

Influence of Acinetobacter in Coming Era

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Abstract

Acinetobacter baumannii is the Gram-negative bacillus that is aerobic, pleomorphic and non-motile. An opportunistic pathogen, A. baumannii has the high incidence among immunocompromised individuals, particularly those who have experienced the prolonged (> 90 d) hospital stay. Commonly allied with aquatic environments, it has been shown to colonize the skin as well as being isolated in very high numbers from the respiratory and oropharynx secretions of infected individuals. So this paper discusses the various aspects of Acinetobacter baumannii

Keywords: - *Acinetobacter baumannii, bacilli, immunocompromised, skin, colonize*

INTRODUCTION

In the recent years, it has been designated as a “red alert” human pathogen, generating alarm among medical fraternity, arising largely from its extensive antibiotic resistance spectrum. This phenomenon of the multidrug-resistant (MDR) pathogens has increasingly become a cause for serious concern with regard to both the nosocomial and community-acquired infections. Indeed, the World Health Organization (WHO) has recently identified the

antimicrobial resistance as one of the three most important problems facing human health. The most common and the serious MDR pathogens have been encompassed within the acronym “ESKAPE,” standing for the Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa and Enterobacter spp (Brisou et al., 1954).

While in the 1980s *A. baumannii* is thought to have been sensitive to most antibiotics, today the pathogen appears to exhibit the extensive resistance to most first-line antibiotics (Baumann et al., 1968). More recently, *A. baumannii* has become the major cause for concern in conflict zones, and has gained specific notoriety in the recent desert conflicts in Iraq, earning it the moniker “Iraqibacter.” In particular, the high incidences of MDR bacteremia (bloodstream infections) have been noted among the US Army service members following Operation Iraqi Freedom (OIF). Interest from the scientific community over the past 14 years has led to significant advances of our understanding of this organism. *Acinetobacter baumannii* is ubiquitous in the nature and can be isolated from drinking water, food, and soil. It is well known as an opportunistic pathogen mainly responsible for nosocomial infections with the considerable morbidity and mortality in hospitalized human patients. These infections include pneumonia in the ventilated patients, urinary tract infections in patients with indwelling urinary catheters, wound infections, bacteremia, and the meningitis after neurosurgical procedures. Its importance aggrandized in recent decades, especially in intensive care units where proportional morbidity of the colonization

at various body sites, was estimated at 3.2 to 10.9 per 1,000 patients. *Acinetobacter* infections accounted for 0.4% of endemic nosocomial infections in critically ill patients. These findings are thought to be due to the aggrandizing invasive nature of diagnostic and therapeutic procedures, the widespread use of the broad-spectrum antibiotics, and the capacity of *A. baumannii* for long-term survival in hospital environment. Such infections usually are difficult to treat because of occurrence of multi resistant strains and frequently require combination therapy.

A. baumannii infestations increase the duration of hospitalization and the cost of treatment.

Due to the widespread use of the antibiotics during the last two years, multidrug-resistance and specifically extensively drug-resistant *A. baumannii* (MDR-AB, and XDR-AB) have accrued therefore cause the critical problem in the world (Lessel, 1970). The transmission of resistant strains among the patients and the application of broad-spectrum antibiotics have been reported between wards within a hospital because of the emergence of MDR-AB. The MDR-AB is allied with high mortality in the hospitalized patients. In the ICU, the mortality rate associated with *A.*

