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Review Article

Acinetobacter: An Emerging Threat to Hospitalized Patients

Siddharth Singh[1] and Pooja Singh Gaur[2], Surya Kant[2] and Rachna Chaturvedi[1]*

[1]*Amity Institute of Biotechnology, Amity University, Uttar Pradesh, Lucknow Campus, Gomti Nagar Extension, Lucknow, India*

[2]*Department of Pulmonary Medicine, KGMU, Lucknow, India*

***Corresponding Author:** Rachna Chaturvedi, Amity Institute of Biotechnology, Amity University, Uttar Pradesh, Lucknow Campus, Gomti Nagar Extension, Lucknow, India.

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Abstract

Over the last few decades, the increase in *Acinetobacter* infections among critically ill patients has been a growing concern and it has become important as a major nosocomial pathogen, partially due to its impressive genetic capabilities to acquire resistance and partially due to its high selective pressure, especially in intensive care units. Bacteraemia, pneumonia, urinary tract, and skin and soft tissue infections are the utmost frequent presentations of Acinetobacter baumannii with attributable death rates considering 35%. *A. baumannii* is progressively connected with several epidemics, demonstrating determined trouble due to the extensive level of antimicrobial resistance and clinical manifestations. Initially a low-virulence bacterium, it has evolved into a multidrug-resistant pathogen that is now a threat to medical professionals and hospitalized patients everywhere. To control hospital outbreaks of multi-drug resistance Acinetobacter infection, we need to contain their dispersion or bear new medicines or rational combination therapy. The best course of action for treating multidrug-resistant *Acinetobacter* infections is still unclear, and practical therapy still depends on understanding the susceptibility patterns of isolates from the patient's institution. Thus, the troublesome distribution of biofilm-producing species in multidrug-resistant inhabitants of *A. baumannii* poses a meaningful treatment task. This review is mainly concentrated on general features and introduction to *Acinetobacter* and its epidemiological status, antibiotic resistance, and strategies to control infection to minimize spread.

Keywords: *Acinetobacter baumannii*; Biofilm Formation; Multi-resistance; Nosocomial Infections; Compromised Immune System

Introduction

Acinetobacter is a genus of aerobic, gram-negative coccobacilli that are widely distributed in nature that includes numerous species, some of which can cause infections in humans. They are found in soil, water, and air, and can also be found on the skin and in the respiratory and digestive tracts of humans and animals. The most clinically relevant species within this genus is *Acinetobacter baumannii* often abbreviated as *A. baumannii*. It has gained attention as a cause of nosocomial infections, particularly in intensive care units (ICUs). It can live on various surfaces and medical apparatus, accepting it to continue in healthcare environments. *A. baumannii* is also known for its ability to develop fighting multiple antibiotics. While some species of *Acinetobacter* are not dangerous and can be in the atmosphere, certain strains can begin infections, remarkably in healthcare settings, making them a concern for nosocomial infections. Nosocomial infections, also known as healthcare-associated infections (HAIs), are infections that are obtained in hospitals or other healthcare surroundings. *A. baumannii* infections principally occur in healthcare settings, such as hospitals, long-term care facilities, and ICUs. *A. baumannii* can cause a range of infections, including bloodstream infections, pneumonia, urinary tract infections, wound infections, and infections of surgical sites. They tend to affect individuals with compromised immune systems, such as individuals who are desperately ill, have principal medical condi-

