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REVIEW

Acinetobacter baumannii Biofilm Formation and Its Role in Disease Pathogenesis: A Review

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Abstract: *Acinetobacter* species, particularly *Acinetobacter baumannii*, is the first pathogen on the critical priority list of pathogens for novel antibiotics to become a "red-alert" human pathogen. *Acinetobacter baumannii* is an emerging global antibiotic-resistant gram-negative bacteria that most typically causes biofilm-associated infections such as ventilator-associated pneumonia and catheter-related infection, both of which are resistant to antibiotic therapy. *A. baumannii's* capacity to develop antibiotic resistance mechanisms allows the organism to thrive in hospital settings, facilitating the global spread of multidrug-resistant strains. Although *Acinetobacter* infections are quickly expanding throughout hospital environments around the world, the highest concentration of infections occurs in intensive care units (ICUs). Biofilms are populations of bacteria on biotic or abiotic surfaces that are encased in the extracellular matrix and play a crucial role in pathogenesis, making treatment options more difficult. Even though a variety of biological and environmental elements are involved in the production of *A. baumannii* biofilms, glucose is the most important component. Biofilm-mediated *A. baumannii* infections are the most common type of *A. baumannii* infection associated with medical equipment, and they are extremely difficult to treat. As a result, health care workers (HCWs) should focus on infection prevention and safety actions to avoid *A. baumannii* biofilm-related infections caused by medical devices, and they should be very selective when using treatments in combination with anti-biofilms. Therefore, this review discusses biofilm formation in *A. baumannii*, its role in disease pathogenesis, and its antimicrobial resistance mechanism.

Keywords: biofilm, *Acinetobacter*, *A. baumannii*, pathogenesis, antibiotics resistance

Introduction

Acinetobacter baumannii is the member of the genus *Acinetobacter* and the family Moraxellaceae of the Eubacteria class *Proteobacteria*.[1] *Acinetobacter baumannii* is non-motile, non-fastidious, non-fermentative, catalase-positive, oxidative-negative Gram-negative coccobacilli.[2] *Acinetobacter baumannii* is an ESKAPE pathogen (*Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa,* and *Enterobacter* species)[3] associated with hospital-acquired antibiotic-resistant infections. Of all hospital-acquired infections caused by Gram-negative; *A. baumannii* is responsible for 2–10% of infections.[4] With invasive operations and frequent antibiotic use as well as immunocompromised hosts, *A. baumannii* has emerged as a major nosocomial pathogen. The pathogen's versatile genetic machinery allows it to rapidly generate resistance factors, as well as a remarkable ability to tolerate harsh environmental circumstances, making it endemic in hospital settings.[2]

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A. baumannii is a low-grade pathogen that can be found in a variety of habitats, including soil, water, and food, and is frequently isolated from medical devices.[5] As a result of colonization and living on much medical equipment, it causes severe infections in immune-compromised people.[6] According to evidence meningitis, wound, pneumonia (hospital and community-acquired), bacteremia, burn, endocarditis, urinary tract infections (UTI) as well as skin and soft tissue infections are the most prevalent *Acinetobacter*-associated nosocomial illnesses.[5,7] Community-acquired pneumonia is more severe than nosocomial pneumonia; it is usually fulminant, and fatality rates can reach 60%.[8] This human pathogen is also responsible for ventilator-associated pneumonia and bloodstream infections, both of which have high death rates of up to 35%.[9] *A. baumannii* infections are more common in men and are linked to advanced age, behavioral factors like alcoholism and excessive smoking as well as chronic disease comorbidities like diabetes, renal disease, and chronic obstructive pulmonary disease (COPD).[8]

The most important virulence factors identified by genomic and phenotypic investigations are outer membrane porins, phospholipases, capsular polysaccharides, lipopolysaccharides (LPS), proteases, iron-chelating systems, and protein secretion systems.[2,7,10] *A. baumannii* infections are often associated with multidrug resistance; Carbapenem and Colistin resistance has been observed. Surprisingly, antibiotic-resistant bacteria have lately surfaced.[9] Modifications of target sites, permeability deficiencies, multidrug efflux pumps, and enzymatic drug degradation, for example, β-lactamases and aminoglycoside-modifying enzymes, are all linked to *A. baumannii* resistance mechanisms.[2,11,12] The fast spread of multidrug resistance in *A. baumannii* is currently posing a severe threat to public health. The ability of *A. baumannii* to colonize and produce biofilm on biotic and abiotic surfaces contributes to chronic and persistent infections, antibiotic resistance, as well as survival in hospital environments and transfer.[13] Hence, the biofilm matrix that surrounds bacteria permits germs to withstand extreme circumstances and resist treatments of antibiotics. As a result, medications now available for treating *A. baumannii* biofilm-associated infections are ineffective.[14]

