Lausanne). 2022;9:793615.
52.El-Sayed Ahmed MAE, Zhong LL, Shen C, Yang Y, Doi Y, Tian GB. Colistin and its role in the Era of antibiotic resistance: an extended review (2000-2019). Emerg Microbes Infect. 2020;9(1):868-85.
53.Gontijo AVL, Cavalieri AVG. Optimal control for colistin dosage selection. J Pharmacokinet Pharmacodyn. 2021;48(6):803-13.
54. Kilic I, Ayar Y, Ceylan İ, Kaya PK, Caliskan G.

Nephrotoxicity caused by colistin use in ICU: a single centre experience. BMC Nephrology. 2023;24(1):302.
55.Schumann A, Gaballa A, Yang H, Yu D, Ernst RK, Wiedmann M. Site-selective modifications by lipid A phosphoethanolamine transferases linked to colistin resistance and bacterial fitness. mSphere. 2024;9(12):e0073124.
56.Jalil AT, Alrawe RTA, Al-Saffar MA, Shaghnab ML, Merza MS, Abosaooda M, et al. The use of combination therapy for the improvement of colistin activity against bacterial biofilm. Braz J Microbiol. 2024;55(1):411-27.
57.Scoffone VC, Trespidi G, Barbieri G, Arshad A, Israyilova A, Buroni S. The Evolution of Antimicrobial Resistance in Acinetobacter baumannii and New Strategies to Fight It. Antibiotics [Internet]. 2025; 14(1).
58.Basavegowda N, Baek KH. Combination Strategies of Different Antimicrobials: An Efficient and Alternative Tool for Pathogen Inactivation. Biomedicines. 2022;10(9).
59.Sabnis A, Hagart KL, Klöckner A, Becce M, Evans LE, Furniss RCD, et al. Colistin kills bacteria by targeting lipopolysaccharide in the cytoplasmic membrane. Elife. 2021;10.
60.Norton MD, Spilkia AJ, Godoy VG. Antibiotic resistance acquired through a DNA damage-inducible response in Acinetobacter baumannii. J Bacteriol. 2013;195(6):1335-45.
61.Kang S-J, Kim D-H, Lee B-J. Metallo-β-lactamase inhibitors: A continuing challenge for combating antibiotic resistance. Biophysical Chemistry. 2024;309:107228.
62.Thacharodi A, Vithlani A, Hassan S, Alqahtani A, Pugazhendhi A. Carbapenem-resistant Acinetobacter baumannii raises global alarm for new antibiotic regimens. iScience. 2024;27(12):111367.
63.Sargianou M, Stathopoulos P, Vrysis C, Tzvetanova ID, Falagas ME. New β-Lactam/β-Lactamase Inhibitor Combination Antibiotics. Pathogens [Internet]. 2025; 14(4).
64.Langley GW, Cain R, Tyrrell JM, Hinchliffe P, Calvopiña K, Tooke CL, et al. Profiling interactions of vaborbactam with metallo-β-lactamases. Bioorg Med Chem Lett. 2019;29(15):1981-4.
65.Xu C, Chen T, Zhang S, Zhou C, Liao W, Fang R, et al. In vitro activity of imipenem-relebactam alone and in combination with fosfomycin against carbapenem-resistant gram-negative pathogens. Diagnostic Microbiology and Infectious Disease. 2022;103(3):115712.
66. Sundermann AJ, Kumar P, Griffith MP, Waggle KD, Srinivasa VR, Raabe N, et al. Genomic Surveillance for Enhanced Healthcare Outbreak Detection and Control. medRxiv. 2024.
67.Resendiz M, Blanchard D, West GF. A systematic review of the germicidal effectiveness of ultraviolet disinfection across high-touch surfaces in the immediate patient environment. J Infect Prev. 2023;24(4):166-77.
68.Chukwu EE, Oshun PO, Osuolale KA, Chuka-Ebene VO, Salako A, Idigbe IE, et al. Antimicrobial stewardship programmes in healthcare facilities in Lagos State, Nigeria: a needs assessment. Journal of Global Antimicrobial Resistance. 2021;25:162-70.
69.Gupta N, Angadi K, Jadhav S. Molecular Characterization of Carbapenem-Resistant Acinetobacter baumannii with Special Reference to Carbapenemases: A Systematic Review. Infect Drug Resist. 2022;15:7631-50.
70.Aldali JA. Acinetobacter baumannii: A multidrug-resistant pathogen, has emerged in Saudi Arabia. Saudi Med J. 2023;44(8):732-44.
71.Iskandar K, Molinier L, Hallit S, Sartelli M, Hardcastle TC, Haque M, et al. Surveillance of antimicrobial resistance in low- and middle-income countries: a scattered picture. Antimicrob Resist Infect Control. 2021;10(1):63.
72.Bianconi I, Aschbacher R, Pagani E. Current Uses and Future Perspectives of Genomic Technologies in Clinical Microbiology. Antibiotics (Basel). 2023;12(11).
73.Murugaiyan J, Kumar PA, Rao GS, Iskandar K, Hawser S, Hays JP, et al. Progress in Alternative Strategies to Combat Antimicrobial Resistance: Focus on Antibiotics. Antibiotics (Basel). 2022;11(2).
74.Struelens MJ, Ludden C, Werner G, Sintchenko V, Jokelainen P, Ip M. Real-time genomic surveillance for enhanced control of infectious diseases and antimicrobial resistance. 2024;Volume 2 - 2024.
75.Garcia R, Barnes S, Boukidjian R, Goss LK, Spencer M, Septimus EJ, et al. Recommendations for change in infection prevention programs and practice. Am J Infect Control. 2022;50(12):1281-95.
76.Aslam B, Asghar R, Muzammil S, Shafique M, Siddique AB, Khurshid M, et al. AMR and Sustainable Development Goals: at a crossroads. Globalization and Health. 2024;20(1):73.
77.Lane HG, Allgood SD, Schexnayder J, Bosworth HB, Baumann AA, Lewinski AA. Recommendations for interdisciplinary research collaboration for early career dissemination and implementation researchers: A multi-phase study. J Clin Transl Sci. 2025;9(1):e39.