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Acinetobacter baumannii, a global health-threatening bacterium: a short review

Abstract

Antibiotic resistance is a worldwide concern that requires quick attention. The overuse and abuse of antibiotics have resulted in the emergence of multidrug-resistant bacteria and led to a global health crisis and economic losses. *Acinetobacter baumannii* is a bacterial pathogen that is commonly linked with hospital-acquired illnesses, such as pneumonia, meningitis, bacteremia, urinary tract, and skin infection. The recent rise in incidence, which has been linked to a substantial rise in the patients infected with the multidrug-resistant (MDR) strains of *A. baumannii*, has boosted the prominence of this opportunistic pathogen. This short review discusses this elusive bacterium and the factors that determine the occurrence of multidrug-resistant *A. baumannii* infections. Epidemiology and current treatments, as well as infection control strategies, are also discussed.

Keywords: antibiotics, multi-drug resistance, *Acinetobacter baumannii*, infection, pathogens

Volume 9 Issue 6 - 2021

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Received: November 05, 2021 | **Published:** November 22, 2021

Introduction

One of humanity's greatest triumphs in the twentieth century was the discovery of antibiotics. The success of the use of antibiotics led to the development of medicine significantly. Unfortunately, any treatment agent's success is constrained by the possibility of resistance developing. Recently, antibiotic resistance has spread across the globe, posing a severe danger to the therapeutic effectiveness of currently available antibiotics and their prescribed regimens.[1] The worldwide impact of this dilemma is already significant and is anticipated to grow, especially among the poorest countries. The overuse and misuse of antibiotics in medicine and agriculture, including unregulated over-the-counter sales, are the main drivers, while poor infection prevention and control in health care facilities, as well as suboptimal hygiene and sanitation in communities, are all exacerbated by poor infrastructure and weak governance of infection control,[2] where a small but growing number of isolates, mostly Gram-negative non fermenters of the genera Acinetobacter and Pseudomonas, are resistant to all 'good' antibiotics, and where a growing number of Enterobacteriaceae are resistant to all except carbapenems, the need for new agents is most pressing. While there is greater availability of anti-staphylococcal drugs, the frequency of methicillin-resistant *Staphylococcus aureus* (MRSA) infections remains exceedingly high in many regions.[3] A recent study conducted by the World Health Organization's (WHO) Global antimicrobial Resistance Surveillance program showed worldwide significant levels of multi-drug resistance in *Acinetobacter spp.* As well as other pathogens namely, *Escherichia coli*, *Klebsiella pneumoniae*, *Salmonella spp.*, *Staphylococcus aureus*, and *Streptococcus pneumoniae.*[4] Therefore, due to the growing global interest in Acinetobacter infections this short review aimed to highlight the global growing phenomenon of multi-drug resistant *Acinetobacter baumannii*.

General characteristics

The first to isolate Acinetobacter was Beijerinck, a Dutch scientist who isolated it from the soil in 1911, using a minimum medium fortified with calcium-acetate. *Micrococcus calcoaceticus* was named for the first time.[5] The species *Acinetobacter baumannii* was not formally named until 1986 after the genus Acinetobacter underwent many taxonomic revisions.[6] *Acinetobacter baumannii* (*A. baumannii*) is a Gram-negative, aerobic, pleomorphic, non-motile and the cells of *Acinetobacter* spp. have different shapes depending on the growth phase, from coccoid to coccobacillary.[7] Generally, *A. baumannii* is an opportunistic infection with a high prevalence among immunocompromised people, especially those who have had a protracted hospital stay (greater than three months). It has been demonstrated to colonize the skin as well as be isolated in large quantities from sick people's respiratory and oropharyngeal secretions.[8] In terms of the MDR phenotype, *A. baumannii* has a varied complement of mobile genetic elements encoding drug-inactivating enzymes and insertion sequences, develops a flexible genome, and hence develops resistance to a wide range of antibiotics. Moreover, *A. baumannii* isolates have also an accessory genome in addition to several genes encoding resistance determinants.[9]

Methods for detection of resistance

Fast detection of resistant strains of *A. baumannii* is of crucial importance to the prevention of the prevalence of this pathogen. Growth media used for detection are diverse. *A. baumannii* may be isolated using a variety of selective and differential media. Bile salts and bromocresol purple are two examples of such a media.[10] Some studies suggest the use of new effective selective media, such as CHROMagar Acinetobacter®.[11] Detection protocols, to differentiate between Acinetobacter species have been effectively identified using phenotypic systems and commercial phenotypic techniques (the API 20 NE system and the VITEK 2 system [Biomerieux]) or DNA-based testing such as PCR (16S rRNA gene amplification). Although, these approaches are time-consuming and take days.[12] Therefore, some rapid-detection assays have been innovated. Among them, The MALDI-TOF-based assay and the MALDIxin test, which allows accurate and rapid detection of colistin-resistant *A. baumannii* pathogen in less than 15 minutes.[13] Recently, a quick diagnostic test based on MALDI-TOF MS detection of modified lipid A (the MALDIxin test) was developed, and it showed great promise as a reliable method for determining colistin-resistance in *Acinetobacter baumannii.*[14] Besides, for quick detection of *A. baumannii*, a set of multiple cross displacement amplification (MCDA) primers was employed to recognize *pgaD* gene and it was found that the detection ability was superior to regular

techniques and conventional PCR, and that it might be a promising tool for the quick detection of *A. baumannii* in hospitals.[15] However, the majority of the above-mentioned techniques are expensive and there is a need for cheap and inexpensive protocols to use in poor and developing countries.