Biofilms are communities of microorganisms which are adhering to biotic and/or abiotic surface encased by extracellular polymeric substance (EPS) matrix and are physiologically different from planktonic (free floating) bacteria.[15] Biofilm-encased cells have limited metabolic activity and are shielded by the extracellularly produced matrix, making them more resistant to antibiotics and innate immune components of the host.[16] *A. baumannii* frequently causes biofilm-related infections, particularly ventilator-associated pneumonia and catheter-related infection, which can be exceedingly resistant to antibiotic therapy, offering a severe challenge to the clinical management of *A. baumannii*-related biofilm infections.[5,17] *A. baumannii* biofilms have become one of the most serious global issues due to the rapid spread of medical device-associated infections and antibiotic resistance.[9,13] Despite these problems causes, the data about *A. baumannii* biofilms in Africa are still limited. Hence, understanding the magnitude of *A. baumannii* biofilm formation; its role in pathogenesis and antimicrobial resistance is important for limiting medical device-associated infections. Therefore, the objective of this review is to discuss *A. baumannii* biofilm formation and its role in disease pathogenesis.

Discussion

Magnitude of *Acinetobacter baumannii* Biofilm Formation

The relationship between biofilm development and multidrug resistance was investigated in a study. There were 156 confirmed *A. baumannii* isolates, 10.26% of which produced biofilms on Congo red agar. However, in test tube, conventional microtiter plate, and modified microtiter plate assays, the percentage of bacterial isolates with positive biofilm was 48.72%, 66.66%, and 73.72%, respectively.[18] The effectiveness of isolated bacteriophage against biofilm-embedded Colistin-Resistant *Acinetobacter baumannii* isolates was investigated in another investigation. It was discovered that 20% of isolates formed a mild biofilm, 40% created an intermediate biofilm, and 40% produced a strong biofilm.[19] Another similar study also revealed that 80–98% of strains were biofilm producers.[20] *Acinetobacter baumannii* isolates from 92 unrelated strains were tested for biofilm production using a microtiter plate assay in a multicenter cohort study, and 63% of the isolates produced biofilm.[21]

Surprisingly, in a study done on 100 *A. baumannii* clinical isolates from immunocompromised hospitalized patients in intensive care unit (ICU); all isolates had the ability to form a biofilm, and 58% of isolates showing high biofilm-forming ability. Molecular typing of biofilm-related genes based on REP-PCR showed that the

distribution of csuE, pgaB, epsA and ptk, bfmS, and ompA genes were 100%, 98%, 95%, 92%, and 81% respectively. Nearly total (98%) of isolates simultaneously carried more than 4 biofilm-related genes.[22] In another similar study, seventy-five biofilm-producing multidrug-resistant Acinetobacter species were identified in a study by the microtiter plate method. Of these 75 isolates 12 (16%), 9 (12%), 30 (40%), and 24 (32%) respectively were weak biofilm producers, moderate biofilm producers, strong biofilm producers, and non-biofilm producers. This study found a clear relationship between *Acinetobacter* isolates' propensity to form biofilm and the development of biofilm and multiple antibiotic resistance.[23]

Moreover, among 125 clinical samples from skin infections in patients of Baghdad, 18 (14.4%) were identified as *A. baumannii*. Different findings were observed across the different techniques used. On the Tissue Culture Plate method 1, 15, and 2 isolates respectively were identified as weak, moderate, and strong biofilm producers among 18 isolates. Biofilm production was not detected in any of these isolates in Congo red agar but on Tube Method 7, 5 and 6 isolates respectively were weak, moderate, and strong biofilm producers.[24] Another study also revealed that 34 isolates (62%) were biofilm producers, with only 11 having the blaPER-1 gene, two of which were significant biofilm producers and the rest were weakly adherent isolates.[25]

The molecular analysis and expression of the bap Gene in biofilm-forming *A. baumannii* were investigated. The genes ompA and csuE were found in all of the isolates, while bap and blaPER-1 were found in 43 (66%) and 42 (64%) of the isolates with strong and moderate biofilm activity (p 0.05), respectively. Furthermore, strong, moderate, weak, and no biofilm activities were found in 23 (35.4%), 18 (27.7%), 13 (20%), and 11 (16.9%) of the isolates, respectively. In the presence of low iron concentrations, overexpression of bap influences biofilm development, according to the findings of this study.[26]