tions, or have experienced invasive procedures. These infections are troublesome because they can be problematic to treat, specifically when the bacteria are opposed to multiple antibiotics. Avoiding and managing *Acinetobacter* infections in healthcare surroundings concerns strict observance of infection control methods, such as proper hand hygiene, environmental cleanup, and sterilization of equipment. Furthermore, proper antibiotic stewardship preparations are necessary to avoid the beginning and coverage of antibiotic-resistant strains. It's the main thing to note that whereas *Acinetobacter* can be life threatening in certain circumstances, not all strains or species within the *Acinetobacter* genus are similarly lethal or resistant to antibiotics. The identifiable quality and occurrence of *Acinetobacter* strains can adjust across changed regions and healthcare capabilities. Over the last twenty years, medical professionals across many nations have seen an increasing number of critically sick patients with infections caused by germs from the *Acinetobacter* genus, mostly strains of the *A. baumannii* species. *Acinetobacter* is a class of Gram-negative, non-fermentative bacteria that can live in aquatic settings and on a range of surfaces with low nutritional needs [1]. It has been demonstrated to be a cause of community-acquired respiratory tract infections, including pneumonia, among immunocompetent individuals residing in tropical regions, in addition to intensive care unit patients. Furthermore, among the most frequent sources of infection among troops who suffered trauma during the Vietnam, Afghanistan, and Iraq conflicts is *Acinetobacter.* Notwithstanding these noteworthy correlations, the extent of the expanding worldwide pandemic of *Acinetobacter* ICU-acquired infections in critically unwell individuals is incomparable [2]. One of the most concerning aspects of *Acinetobacter* infections is that many strains are resistant to multiple antibiotics. This is due in part to the overuse of antibiotics, which has allowed *Acinetobacter* to develop resistance mechanisms. Because of its multidrug resistance, it has been termed an "ESKAPE" pathogen (*Enterococcus faecium*, *Staphylococcus aureus, Klebsiella pneumoniae*, *Acinetobacter baumannii, Pseudomonas aeruginosa*, and *Enterobacter sp.* [3]. To determine the prevalence and patterns of antibiotic resistance of *Acinetobacter* in critically ill patients throughout the globe, we reviewed surveillance data as well as other prospective and retrospective investigations of ICU-acquired infections. *Acinetobacter* infections are most common in hospitalized patients, especially those who are critically ill or who have weakened immune systems. However, community-acquired *Acinetobacter* infections are also becoming more common. During their stay in an ICU, a significant percentage of critically ill patients get an infection; the occurrence of these infections varies greatly among various groups and clinical settings. They are often referred to as nosocomial or hospital-acquired infections. *A. baumannii* can survive on surfaces and medical equipment, allowing it to persist and spread within healthcare environments. Prolonged stays in the intensive care unit are closely linked to the development of infections acquired there, which is linked to worse outcomes such as higher rates of morbidity and death.

Taxonomy and classification

The taxonomy and classification of *Acinetobacter* have evolved with advancements in molecular techniques and genomic analyses. Here is an overview of the current taxonomy and classification of *Acinetobacter*.

Acinetobacter is a diverse genus comprising more than 50 species, including both pathogenic and non-pathogenic strains while *A. baumannii* is the most extensively studied and medically important species [4]. The taxonomy and classification of *Acinetobacter* have evolved with advancements in molecular techniques and genomic analyses.

Acinetobacter is a diverse genus encompassing several species, containing both pathogenic and non-pathogenic strains. Some of the clinically relevant species within the genus *Acinetobacter* include *Acinetobacter baumannii, Acinetobacter calcoaceticus, Acinetobacter nosocomialis, Acinetobacter pittii,* and *Acinetobacter lwoffii.* These species are associated with various infections, particularly in healthcare settings. It is significant to remark that taxonomic revisions may occur over time as new knowledge is available. To retrieve the most up-to-date and complete information on the taxonomy and classification of *Acinetobacter*, refer to reliable scientific resources for example.

- **Bergey's Manual of Systematic Bacteriology:** The definitive reference for bacterial taxonomy and classification. The latest edition, "Bergey's Manual of Systematics of Archaea and Bacteria," provides thorough information on *Acinetobacter* and its classification.

