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Clinical Significance, Antibiotic Resistance and Biofilm Formation of *Acinetobacter baumannii*: Review

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Abstract

Acinetobacter baumannii is a gram-negative, non-fermentative aerobic, multi-drug resistant coccobacillus that is prominently seen in the healthcare settings. It is present in normal flora of human skin, upper respiratory tract and gastrointestinal tract. They have emerged as significant nosocomial pathogen and occasionally referred to as causative agent for community-acquired infection. The main characteristics of *A. baumannii* is the capacity to remain in hospital environment on various inanimate materials paving a way for infection in vulnerable patients The natural habitat of *A. baumannii* is not clearly understood, it is not only isolated from hospitalized patients but also from sick animals. *A. baumannii* colonizes cutaneous layer, mucosal membranes as well as hospital equipments like tap water, sink, lotion dispensers, mattresses, respiratory equipment, pillows, curtains, blankets, telephone, door handles, dustbins, steel trolleys and computers.

A. baumannii has the capacity to adapt to a wide range of antibiotics, rapid transformation and it has a great ability to persist in the environment for a very long time. The hospital acquired infections in majority affects the patients in Intensive Care Units. *A. baumannii* has led to epidemic outbreaks or endemic occurrences, which has shown high mortality rates in past reports. The major cause of high mortality rate is due to the emergence of multi-drug resistant strains.

Keywords: *A. baumannii*; Clinical significance; Biofilm formation; Antibiotic resistance

Introduction

A. baumannii and its clinical significance

Acinetobacter baumannii is a multidrug resistant (MDR) organism responsible for community as well as hospital-required infections. They are very difficult to control and treat due to its increased multidrug resistance [1]. In a survey conducted by US hospital laboratories (2004), 1.3% of health-care-associated bloodstream infections were due to *A. baumannii*. A nationwide survey was conducted in Benin, West Africa on the prevalence of nosocomial infections, in which it was identified that 972 nosocomial infections were found among 597 patients, which was highly due to *A. baumannii* which showed complete resistance to ceftazidime. In India, the prevalence of *A. baumannii* was raised to 11.6% for a period of 25 years [2]. There are different species of *Acinetobacter*, out of which only *A. baumannii*, *A. lwoffi* and *A. calcoaceticus* are leading causes of nosocomial infections in Intensive Care Units, around the world. Urinary tract infections, ventilator associated pneumonia, surgical site infection, meningitis, skin and soft tissue infections are various kinds of infections caused due to *A. baumannii* [3].

It has been reported that there are many sequence types of *A. baumannii* which is the highly responsible for causing inconvenience to mankind. A phylogenetic tree has been constructed with *A. baumannii* of 50 genospecies based on *rpoB* sequences via RFLP analysis [4]. It has been reported that the resistance to carbapenem by *A. baumannii* is highly increasing. In Europe, it has been reported that the resistance to meropenem is increased to 57.4% and the resistance to imipenem is raised to 47.9%. It has been reported in Taiwan, the percentage of carbapenem resistance *A. baumannii* has increased from 3.4% to 58.7% between 2002 to 2011. The infections due to carbapenem resistance has increased from 20% to 70% during the period between 2003 to 2007 in intensive care units, which was found by the data collected from Taiwan Nosocomial Infections Surveillance (TNIS). It has been reported that the mortality rate due to carbapenem resistant *A. baumannii* infections has increased to 50% [5].

Antibiotic resistance of *A. baumannii*

It has been found that over past three decades traditional antibiotics were used to treat infections caused by *A. baumannii* but now a days it started showing resistance to major classes of antibiotics like tetracyclines, fluoroquinolones, carbapenems, chloramphenicol, penicillins, cephalosporins and aminoglycosides and moreover due to its increased incidence and faster emergence of resistance *A. baumannii* is regarded as "red-alert" [3]. Therefore the control of these infections demands *A. baumannii* removal from medical settings [6]. Inspite of the introduction of new alternate treatments, the ability to form biofilm and lower permeability of the outer membrane of *A. baumannii* has led to complicated situation [7]. Contagion strains of *A. baumannii* are prominent for both intrinsic resistance to antibiotics and their abilities to attain genes, encoding resistance determinants. The mechanism of resistance to β lactams and aminoglycosides are through the production of β lactamases and aminoglycoside modifying enzymes. Moreover, the diminished appearance of outer membrane

proteins, mutation in topoisomerase and up-regulation of efflux pumps contributes a vital role in antibiotic resistance [8].