Clinical Significances

Acinetobacter baumannii is a common bacterium that causes nosocomial or hospital-acquired illnesses. Due to the rise of multidrug-resistant strains and high morbidity and mortality, *A. baumannii* has been added to the World Health Organization's (WHO) drug-resistant bacteria and antimicrobial resistance research priority list.[27] *A. baumannii* is causing a wide range of infections related to medical devices, eg, vascular catheters, cerebrospinal fluid shunts, or Foley catheters[21] as well as a postoperative infection like urinary tract infections (UTI) in hospitalized patients.[4] Moreover, *A. baumannii* causes respiratory tract infections (RTI), meningitis, UTI, wound infections, endocarditis, and bacteremia all of which involve the formation of biofilm.[4,28] Antibiotic resistance in biofilms is thought to be 1000 times higher than in planktonic organisms. Hence, the high prevalence of *A. baumannii* infections is biofilm mediated which poses a global health concern.[29]

Stages of Biofilm Development

Biofilms are bacteria that have accumulated in an extracellular polymeric material matrix made up of polysaccharides, lipids, proteins, and nucleic acids. Biofilm development is a complicated process in which microorganism cells transform their growth mode from planktonic to sessile mode, and it is influenced by a variety of environmental conditions such as surface porosity, fluids flow, and availability of nutrients.[30]

The common steps in the development of biofilm are initial contact/attachment to the biotic and/or abiotic surface, micro-colony formation, maturation and formation of the architecture of the biofilm, and lastly detachment/dispersion of the biofilm, which are all controlled by quorum sensing (QS).[30] Biofilm formation begins with the planktonic cell adhering to an abiotic or abiotic surface. A reversible connection follows adhesion cells. Microorganisms adhere more quickly to hydrophobic, nonpolar surfaces like Teflon and other plastics than to hydrophilic surfaces like stainless steel, implying that some sort of hydrophobic interaction occurs, allowing the cells to overcome the repulsive forces.[31] After the attachment is stable; the EPS matrix fixes the initial adhesion then multiplication of microbial cells starts and the basic structural unit of the biofilm (ie, micro-colony) formation has occurred. The closeness of cells within the micro-colony or across micro-colonies plays a significant role in the interchange of the substrate, as well as distribution of major metabolic products and excretion of metabolic end-products.[32]

Biofilm maturation occurs when the irreversibly attached cells develop a more organized and complex structure and shape that is dependent on the source of nutrients. Microbial cells communicate with one another via a cell-to-cell signaling mechanism known as quorum sensing to control their population density using signaling molecules known as auto-inducers.[33] Quorum sensing also aids in the transmission of favorable mutations in the

biofilm colony, improves access to resources, and contributes to antibiotic tolerance. In this stage, the matrix also produces interstitial spaces (channels) that are filled with water and act as a circulatory system.[34] Finally, the sessile form converts into motile form; ie, dispersion of biofilm occurred. Detachment/dispersion of biofilm is initiated by oxygen or nutrient starvation and dissolution of EPS by saccharolytic enzymes, allowing the bacteria surface to be released into a new location for colonization.[32]

Biofilm in Disease Pathogenesis

Infections associated with biofilms are first restricted to a specific location before detaching over a while. The detachable biofilms may then cause infections in the bloodstream or urinary system, as well as restriction of blood flow.[35] On the contrary, sessile cells or biofilms are resistant to harsh environmental conditions, antimicrobial agents as well as host immune systems than planktonic bacteria. As a result, removing biofilms from living hosts is quite challenging.[36]

The ability of *A. baumannii* to survive in harsh environmental condition, dormancy of bacterial cells deep in the biofilm, multiple antibiotic resistance mechanisms, prolonging survival on inanimate objects and resistant to environmental stress plays a role in its environmental survival, resulting in biofilms causing a wide range of subacute or chronic infections which are very challenging to eradicate.[37,38] *A. baumannii* has been designated as a "red-alert" human pathogen due to its ability to acquire resistance to all currently available antimicrobial agents.[39]

Even though *A. baumannii* infections are becoming increasingly important in clinical practice and are a global health concern, relatively little is known about the factors influencing its pathogenesis. Pieces of evidence elucidated that outer membrane protein A (OmpA), phospholipids, extracellular polysaccharides,[2,10,38–40] the K1 capsule, a siderophore-mediated iron-acquisition system, and phospholipases are virulence factors that have an important role in bacterial pathogenicity[2,10,38] (Table 1).