A. baumannii has been found to be 55% (Gerner-Smidt et al., 1991). The MDR-AB in the burn wounds of the infected patients is a main risk factor for high mortality rate around the world. The prevalence of these resistant strains is the paving cause of infections. Emergence of XDR-AB limits the therapeutic options and causes the serious concern to control the HAIs. For a period of 4 years (2005-2010), the frequency of XDR-AB in the clinical isolates had increased from 15% to over 42% (Di Nocera et al., 2011). For the medical communities, the management of MDR-AB and XDR-AB infections is one of the essential problems. It is very difficult to treat the infections caused by *A. baumannii* due to various and multiple antibiotic resistant strains (Juni, 1972). Various mechanisms of the antibiotic resistance have been recognized in these microorganism, such as the enzymatic degradation and modification of antibiotics, enhanced expression of efflux pump genes, decreased permeability, ability of forming the bio film formation and altered drug targets, and the combination therapy is usually required for effectual treatment of the nosocomial infections from *A. baumannii*. It is ubiquitous in the hospital environment and can also survive for longsome periods on dry inert surfaces. The infected patients are one of the key

reservoirs of *A. baumannii*, who might make contamination in their hands, resulting in the cross transmission of the bacteria (Seifert et al., 1997). The specified risk factors for the *A. baumannii* colonization and infection are the protracted hospitalization, long stay in the ICU, mechanical ventilation, central venous catheterization, urinary catheterization, previous exposure to antimicrobials. One of the major key factors in these infectious diseases is the ability of the bacteria to form biofilm, the antibiotic resistance and in-hospital survival causes of this organism have been shown to be due to its bio film, the formation ability, due to virulence factors, such as the auto inducer synthase *abaI* as a part of quorum sensing complex, and the *pga* ABCD operon responsible for producing poly-b-1,6-N acetyl glucosamine (PNAG). A direct relationship has been found specifically between the biofilm formation and drug resistance in *abaI* and *pga* genes in the *A. baumannii* (Vanechoutte et al., 1995).

CLINICAL IMPORTANCE OF ACINETOBACTER SPP

Acinetobacters have been isolated from several types of opportunistic infections, including skin and the wound sepsis, septic aemia, pneumonia, endocarditis,

meningitis, and UTI. The distribution by site of the acinetobacter infections does not differ from that of other nosocomial gram-negative bacterium. The major sites of infection are the lower respiratory tract and the urinary tract (Janssen et al., 1997).

Respiratory infection: nosocomial pneumonia. Nosocomial respiratory tract infection with the *Acinetobacter* spp occurs frequently in hospitals, especially in ICUs. Large outbreaks of the acinetobacter-associated pneumonia have been delineated in which all the patients had severe underlying disease requiring assisted ventilation and most had tracheostomies or were intubated. *Acinetobacters* represent 15.7% of the total gram-negative bacilli involved in nosocomial pneumonia in France (Gerner-Smidt et al., 1992).

UTI

Acinetobacters have been allied with 2-61% of nosocomial UTIs. A recent investigation in France implicated acinetobacters in 30.6% of nosocomial UTIs. Factors predisposing patients to this infection do not seem to typically differ from those for other nosocomial bacteria. Occasionally, *Acinetobacter* spp may also cause community-acquired UTIs in the absence of known predisposing factors. Meningitis (Ehrenstein et al., 1996).

Nosocomial meningitis is an in frequent manifestation of the acinetobacter infection. The first case report appeared in 1907 (the responsible organism, then designated *Diplococcus mucosus*, was then renamed *Mima* because of its resemblance to the meningococcus following Gram's stain). Cases of meningitis caused typically by acine to bacters have been reported after neurosurgical procedures, but rare cases of the primary meningitis, especially in children, have also occurred. *Acinetobacter* meningitis may result from direct introduction of the organism into the central nervous system during intracranial surgery, but has also been allied with the presence of the indwelling ventriculostomy tubes or cerebro spinal fluid (CSF) fistulae in patients receiving antimicrobial therapy (Dolzani et al., 1995).