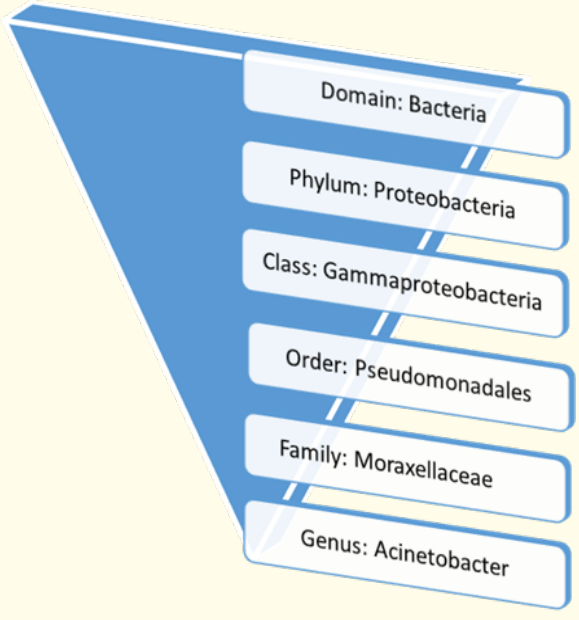

Figure 1: Graphic representation of classification of Acinetobacter sp.

- **International Journal of Systematic and Evolutionary Microbiology (IJSEM):** Consistently announces taxonomic updates and explanations of newly detected species. Examining specific *Acinetobacter* species in the IJSEM can give the newest taxonomic information.
- **PubMed:** A database of biomedical text, involving systematic commentaries on *Acinetobacter* taxonomy and classification. Seeking appropriate review articles or research papers can provide designated information on specialized phases of *Acinetobacter* taxonomy.

Watch in object that the field of bacterial taxonomy is vibrant, and new findings can manipulate the classification of microbes. It is always sensible to discuss the latest scientific literature and resources for the maximum precise and recent information.

Epidemiology

Acinetobacter infection epidemiology is extensive and includes illnesses linked to tropical settings, armed conflicts, natural catastrophes, and hospital epidemics in temperate regions.

It lives naturally in soil and water, but it may also be found in pets, arthropods, and food animals. They are ubiquitous and can be found in diverse environments, including soil, water, and hospital settings. They can persist in the environment and survive on various surfaces, contributing to their prevalence of healthcare-associated infections [5].

Acinetobacter is a genus of bacteria that includes several species known to cause opportunistic infections in humans. In humans, *Acinetobacter* can colonize skin, wounds, and the respiratory tract and gastrointestinal tract [6]. *Acinetobacter* has a reputation for forming biofilms and is a skilled colonizer. Additionally, the results show a favorable association between *Acinetobacter* multidrug resistance (MDR) status and its ability to produce biofilms. These traits can mediate epidemics. The pathogenicity of *A. baumannii* is multifactorial, as evidenced by recent research, which has led to the proposal of several models. These models elaborate on the role of virulence attributes such as iron acquisition resistance to the serum, resistance to desiccation, adherence, and colonization, epi-

thelial cell invasion, and the remarkable ability to gather foreign genetic material by lateral transfer for its survival. *A. baumannii* can last for a considerable amount of time in situations like dry, alive, and inanimate surfaces.

In recent years, the epidemiology and ecology of *Acinetobacter* have obtained noteworthy consideration due to its capability to develop resistance to multiple antibiotics, leading to increased morbidity and mortality rates. Here is an overview of *Acinetobacter* epidemiology and ecology, supported by references.

- **Global Distribution:** *Acinetobacter* species are found globally and can be separated from various environmental sources such as soil, water, and hospital settings. Studies have reported higher rates of *Acinetobacter* infections in tropical and subtropical regions, although it is a growing concern in healthcare facilities globally [5,7].
- **Nosocomial Infections:** *A. baumannii* the most clinically appropriate species within the genus, is repeatedly associated with nosocomial (hospital-acquired) infections. These infections principally affect essentially ill patients, remarkably those in ICUs. Risk factors for *Acinetobacter* infections taken into notice as prolonged hospital stays, invasive procedures, mechanical ventilation, and negotiated immune systems [5,8].
- **Antibiotic Resistance:** *Acinetobacter* species are known for their capability to develop resistance to numerous antibiotics, including carbapenems, which are contemplated last-line agents for many bacterial infections. This resistance is often due to the existence of various resistance mechanisms, such as the production of beta-lactamases and efflux pumps, as well as alterations in outer membrane proteins [5,9].
- **Environmental Reservoirs:** *Acinetobacter* can continue in the environment, remarkably in soil and water. Numerous studies have exhibited the existence of *Acinetobacter* in genuine and human-made water supplies, as well as in soil samples. Environmental basins can act as resources for nosocomial outbreaks and promote the spread of antibiotic-resistant strains [5,7].
- **Clonal Dissemination:** *Acinetobacter* epidemics in healthcare backgrounds are repeatedly connected with the clonal diffusion of specific strains. Molecular typing methods, such as pulsed-field gel electrophoresis (PFGE) and multilocus sequence typing (MLST), have exposed the clonal distribution of certain strains within and between healthcare facilities, suggesting both limited and global transmission [5,8].