Biofilm formation, integron formation, inactivating or deactivating enzyme, outer membrane permeability, drug exocytocysis are the resistance mechanisms of *A. baumannii* that makes the strain complex [9]. Due to its high resistance to clinically functional antibiotics, the approach to the treatment for this bacterial infection is limited [6]. In a study conducted with patients suffering from pneumonia and blood stream infections at Poland, Sosnowiec Hospital Intensive Care Unit, it was found that 13.5% of the clinical isolates were *A. baumannii*. Moreover, 76.5% of the strains were extremely drug resistant. There was greater than 90% of *A. baumannii* resistant to fluoroquinolones, amikacin and trimethoprim/sulfamethoxazole. The resistance to imipenem and meropenem accounts for 95% whereas, 100% of the strains showed resistance towards cephalosporins and tetracyclins. According to the report by Antimicrobial Resistance Surveillance Network Poland, it was found that in 2012, 38.3% of *A. baumannii* were carbapenem resistant which was then increased to 49.7% after one year. There was also increase in resistance to fluoroquinolones from 78% during 2012 to 81.4% by the year 2013. Moreover, the resistance to aminoglycosides was increased to 73.8% from 63.4% in 2012 [10].

The colistin hetero resistance in *A. baumannii* has been reported to increase from 23% to 100%. It was found that in blood isolates *A. baumannii* hetero resistance to colistin was 92% and in respiratory isolates it was found to be 75% [11].The mortality rates in hospitals due to pneumonia and blood stream infections caused by multidrug resistant *A. baumannii* isolates is reported to be 60% and 35%. Through a study conducted in US hospitals during a period of 2009-2011, it was found that almost 50% of *A. baumannii* showed resistance to most antibiotics, expect colistin. Later, it was found that colistin treatment showed severe side effects by developing neurotoxicity and nephrotoxicity [6].

Biofilm formation of *A. baumannii*

The arrangement of cells that differ morphologically, physiologically and metabolically from their planktonic systems constitute biofilm. The antimicrobial resistance of the strain is mainly due to the biofilm formation. The ability to form biofilm helps *A. baumannii* to survive on abiotic surfaces. The external factors like dehydration and less nutrient availability is well managed by the biofilm formed by *A. baumannii* [12]. The cultures stagnantly incubated at liquid-air interface are more convenient for the strain to attach and form biofilm. The strain forms exopolysaccharides as a part of cell aggregates which is confirmed by electron and fluorescence microscope. In medical devices the biofilm formation is found in catheters, artificial heart valves etc. The pilli and flagella mediate the bacterial motility and therefore helps in biofilm formation [3].

Biochemical assays are done for the identification of the strain. The presence of the strain is detected by methods like urease, catalase and oxidase. A specific cell surface protein is directly involved in biofilm formation of *A. baumannii* which is known as (Bap) Biofilm associated protein [13]. It has been found that Bap of *A. baumannii* is similar in homology to Bap of *S. aureus*. Bap of *A. baumannii* is a large surface protein containing 8,620 amino acids. It has been reported that the Bap plays a major role in biofilm formation, maturation and maintenance of *A. baumannii* strains on biotic and abiotic surfaces. Moreover, it is very important for maintenance of thickness on various abiotic surfaces and for stabilization. Therefore, research on an inhibitor against Bap of *A. baumannii* is required to prevent the biofilm formation [14].

Conclusion

Therefore there is a need for alternate method of treatment for the infections caused by multidrug resistant *A. baumannii*. More research activities are needed to be carried out against these types of multidrug resistance microorganisms which are an upcoming crisis in the medical field.

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