Furthermore, the formation ability of biofilm (due to fimbriae and pili) is a significant factor that aggravates the disease process of *A. baumannii* infections.[10,38,40] After initial attachment to abiotic surfaces, pili assembly and synthesis of the biofilm-associated protein (Bap) surface-adhesion protein play a significant role in the initiation and maturation of biofilm.[41] Biofilm increases *A. baumannii* adherence and long-term survival on both biotic and abiotic surfaces. Adhesion to abiotic surfaces such as medical equipment and environmental surfaces;[7,38,39] the adherence capacity of cells and the expression level of OMPs mRNAs are determinant virulence factors for *A. baumannii* pathogenesis.[40] Additionally, OmpA contributes to biofilm formation on biotic surfaces like epithelial cells and mediates bacterial adherence to lung epithelial cells by interacting with fibronectin on the surface of cells and may induce apoptosis in human epithelial cells.[40,42]

Factors Influencing Biofilm Formation

A. baumannii is at least three times higher biofilm former at the solid–liquid interface than the other *Acinetobacter* species. Clinical strains can form stronger biofilms than environmental strains, and biofilm development on medically important surfaces affects their ability to resist nutrition availability stress, desiccation, and antimicrobial therapy.[28] The formation of biofilms is a complicated process that is influenced by a variety of cell properties. Cell surface, hydrophobicity, surface charge, adhesion proteins, and extracellular polymeric compounds all have an impact on the production of *A. baumannii* biofilms.[28,62,63]

Furthermore, the formation of the biofilm process of *A. baumannii* on abiotic surfaces has a positive correlation with multidrug resistance and with virulence factors expression such as the OmpA, the extracellular polysaccharide poly-β-^{1,6}-N-acetyl glucosamine (PNAG), type I pili, Rec A, Bap, and the Omp CarO. On an animate surface, it needs chaperone-usher pili to produce biofilm.[62] *A. baumannii* has biofilm-related virulence genes and proteins, which aid in its capacity to cling to biotic and abiotic surfaces and form biofilms.[29]

Environmental changes in physical and chemical settings have an impact on phenotypic characteristics and the expression of key functions.[29] Several environmental elements influence biofilm growth in a highly regulated manner at each stage. Temperature, osmolarity, ferrous iron concentration, nutrients availability, quality of materials where biofilms are formed, light, and ambient acidic conditions are the most major environmental elements affecting biofilm formation.[64] Glucose is also the key determinant factor in *A. baumannii* biofilm formation. Moreover, *A. baumannii* biofilm formation has been influenced by surface hydrophobicity and oxygen content.[29]

Biofilm and Antimicrobial Resistance

A. baumannii is inherently antibiotic-resistant. Due to the increasing usage of antibiotics, multidrug-resistant (MDR) and extensively drug-resistant (XDR) bacteria have

Table 1 Summary of Known *Acinetobacter baumannii* Virulence Factors

Virulence Factors (Genes)	Possible Role in the Pathogenesis	References
1.Outer membrane protein A (OmpA)	Epithelial cell adhesion and invasion, biofilm development, serum resistance, surface motility, and induction of apoptosis in host cells or induces cytotoxicity	[40,42–45]
2.Biofilm-associated protein (Bap)	Biofilm formation and subsequent intercellular adhesion within the mature biofilm	[46]
3.Lipopolysaccharide(LPS)	Host immune response evasion, resistance to cationic antimicrobial peptides, triggering the host inflammatory response, reduces TLR4 signaling and desiccation survival	[47,48]
4.Penicillin-binding protein 7/8 (pbpG)	Biosynthesis of peptidoglycan, cellular stability, and growth in serum	[49]
5.Outer membrane vesicles (OMV)	Delivering virulence genes to host cells cytoplasm and transferring of genetic material across bacterial cells	[50,51]
6.Phospholipase D	Bacterial survival in vivo, serum resistance, and dissemination of bacteria	[52]
7.Acinetobactin or Siderophore mediated iron acquisition mechanism	Provides iron for the survival of the bacterium the host and induce cell death	[53,54]
8.Capsule	Mediates cationic antimicrobial peptide resistance, as well as serum resistance and in vivo survival	[10,55]
9.Phospholipase C	Exhibiting hemolytic action against human red blood cells and assisting in the uptake of iron	[56,57]
10.Poly-β-1-6-N-Acetylglucosamine (PNAG)	Formation of biofilm, cell-cell adherence as well as protection against innate host defenses	[39,58]
11.Two-component regulatory system, BfmRS	Csu pili chaperone–usher assembly system expression, biofilm formation, and cellular morphology	[59]
12.AbaI autoinducer synthase	Normal biofilm development	[60]
13.CsuA/BABCDE chaperone usher pili assembly system	Pilus assembly, biofilm formation on abiotic surfaces	[39,61]