Clinical significance

A. baumannii is a foremost cause of nosocomial infections, incorporating bloodstream infections, ventilator-associated pneumonia, surgical site infections, and urinary tract infections. It creates a significant challenge in healthcare surroundings due to its capability to acquire antibiotic resistance mechanisms [10]. Here is an overview of the clinical significance of *Acinetobacter*, supported by references:

- **HAIs:** *A. baumannii* relates to a range of healthcare-associated infections, including bloodstream infections, ventilator-associated pneumonia, urinary tract infections, surgical site infections, and catheter-related infections [11,12]. These infections primarily influence persons with compromised immune systems, such as acutely ill patients, those who go through invasive procedures, and individuals with prolonged hospital stays [13].
- **Antibiotic Resistance:** *Acinetobacter sp.* has an increased unsavory reputation due to its capability to grow resistance to multiple antibiotics, including carbapenems, which are commonly used as a last resort for treating multidrug-resistant infections. The development of carbapenem-resistant *A. baumannii* (CRAB) has presented noteworthy trials in clinical settings, limiting medication opportunities, and encouraging mortality rates [14,15].
- **Outbreaks and Clonal Spread:** *Acinetobacter* occurrences have been described in healthcare facilities internationally, often concerning multidrug-resistant strains. These outbreaks are repeatedly accompanied by the clonal distribution of specific strains within a healthcare setting, indicating the significance of infection control measures to avoid transmission [16,17].
- **Community-Acquired Infections:** Although less common, *Acinetobacter* infections can also appear in the group, remarkably in individuals with causal risk factors or preceding healthcare coverage. Community-acquired strains may show antibiotic resistance, further causing difficulties in treatment [18].
- **Wound Infections in Combat Casualties:** *A. baumannii* has been an alarm in army healthcare settings due to its capability to be a source of severe wound infections, remarkably in combat fatalities. These infections have determined resistance to multiple antibiotics, pretending challenges for treatment [19,20].

Virulence

The genuine disease impact of *Acinetobacter* has been a source of contention for many years, due to the difficulty in distinguishing colonization from infection with these organisms. Biofilm formation has been associated with *A. baumannii* virulence [21]. The ability to produce biofilm promotes colonization of host mucosa and bacterial growth on abiotic surfaces, hence leading to medical device-associated infections and survival in the environment [22]. The recent military experience with *Acinetobacter* found no related mortality in our young, healthy group, but rather a link with longer hospital stays and more surgical operations [23]. Some investigations have found attributed mortality, particularly in individuals with imipenem-resistant isolates who were not initially treated well [24]. Underlying chronic disease, mechanical ventilation, repeated trauma, neutropenia, and past antibiotic exposure are all risk factors for poor *Acinetobacter* infection outcomes [25]. Some of the virulence factors of *A. baumannii* have been illustrated in Figure 2.

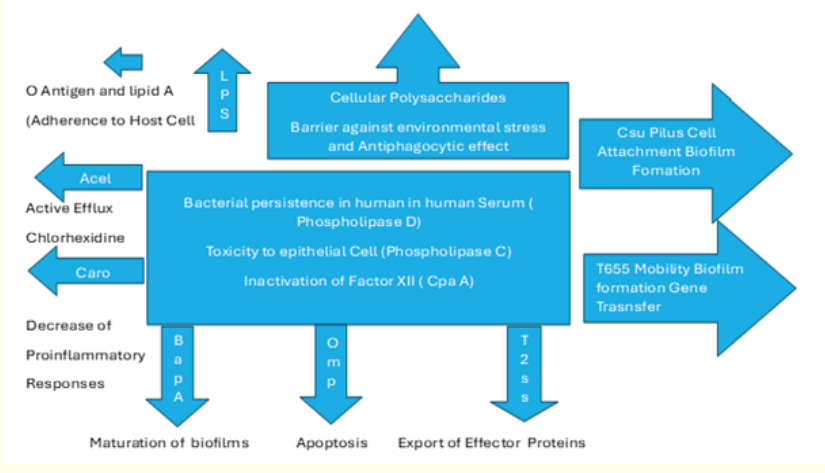

Figure 2: Virulence factors of *A. baumannii*.