Other miscellaneous infections. *Acineto bacter* skin and the wound infections, abscesses, septicaemia, endocarditis, peritonitis and the burn wound superinfections have all been described in the literature (Chang et al., 2005). Their rate differs according to the hospital, the ward and the type of patients involved. Sporadic cases of the acinetobacter infections are seen in many hospitals, with the periodic outbreaks in ICUs, in burn units, or in pediatric wards. Strains of the

multiresistant *Acinetobacter* spp, particularly *A. baumannii*, can survive in the hospital environment and may persist for 8-10 days or more on dry surfaces. They also persist on the skin, in the throat and in the gut of the colonized patients. All of these multiple sources may contribute to periodic outbreaks of infection that are often observed (La Scola et al., 2004).

GENUS *Acinetobacter*

The Dutch microbiologist Beijerinck first isolated the organism in 1912 from soil using minimal media enriched with the calcium acetate. Originally described as *Micrococcus calco-aceticus*, genus *Acinetobacter* (coming from the Greek “*akinetos*,” meaning non-motile) was proposed some 44 years later by Brisou and Prevot to differentiate it from the motile organisms within genus *Achromobacter*. The genus *Acinetobacter* was widely accepted by 1967 after assessed a comprehensive study of organisms such as *Micrococcus calco-aceticus*, *Alcaligene* ssp, *Mimopoly morpha*, *Moraxella lwoffii*, *Herellea vaginicola* and *Bacterium anitratum*, which concluded that they belonged to the single genus and could not be further sub-classified into different species based on phenotypical characteristics. In 1972, the sub-committee on the Taxonomy of *Moraxella* and the

Allied Bacteria officially acknowledged the genus *Acinetobacter* based on results of Baumann’s 1967 publication (Fournier et al., 2006). The genus *Acinetobacter*, as currently defined, encompasses Gram-negative, strictly aerobic, non-fermenting, non-fastidious, non-motile, catalase-positive, the oxidase-negative bacteria with a DNA G + C content of 39% to 49%. Following DNA-DNA hybridization studies performed by Bouvet and Grimnot in 1987, the *Acinetobacter* genus now consists of 26 named species and nine genomic species. Four species of *Acinetobacters* (*A. calcoaceticus*, *A. baumannii*, *Acinetobacter* genomic species and *Acinetobacter* genomic species 13TU) they have such phenotypic similarities that they are difficult to differentiate, and as such and are often referred to as the *A. calcoaceticus*-complex. This nomenclature can be misleading as the environmental species *A. calcoaceticus* has not been much implicated in clinical disease, while the other three species in the *A. calcoaceticus*-complex are perhaps the major clinically significant species, being implicated in both community-acquired and nosocomial infections (Turton et al., 2006).

ANTIBIOTIC RESISTANCE

The rapid emergence of the multi- and pan drug-resistant strains of *Acinetobacter*

highlights the organism's ability to quickly acclimatize to the selective changes in environmental pressures. The upregulation of organism's innate resistance to mechanisms coupled with the acquisition of foreign determinants have played the crucial role in the express route the organism has taken to becoming a multidrug-resistant pathogen. A 2007 study undertaken compared the genome of the AYE and SDF *Acinetobacter* using whole shotgun genome sequences.

In France, the epidemic AYE strain had a 27% mortality rate in infected patients, while the SDF strain came from same geographical region, but was allied with human body lice, and was fully susceptible to the antimicrobial agents. The genomic comparisons revealed that the genome of the virulent AYE strain contained an 87 kb region called a resistance "island" that contained a cluster of 46 resistance genes. The homologous location in the susceptible strain exhibited a 21 kb genomic island that is devoid of these resistance markers (Gopinath Prakasam et al., 2011).

This ability to "switch" its genomic structure typically goes some way to explaining the speed with which the *Acinetobacter* captures resistance markers when under antibacterial pressure, such as

may occur in the high risk environment, such as in hospital intensive care units (where broad spectrum antimicrobials are commonly available). Sequence similarity and the phylogenetic analyses confirmed that most of the resistance genes found in the *Acinetobacter* strain AYE had been recently acquired from the bacteria of the genera *Pseudomonas*, *Salmonella* or *Escherichia*. All genomic variants of the *A. baumannii* contain the non-inducible chromosomal Amp C cephalosporinase, also known as *Acinetobacter*-derived cephalosporinases (ADCs).