Epidemiology of *A. baumannii*

To date, there are around 50 Acinetobacter species, the vast majority of which are nonpathogenic; nevertheless, only a few species are opportunistic human infections. The most clinically important species of the Acinetobacter genus are *Acinetobacter calcoaceticus* and *Acinetobacter baumannii*.[16] Natural reservoirs of these pathogens outside hospitals are not yet known.[17] *A. baumannii* causes a variety of diseases in both hospitals (nosocomial) and the general public, including skin and soft tissue infections, bacteremia, meningitis, pneumonia and urinary tract infections (Figure 1).[18] Regretfully, about 2% of all health-care-associated infections caused in the United States and Europe are from *A. baumannii*, and it is expected to be much higher in Asia, where around 45% of *A. baumannii* isolates are classified as multidrug-resistant (MDR) pathogen and this percentage is anticipated to be as high as 70% in the Middle East and Latin America.[19-21] Due to various outbreaks occurred by MDR *A. baumannii* infections, the WHO has declared that *A. baumannii* is one of the most serious resistant pathogens that successfully evade the action of most available antibiotics.[22] Resistance mechanisms in *A. baumannii* include beta-lactamases, efflux pumps, aminoglycoside-modifying enzymes, target site alterations, and permeability deficiencies. Internationally, the proportion of *Acinetobacter* spp. causing pneumonia in the Intensive care units (ICU) in the United States grew from 1.4 % in 1975 to 6.9% in 2003.[23] In China, the imipenem-resistant *A. baumannii* of has spread dramatically in Western China in 2011.[24] In Latin America, an outbreak of an MDR *A. baumannii* strain has been documented initially in 2011 in the ICU that lasted until 2015.[25] While *A. baumannii* outbreaks have been documented in various parts of the world, there are limited data from Africa. In Nairobi, Kenya, an outbreak of MDR *A. baumannii* strains was reported between September 2010 and September 2011.[26] Then, came the Covid-19 pandemic and the health authorities have taken up the fight against it and this led to a decrease in surveillance studies on the prevalence of *A. baumannii* infections worldwide. However, in a Covid-19 devoted hospital, there was an outbreak of carbapenem-resistant *A. baumannii*. The hands or equipment of healthcare personnel were suspected as the means of transmission.[27] This outbreak shows that during the COVID-19 pandemic, procedures to limit the spread of MDR *A. baumannii* must not be overlooked.

Drug-resistance mechanisms

Despite the increasing prevalence of *A. baumannii* particularly in hospitals, the rapid development of antibiotic resistance and especially the mechanisms of beta-lactamase resistance in *A. baumannii* is still unknown.[28] In *A. baumannii*, there are three main mechanisms of resistance exist: enzymes that inactivate antibiotics, limited access into the bacteria's target site, and gene mutations.[29] On mobile gene cassettes placed in the variable region of integrons, both bla_{VIM} and *blaIMP* gene cassettes were identified.[30] Resistance to carbapenems in *A. baumannii* linked to the development of OXA-type or NDM-type enzymes and the existence of Omp 33–36 kDa, as well as high levels of colistin resistance linked to the loss of LPS, may all play a role in *A. baumannii*'s virulence profile.[31] Moreover, Beta-lactamase genes, efflux pump genes, and mutations in the outer membrane protein-producing gene may all play a role in imipenem resistance in *A. baumannii*. ST11 genotype was shared by the majority of *A. baumannii* genotypes, which might be attributed to horizontal patient transfers from hospitals.[32] Therefore, understanding the genetic mechanisms behind the acquisition and spread of these multi-drug resistant *A. baumannii* strains could lead to the development of more effective prevention and control strategies, allowing for more effective treatment and reducing resistance development.[33]

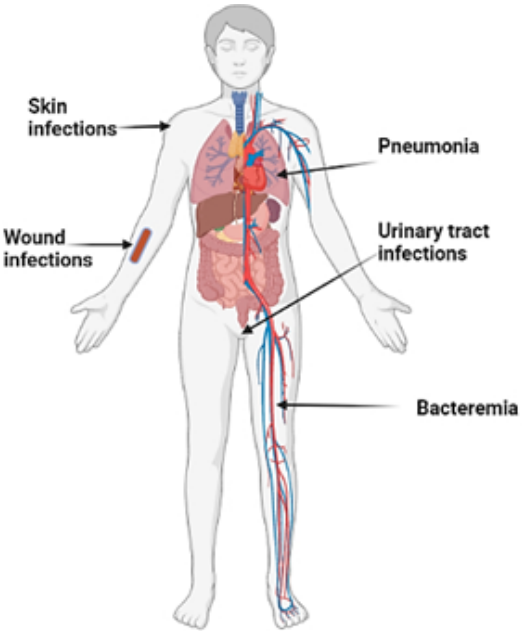

Figure 1 Major diseases caused by *A. baumannii* in both hospitals and the general public.