evolved. As a result, the worldwide emergence of *A. baumannii* is becoming a critical problem.[28] The emergence of MDR strains is a major cause of the high mortality rate.[65] Even though the link between biofilm production and antibiotic resistance phenotypes is still debated.[28] Pieces of evidence revealed that biofilm formation and multidrug resistance have a positive correlation.[28,66] In comparison to imipenem and piperacillin, biofilm formers demonstrated increased resistance to ampicillin-sulbactam, amikacin, ciprofloxacin, and ceftazidime. Moreover, biofilm formation and multidrug-resistant have a statistical association.[66] Another study found that clinical isolates of *A. baumannii* have a high proclivity for biofilm formation and that biofilms are associated with multiple drug resistance. This study also showed that the resistance pattern of antibiotics was also found to be higher among biofilm producers than among non-biofilm producers.[25]

A similar study was conducted on *A. baumannii* strains isolated from hospital-acquired infection for the relationship between biofilm production and drug susceptibility. Paradoxically, ceftazidime-sensitive strains formed less biofilm than ceftazidime resistant as well as tobramycin and amikacin sensitive strains produced more biofilm than strains showing resistance to these antibiotics. On the other hand, strong biofilm producers from ICUs are often more susceptible to antibiotics which are related to the fact that bacteria protected in biofilm do not need resistance mechanisms responsible for resistance by planktonic cells.[20] Other studies showed that biofilm-forming isolates were less commonly resistant to imipenem and ciprofloxacin than non-biofilm-forming isolates.[21] Similarly, meropenem-resistant *A. baumannii* isolates had a lower ability to form biofilms than meropenem-susceptible isolates.[67]

Generally, *Acinetobacter* strains with multidrug resistance and biofilm production continue to pose a substantial hazard in the hospital setting, since they rapidly become resistant to routinely used routine medications, and their ability to produce biofilm is statistically significant with imipenem resistance.[68] Enzyme-mediated neutralizations, the existence of persistent (non-dividing) cells, and the biofilm phenotype are all antimicrobial resistance mechanisms.

Detection of Biofilm

Different phenotypic techniques such as Qualitative biofilm production assays (ie, tube method and tissue culture plate method) and Quantitative biofilm production assays (ie, Congo red agar method) are used to detect biofilm formation *A. baumannii*.[13,18,24] Additionally, Microscopic examination of the ability of *A. baumannii* strains to produce biofilms is seen using a scanning electron microscope (SEM), and detection of genes related to biofilm such as; ompA bap, blaPER-1and csuE genes are screened using Polymerase chain reaction (PCR).[13] The modified microtiter plate assay for detecting *A. baumannii* biofilm is a sensitive, accurate, repeatable, and reliable quantitative assay.[18,24]

Tube Method and Tissue Culture Plate Methods need staining to visualize the presence of biofilm on different days using crystal violet dye. However, Congo red agar does not need stain and it can detect by culturing from another culture and producing a distinct color, which may be used to identify it. The biofilm producers become black colonies with a dry crystalline consistency and the non-producers remain red or move.[18,24] Biofilm production is graded into strong, moderate, and non/weak. Strong and moderate results are interpreted as positive biofilm production, while non/weak results are interpreted as negative biofilm production.[24]

Therapeutics Options

Despite this, early detection of biofilm infection is challenging at the moment, and the majority of clinical biofilm infections are mature biofilms that are difficult to eliminate with antibiotics. Because nascent biofilm can be eliminated more easily than matured biofilm, early and strong antibiotic therapies are indicated for biofilm infections.[69]

Because of the persistent nature of biofilm-associated *A. baumannii* infections, therapy can be difficult. However, because biofilm formation increases antibiotic resistance, combination therapy may be beneficial in treating biofilm-related infections.[29] Therefore, the treatment of biofilm consists of a selection of antibiotics as sensitive and well penetrating.[70] Well-established interdisciplinary teamwork is required for the effective treatment of biofilm infections. As a result, contaminated foreign bodies removal, use of biofilm-active, sensitive, and well-penetrating antimicrobials, use of anti-quorum sensing or biofilm dispersal agents and systemic or topical antibiotic administration in high doses and combinations can be used for efficient treatment of biofilm-related infections.[70,71]