The presence of an upstream IS element known as ISAba1 determines the regulation of AmpC gene. Over expression of AmpC cephalosporinase and the resistance to extended spectrum cephalosporin is intrinsically linked to the presence of ISAba1. Cefepime and carbapenems, however, appear to be quite stable in response to these enzymes (Seifert et al., 1995).

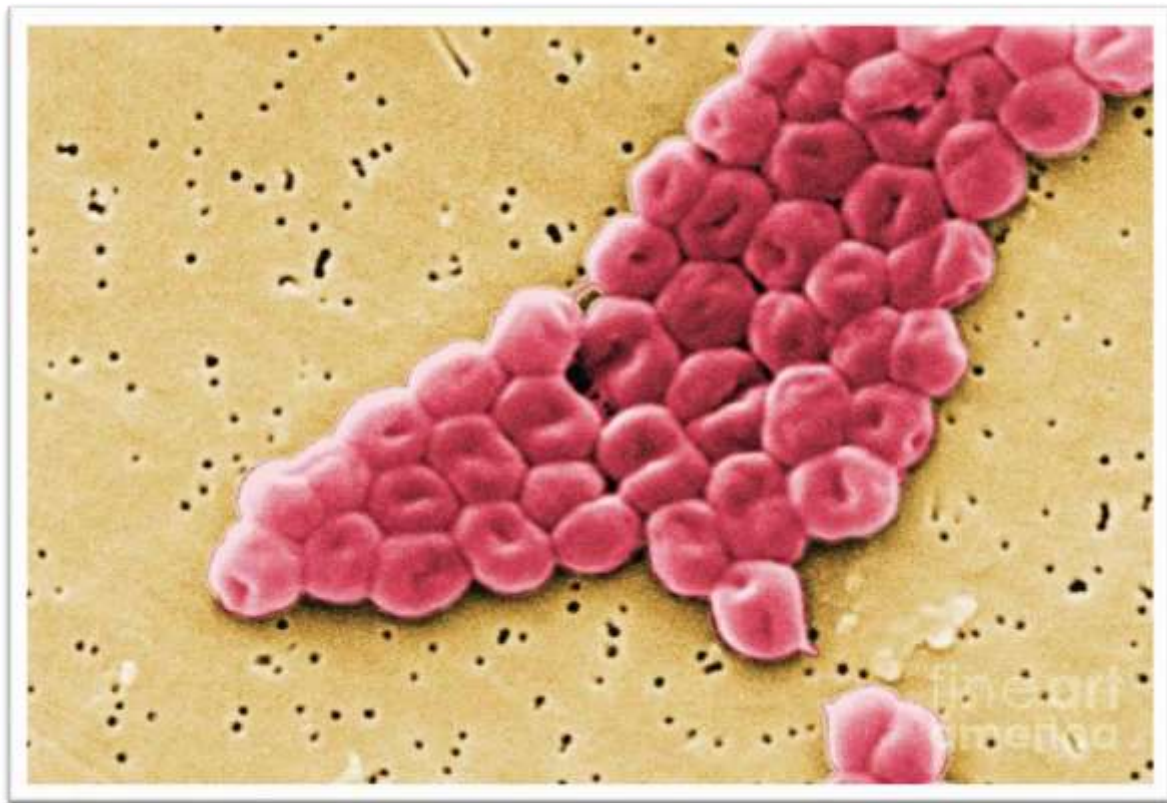


Figure: 1 *A. baumannii*

A. baumannii also possess an intrinsic class D oxacillinase belonging to the OXA-51-like group of the enzymes that constitutes over 40 sequence variants (fig:1). The ubiquitous nature of the OXA-51-like genes in *A. baumannii* has led to this gene becoming an important genetic marker in identification of the organism to the species level. OXA-51-like enzymes are able to mainly hydrolyze penicillins (benzylpenicillin, ampicillin, ticarcillin and piperacillin) and carbapenems (imipenem and meropenem) but do so only much weakly. A significant contribution to the lactam resistance by OXA-51-like enzymes therefore requires the presence of an