Figure 2 introduces several new terms, pathways, and mechanisms that may not have been fully discussed in the main text. *A. baumannii* employs a variety of virulence factors that contribute to its persistence, immune evasion, and antimicrobial resistance. Lipopolysaccharides (LPS) act as a barrier against environmental stress and have an antiphagocytic effect, making it harder for the immune system to clear the infection. Csu pili facilitate bacterial adhesion and biofilm formation, a crucial factor in colonization and survival on medical devices. Type VI Secretion System (T6SS) allows the bacterium to inject toxic effector proteins into host cells or competing bacteria, aiding in survival and infection. Additionally, Type II Secretion System (T2SS) exports various enzymes that degrade host tissues, further contributing to virulence.

Moreover, several enzymatic and structural factors enhance *A. baumannii*'s pathogenicity. Phospholipase D and C promote bacterial persistence by disrupting host cell membranes and causing cytotoxicity, while CpaA inactivates Factor XII, interfering with host immune responses. Outer membrane proteins (Omp) contribute to apoptosis, facilitating bacterial dissemination. Biofilm-associated proteins like BapA enhance biofilm maturation, ensuring long-term colonization and resistance to treatment. Additionally, efflux pumps (Acel and Caro) actively expel antibiotics, leading to multidrug resistance. These mechanisms collectively make *A. baumannii* a formidable nosocomial pathogen, particularly in immunocompromised patients and those with prolonged hospital stays.

Antimicrobial resistance

A. baumannii is gaining popularity due to a growth in antimicrobial resistance and the emergence of strains that are resistant to nearly all existing medicines [26]. This organism is naturally resistant to many antibiotics, including aminopenicillins, third-generation cephalosporins (Ceftazidime), chloramphenicol, Imipenem, Chloramphenicol, Ciprofloxacin, Doripenem, and Tobramycin. Its resistance mechanisms involve β-lactamase production, efflux

pumps, porin mutations, and aminoglycoside-modifying enzymes, making treatment options increasingly limited. The rapid evolution of MDR *A. baumannii* highlights the urgent need for novel therapeutic strategies and strict antibiotic stewardship to control its spread.

Chandra., *et al*. (2017) conducted a study on the isolation, characterization, and antibacterial susceptibility of *Acinetobacter* species obtained from a tertiary care hospital. The study found varying resistance levels across different antibiotics. Aminopenicillins showed the lowest resistance at 26.6%, while imipenem resistance was alarmingly high at 76.6%, indicating the widespread presence of carbapenemase enzymes. Similarly, ceftazidime resistance was recorded at 70%, suggesting the role of extended-spectrum β-lactamases. Other antibiotics, including chloramphenicol (63.3%), ciprofloxacin (60%), doripenem (60%), and tobramycin (66.6%), also exhibited high resistance rates. These findings highlight the increasing challenge of multidrug-resistant *Acinetobacter baumannii* infections and emphasize the urgent need for alternative treatment strategies and effective antibiotic stewardship programs [27].

It also has a remarkable ability to develop resistance mechanisms to broad-spectrum --lactams, aminoglycosides, fluoroquinolones, and tetracyclines. Numerous investigations have found an increase in the number of *A. baumannii strains* that are resistant to these drugs. MDR isolates from geographically different places have also been shown to be clonally related, whereas susceptible strains are genotypically heterogeneous, implying that the problem of resistance may be associated with a limited number of successful *A. baumannii* lineages. Despite the difficulties associated with assessing resistance trends, *A. baumannii* has the potential to develop resistance to practically all existing medicines. Resistance to carbapenems, which were introduced in 1985 and have been the most important drugs for the treatment of MDR *A. baumannii* infections for many years, is of special concern. Even though clinical *A. baumannii* were shown to be invariably susceptible to these drugs in early studies [28] hospital outbreaks caused by carbapenem-resistant strains had already been reported by the early 1990s [29] indicating that *A. baumannii* can cause infections that are completely resistant to the currently available antimicrobial arsenal.