Current treatment

Unfortunately, the emergence of multiple resistance mechanisms in *A. baumannii* has steadily reduced the number of antibiotic classes accessible in clinical practice to treat *A. baumannii* infections.[34] Formerly, before the escalation of *A. baumannii* resistance, this bacterium was highly susceptible to several antibiotics, including ceftazidime, cefepime, imipenem, meropenem, and beta-lactam/beta-lactamase inhibitor such as sulbactam or carbapenem.[35] Figure 2 shows some treatment options recommended against *A. baumannii* infections. Polymyxins, such as colistin was found to be effective and usually have *in vitro* activity against Acinetobacter, although resistance to polymyxins has been observed. However, several studies have been conducted to find a new alternative to carbapenem or colistin. Engineered endolysins (artilysins) are particularly intriguing among them, despite their obvious flaws. To find new antibiotic classes, innovative, rationally designed techniques and screening-based methodologies are necessary.[36]

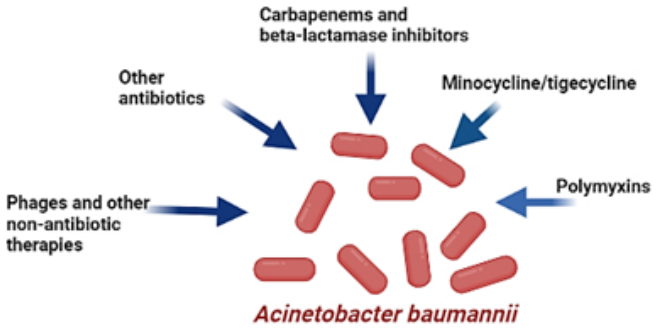

Figure 2 Treatment options against *A. baumannii* infections.

Citation: Abdallah EM, Abdalla RM. *Acinetobacter baumannii*, a global health-threatening bacterium: a short review. *J Mircobiol Exp.* 2021;9(6):181–184. DOI: 10.15406/jmen.2021.09.00341

Infection control

For infection control of *A. baumannii*, it is recommended that the introduction of the infections surveillance system is a critical step in identifying and controlling this disease in a timely manner and for monitoring *A. baumannii* and differentiating phenotypically similar strains, whole-genome sequencing is a valuable tool.[37] Successful attempts to control this pathogen has been reported, it was published that within one year in South Korea, MDR *A. baumannii* in ICUs was under control by implementing stringent antimicrobial stewardship and comprehensive infection control measures at the same time. After the treatments, the incidence density rate of hospital-onset MDR *A. baumannii* reduced from 22.82 cases per 1,000 patients/days to 2.68 cases per 1,000 patient/days.[38] In Spain, between 2012 and 2016, a multimodal intervention program based on environmental decontamination, hand hygiene, antimicrobial stewardship, contact precautions, active surveillance, weekly reports, and regular meetings was effective in eradicating the endemic MDR-*A. baumannii*. Antibiotic consumption in the ICU was significantly reduced, and the incidence density of MDR-*A. baumannii* in the ICU gradually dwindled.[39] Suggested successful control and eradication of MDR *A. baumannii* is based on using a combination of techniques, including hand hygiene and contact precautions, environmental cleaning, antimicrobial therapy stewardship, human microbiome restoration and bacteriophage therapy.[26] Finally, effective control of *A. baumannii* infections can be achieved if we continue to make every effort to keep the current efficacy of antibiotics used and develop new treatments.

Conclusion

In recent years, antibiotic resistance has grown among strains linked to severe nosocomial infections. Due to its numerous adaptability strategies, *A. baumannii* is one of the most troublesome opportunistic agents, allowing it to live in harsh settings Moreover, antibiotics administered incorrectly have resulted in an uncontrolled spread of resistance among *A. baumannii* isolates. Acinetobacter infections have a diverse and complex epidemiology that includes hospital-acquired infections, community-acquired infections, and infections that arise during conflicts and natural catastrophes. Some strains may withstand months of desiccation in the environment. More scientific efforts are needed to control challenges surrounding *A. baumannii* infections, as well as to look into treatment options and develop or innovate new antibacterial drugs with different mode of actions to control the dramatic spread of this elusive pathogen. Modern biotechnology, such as artificial intelligence, automated machine learning, and nanoparticle phytotherapy, should also be considered.

Acknowledgments

None.

Conflicts of interest

Authors declare that there is no conflict of interest.

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Citation: Abdallah EM, Abdalla RM. *Acinetobacter baumannii*, a global health-threatening bacterium: a short review. *J Mircobiol Exp.* 2021;9(6):181–184. DOI: 10.15406/jmen.2021.09.00341