insertion element IS_{Aba1} upstream of the gene, which acts as the strong transcriptional promoter. The common enzymatic mode of carbapenem resistance is the synthesis of oxacillinases encoded by genes of the bla_{OXA-23}, bla_{OXA-40} and bla_{OXA-58}-like lineage (Bernards et al., 1998).

In Europe, spread of multidrug-resistant *Acinetobacter* is not confined to the hospitals within a city but also occurs on the national scale, mostly through inter-hospital patient transfers, for example the spread of so-called Southeast clone and Oxa-23 clones 1 and 2 in southeast

England. International transfer of the colonized patients has led to the introduction and subsequent epidemic spread of multidrug-resistant *A. baumannii* strains from the southern into northern European countries, such as Belgium and Germany. In an industry-supported surveillance report (MYSTIC) from 47 European hospitals for the period 2002–2004, just 73.1% of *A. baumannii* isolates were susceptible to meropenem and 69.7% were susceptible to imipenem. Susceptibility to other antibiotics was also very low, with 32.2%, 34.0% and 47.5% being susceptible to ceftazidime, ciprofloxacin and gentamicin, respectively (Joshi et al., 2006). There is a long history of multidrug-resistant *A. baumannii* infections occurring in United States. In 1991 and 1993, outbreaks of carbapenem-resistant *A. baumannii* were observed in the hospital in New York City. This followed an outbreak of the infections due to ESBL-producing *Klebsiella pneumoniae* during which use of the imipenem increased substantially. In more recent industry supported surveillance study encompassing the isolates of *Acinetobacter* collected between 2004 and 2006 from 76 centers throughout the United States, only 60.3% were susceptible to imipenem. Numerous outbreaks of pan drug-resistant *A. baumannii* have been mainly documented

in Asian and Middle Eastern hospitals. Rates of non-susceptibility in SENTRY (Anti-microbial Surveillance Program) isolates (2001–2004) exceeded 26% for imipenem and meropenem, 40% for cefepime and ceftazidime, 40% for ampicillin-sulbactam, 35% for amikacin, and 46% for ciprofloxacin. It is worth noting that resistance to tigecycline and polymyxin B (drugs relied on heavily to treat the infection with *A. baumannii*) both already exist in this region (Jones et al., 2005). Like *Mycobacterium kansasii*, *A. baumannii* is a chronic infective pathogen (Sreeremya, 2018).

CLINICAL SYMPTOMS

A. baumannii infections are implicated across a broad range of anatomical regions and with varying severity and patient outcomes. There is considerable debate connecting to the actual clinical impact of infection and its relationship to patient mortality. While the numbers of studies have concluded that the infection with *Acinetobacter* has a detrimental effect on patient outcome, other similar analysis implied little or no effect on patient outcome as a result of infection. The lack of consensus is majorly likely due to the difference in the approaches of the various analysis; some being prospective while others have been of retrospective samples.

The results generated by some studies have also only identified the organism to the genus level but not to species level, with many referring to infection with *Acinetobacter calcoaceticus- baumannii* complex which could conceivably indicate the colonization with the environmental species *Acinetobacter calcoaceticus* coupled with a polymicrobial infection, rather than the monomicrobial infection with a virulent *Acinetobacter* species such as MDR *Acinetobacter* (Seifert et al., 1997).

CONCLUSION

Acinetobacter baumannii is a gram negative aerobic bacteria. It is a pathogen. It causes several nosocomial infection. It also causes UTI. The various dynamics of *Acinetobacter baumannii* are discussed in this paper.

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