Prevention and Control

Biofilm infections induced by *A. baumannii* are notoriously difficult to treat. However, preventing these organisms from forming biofilms is critical. To inhibit biofilm growth, three basic strategies have been studied such as inhibition of the initial attachment of bacteria to biotic and/or abiotic surfaces, disruption of targets of biofilm during the maturation process, and signal interference approach or Quorum Quenching (QQ).[72] Inhibition of initial biofilm attachment is mediated by alteration of chemical and changing physical properties of biomaterials whereas removal of biofilms is done through matrix-degrading enzymes, surfactants, physical forces and amino acids, free fatty acids, and nitric oxide donors. Moreover, Biofilm inhibition by quorum quenching strategy is carried out through degradation of QS signals, antagonizing signaling molecules, inhibition of signal synthesis, signal transduction, and signal transport.[28,72]

Biofilms provided disinfection resistance at doses that wiped out planktonic populations. As a result, biofilm isolates of *A. baumannii* are more resistant to disinfectants than planktonic bacteria.[73] A positively charged bispyridinamine exhibiting antibacterial action against plaque-producing bacteria called Octenidine dihydrochloride (OH) is effective for the inactivation of *A. baumannii* biofilms on all three matrices, such as stainless steel, polystyrene, and urinary catheters, in the presence and absence of serum protein.[74] Additionally, cinnamaldehyde possesses high antibiofilm capabilities, implying that it could be used to treat biofilm-related clinical problems produced by *A. baumannii*.[75]

Both growth and biofilm formation is inhibited by prebiotic metabolites such as riboflavin, raffinose, citrate, inulin, trehalose, and sorbitol. As a result, prebiotics had significant anti-biofilm efficacy against the biofilm of *A. baumannii*. The ability of *A. baumannii* to produce

biofilms is reduced by 75%±6.5% in the presence of *Lactobacillus rhamnosus* with inulin.[76] Moreover, phage therapy such as phage ΦAB6 and its Tail Fiber (TF) protein prevents and degrades the biofilm of multidrug-resistant *A. baumannii* by 78% and 62% with their respective order.[77]

Conclusion & Recommendation

Acinetobacter baumannii is an ESKAPE pathogen placed under the first in the critical priority list of pathogens for novel antibiotics.[3] It is responsible for epidemics of *Acinetobacter*-associated nosocomial infections such as community and hospital-acquired pneumonia, central nervous system infection or meningitis, bacteremia, endocarditis, skin and soft tissue infections, wound, burn, and UTI. The biofilm formation ability of *A. baumannii* on the biotic and abiotic surface is the most essential feature contributing to chronic and persistent infections, antimicrobial resistance, and strong survival in the hospital environment. Hence, multi-drug resistance (MDR) of *A. baumannii* becomes a serious public health concern associated with modifications of target sites, multidrug efflux pumps, permeability defects, and enzymatic degradation of drugs named β-lactamases and aminoglycoside-modifying enzymes. Due to its capacity to develop resistance to all currently known antibiotics, *A. baumannii* has been designated as a "red-alert" human pathogen.

Biofilm formation is most common in *A. baumannii* clinical isolates from immunocompromised patients in intensive care units. Biofilm promotes *A. baumannii* adherence and long-term survival. So, it is an important factor in the pathogenesis and it makes the treatment options complex. The formation of *A. baumannii* biofilms is influenced by several biological and environmental variables. The primary determinant of *A. baumannii* biofilm development is glucose.[29] Although evidence suggests a link between biofilm formation and multiple drug resistance in *A. baumannii*, imipenem remains the drug of choice for multi-drug resistant *Acinetobacter* infections. The high incidence of *A. baumannii* infections linked to medical devices is caused by biofilms, making treatment and control of infection very problematic. Therefore, health care workers (HCWs) should focus on infection prevention and control (IPC) measures or activities to control device mediated *A. baumannii* biofilm-related infections and they should be strongly selective in the utilization of therapeutics in combination with anti-biofilms. Moreover, researchers shall undergo further studies which explore the exact magnitude, pathogenesis, aggravating factors, as well as mechanisms involved in biofilm formation of *A. baumannii* and the most possible therapeutics options.

Author Contributions

All authors contributed significantly to the paper's conception and design, data collection, and writing the paper; agreed to submit the manuscript to the current journal; granted final approval of the version to be published.

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