Resistance mechanisms

A. baumannii's resistance to antimicrobial agents is mediated by all the primary resistance mechanisms known to occur in bacteria, including target site alteration, enzyme inactivation, active efflux, and decreased drug influx. Beta-lactamases are the most diverse group of enzymes linked with resistance, with more than 50 distinct enzymes or their allelic variants found in A. *baumannii so* far. Mechanism of multidrug resistance in A. *baumannii NCCP* 16007 (Figure 3).

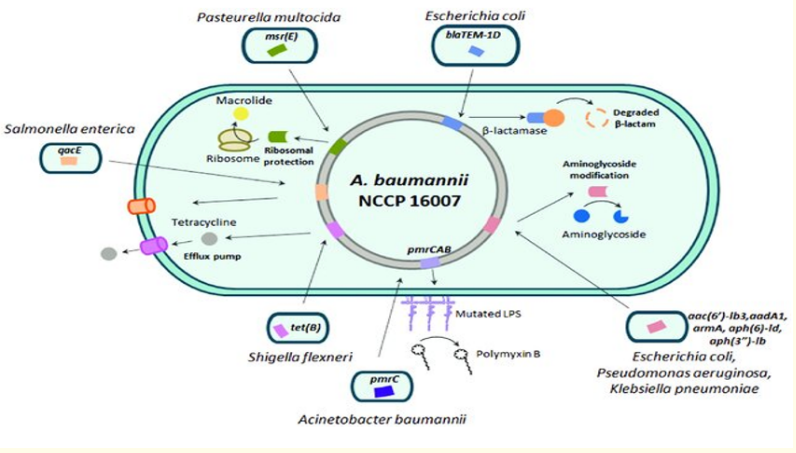

Figure 3: Diagram of multidrug resistance mechanisms in *A. baumannii* NCCP 16007. The β-lactamase (blaTEM-1D) potentially transferred from *E. coli* decomposes the β-lactam ring through hydrolysis. Acquired genetic determinants including aadA1 and aph (6)-ld express aminoglycoside transferases and modify gentamicin, kanamycin, and spectinomycin, leading to cell growth arrest. The Msr(E) transferred from *P. multocida* binds to the exit site of the ribosome and protects the ribosome from macrolides. An efflux pump (Tet(B)) acquired from *S. flexneri* actively eliminates tetracycline and chlortetracycline from the cell. Two additional copies of pmrC-encoded PetN transferase modulate the charge of lipid A and inhibit the binding of PMB to the OM [30].

The following are the mechanisms of antibiotic resistance:

Reduced Permeability of the outer membrane: Beta-lactamases can greatly increase antibiotic resistance when they combine with outer membrane proteins (OMPs). The principal non-specific porin in *A. baumannii* is the low permeability outer membrane protein A (OmpA, 40 kDa) [31] which serves primarily structural functions. It is thought that OmpA aids in the transfer of antibiotics from the periplasmatic region. Iyer., *et al*. on the other hand, revealed that OmpA specifically allows the absorption of small compounds such as sulbactam, imipenem, and ETX2514 [32]. Finally, Zhong., *et al*. recently demonstrated that the OmpA C-terminal domain is also responsible for anchoring beta-lactamases in the periplasmatic region, which may explain why OmpA deletion increases susceptibility [33].

Efflux pumps

Increased expression of efflux pumps synergistically contributes to antibiotic resistance with beta-lactamases [34]. Overexpression of the Ade ABC efflux pump is linked to carbapenem and cephalosporin resistance in *A. baumannii* [35,36]. The Ade ABC is a three-component efflux pump of the resistance-nodulation-division type (RND). AdeB, a membrane fusion protein, and AdeC, an outer membrane protein, both expel antibiotics from the cell [37]. AdeB substrates can be various; they can range from hydrophilic to hydrophobic and can be either positively charged or neutral [38]. The AdeRS two-component system regulates how this efflux pump functions.

Penicillin-binding proteins: Penicillin-binding proteins (PBPs) are enzymes that catalyze peptidoglycan polymerization and are responsible for peptidoglycan insertion into the cell wall [39]. PBPs bind to beta-lactams because they mimic their substrate. PBP inhibition by beta-lactams results in an imbalance in cell wall metabolism and, as a result, cell death [40]. This resistance mechanism appears to have little function, yet it cannot be overlooked. Although hot spot mutations in PBP genes were found, the accompanying variations in amino acid sequences were not directly related to beta-lactam resistance [41].

Infection control

Given the wide range of resistance associated with *Acinetobacter*, the function of avoiding the pathogen's spread to additional patients is critical. According to the Centers for Disease Control and Prevention (CDC) infection control recommendations, hospitals with high rates of multidrug-resistant *Acinetobacter* should implement more aggressive infection control measures to control and prevent further nosocomial transmission [42]. Although difficult, strong infection control techniques can control *Acinetobacter* infection outbreaks. Increased staff education, single-use goods for specific patients, hand cleanliness, cohorting, and isolation are all more likely to be effective measures. Antibiotic control programs appear to be effective in modifying the development of antibiotic resistance under restriction [43]. Controlling the use of ciprofloxacin and ceftazidime, for example, has been linked to a rise in *Acinetobacter*-associated imipenem and amikacin resistance [43]. Antibiotic control strategies can also change (select for other) microorganisms that cause illnesses in hospitals. Because antibiograms cannot always predict the clonality of an epidemic strain, *Acinetobacter* isolates should be molecularly typed. *A. baumannii* has been known to propagate clonally (from one clone to another) in several hospitals in Europe and Asia. This strain was limited to colistin and tigecycline resistance [44].

Future problem

The control of multidrug resistance and its spread in *A. baumannii* is a difficult task. While multiple drug resistance in this organism is developing and carbapenem resistance is rapidly expanding across the continent, there is a steep decline in the discovery of novel antimicrobial medicines that can manage MDR *A. baumannii*. There is no new medicine in the pipeline, and none of the FDA-approved antimicrobial agents evaluated had a significant effect on MDR *A. baumannii* control. Existing antibiotics have also failed to limit resistance development and effectively eliminate MDR forms. A logical synergistic approach to several combination medicines, while effective, requires greater in-depth understanding and rigorous trials to control likely outbreaks. The development of pan-drug resistance variations must be avoided, and efforts must be made to find new anti-*Acinetobacter* drugs.

Conclusions

Microbiological monitoring plays a crucial role in tracking bacterial trends and antibiotic resistance patterns in hospitals. It helps in identifying emerging resistance mechanisms, shaping antimicrobial stewardship policies, and contributing epidemiological data

for infection control strategies. This review highlights that longer hospital stays, ICU admissions, total parenteral nutrition, invasive procedures such as endotracheal intubation and nasogastric tube insertion, and prior antibiotic use are significant risk factors for *Acinetobacter* infections.

MDR *Acinetobacter* species, particularly in hospital ICUs, present a serious global public health challenge, leading to high mortality rates. The geographical variability in resistance patterns underscores the importance of local surveillance in guiding appropriate treatment strategies. With limited treatment options available for MDR organisms, further pharmacokinetic and pharmacodynamic studies are essential to optimize combination therapies until novel, more effective drugs are introduced into clinical practice. While some *Acinetobacter* environmental isolates remain susceptible to commonly used antibiotics and rarely cause outbreaks, infection control efforts must focus on highly resistant strains, especially those belonging to the *A. baumannii* complex. These strains are often responsible for hospital outbreaks and exhibit unique propagation patterns. Strengthening infection control measures, enhancing antimicrobial stewardship, and fostering research on alternative therapeutic strategies will be key to combating the growing threat posed by MDR *Acinetobacter* infections.

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