

Infections Due to *Acinetobacter baumannii* in the ICU

Authors :

Dr Elaheh Dolatshahi Pirooz¹ Robabeh Haghverdi²- Shahrbanoo Akbari³- Zeynab Rahimi⁴-Rasrghoo⁵

Aderss:

Clinical Research Development Unit ,Shide Rajaei Educational &Medical Center .Alborz University of Medical Sciences, Karaj,Iran

Background:

Bacteria within the genus *Acinetobacter* are encapsulated, non-lactose fermenting, oxidase-negative gram-negative coccobacilli that may cause infections in health care or community settings, particularly in patients with comorbidities or skin/soft-tissue injuries.^{1–3} More than 20 *Acinetobacter* species have been identified,¹ but the vast majority of clinical infections are caused by organisms within the *A. calcoaceticus*-*A. baumannii* complex (ABC). This complex comprises four species; *A. baumannii*, *A. nosocomialis*, and *A. pittii* cause clinical infections in humans, whereas *A. calcoaceticus* is an environmental organism of negligible clinical significance. *A. baumannii* is the most common species in most regions; the prevalence of *A. pittii* and *A. nosocomialis* is higher in Southeast Asia and *A. pittii* may be more common in Scandinavian countries. *A. baumannii* has been associated with heightened mortality and a higher degree of antimicrobial resistance compared with other *Acinetobacter* spp.

Clinical Features:

Acinetobacter species (spp.) most frequently cause nosocomial infections in critically ill or debilitated patients, including ventilator-associated pneumonia (VAP), bloodstream infections (BSI), device-associated infections (DAI), wound or skin and soft-tissue infections (SSTI), burns, urinary tract infections (UTI), intraabdominal infections (IAI), and meningitis. Additionally, *Acinetobacter* spp. have been implicated in SSTI sustained during disasters, including earthquakes tsunamis, terrorist attacks, and combat injuries in Vietnam, Iraq and Afghanistan, Ukraine, Lebanon, and Syria. Infections due to *Acinetobacter* spp. occur more frequently in subtropical or tropical regions; in temperate climates, infections are more common in the summer. Community-acquired pneumonia (CAP) due to ABC rarely occurs in temperate climates, but fulminant CAP, sometimes with septic shock, has been described in Asian-Pacific regions. Factors predisposing to ABC-associated CAP include alcoholism, diabetes mellitus, male gender, renal or pulmonary disease, cirrhosis, advanced age, smoking.

Prognosis of Infections Due to *A. Baumannii* Mortality rates with VAP or BSI due to *Acinetobacter* spp. are 30 to 75%; these high mortality rates in part reflect comorbidities and severity of illness. In the EPIC II study, a multinational study of ICU patients, infection with ABC was independently associated with a

greater risk for hospital death . Within the past three decades, resistance rates among ABC have escalated globally. Emergence of multidrug-resistant (MDR) strains has undoubtedly contributed to mortality. Not surprisingly, inappropriate initial empiric antibiotic therapy (IET) for pneumonia or sepsis due to ABC has been associated with heightened mortality. In a recent retrospective review of 1,423 patients hospitalized with sepsis or pneumonia due to ABC, 82.3% of isolates were MDR. MDR-ABC strongly predicted receipt of IET and IET was associated with higher hospital mortality .In light of the rising incidence of MDR-ABC, a multinational consensus statement was recently published regarding the management and prevention of *A. baumannii* infections in the ICU.

Infections Due to ABC in the Hospital Setting ICU Infections

Most ABC infections occur in hospitalized patients in the ICU, often with multiple comorbidities. Device-related infections (DRI) are typical (i.e., VAP, central venous catheter [CVC]- associated BSI, surgical site infections (SSI), catheter-associated UTIs). The EPIC II point prevalence study in 2007 comprising 75 countries implicated *Acinetobacter* spp. in 8.8% of all ICU infections, with rates of 19% in Asia and 17% in Eastern Europe. In the SENTRY study from January 2009 to December 2011, ABCs were implicated in 7% of ICU infections in the United States and Europe. Even higher rates of ABC infections have been reported in Latin America and Asia. In a review of Vietnamese pediatric ICUs, ABC was implicated in 18.4% of hospital-acquired infections (HAI); 65% of isolates were carbapenem resistant (CPR). In a prospective study from six hospitals in Iran (2011–2012), ABC was implicated in 35% of DRI among hospitalized adults.¹⁶ Importantly, 70.5% were CPR.

Risk Factors for Colonization or Infection with *Acinetobacter* spp.

In critically ill patients, *Acinetobacter* spp. may colonize the gastrointestinal (GI) tract, skin, and respiratory tract, and may cause serious infections. Risk factors for acquisition of *Acinetobacter* spp. include invasive procedures or devices, prolonged ICU stay, mechanical ventilation (MV), enteral feedings, burns, and recent use of broad-spectrum antibiotics, particularly cephalosporins (CEPHS) or fluoroquinolones (FQs).

Mechanisms of Antimicrobial Resistance *Acinetobacter* spp.

have innate (chromosomal) resistance mechanisms against multiple antimicrobials but also can acquire new resistance determinants via mobile genetic elements such as plasmids, transposons, integrons, insertion sequences, and resistance islands. Mechanisms of antimicrobial resistance are numerous and include (1) enzymatic inactivation or modification of antimicrobials; (2) alteration in the bacterial target site(s); (3) permeability barriers to uptake of antimicrobials; (4) active efflux pumps (that extrude antibiotics from bacterial cells); (5) combinations of mechanisms, which may occur as the result of large genomic islands containing multiple resistance genes.

Treatment of Infections Due to Acinetobacter spp.

Nosocomial infections due to ABC have been associated with high mortality rates (particularly with BSI or VAP). Early appropriate antimicrobial therapy is critical. Optimal therapy for serious ABC infections has not been established, as prospective randomized trials have not been done. For BSI, removal of invasive devices within 48 hours may reduce mortality. For SSTI or SSIs, debridement is an essential part of therapy. Carbapenems, alone or combined with a second agent, has been considered the best therapy for ABC infections. However, the emergence of CPR strains limits the use of these agents as monotherapy for empirical treatment when CPR is a consideration. We believe a combination of a carbapenem plus colistin is appropriate as initial empirical therapy for serious *A. baumannii* infections when CPR is suspected. Other agents (e.g., β -lactam/ β -lactamase inhibitors, ceftazidime, or FQs) may be used, provided isolates are susceptible.

Treatment of Infections Due to Acinetobacter spp.

In view of the high incidence of MDR-ABC, initial empirical therapy with combination therapy (typically CP plus colistin) is often employed while awaiting antimicrobial susceptibility results. Optimal therapy is not clear, as randomized, controlled studies are lacking. In the next sections, we will discuss antibiotics that are often used either as monotherapy or part of combination therapy for MDR-ABC.

Prevention

Hospital outbreaks of *Acinetobacter* infections may reflect environmental contamination or carriage of *A. baumannii* on the hands of health care workers. Aggressive infection-control measures including identifying sources of transmission environmental cleaning, contact precautions, and hand hygiene and isolating or cohorting infected and colonized patients may be critical to stop or prevent outbreaks. In one study, daily chlorhexidine baths in ICU patients reduced the development VAP due to *Acinetobacter*.

Conclusion

The dramatic global rise of antimicrobial resistance among ABCs reflects acquisition of novel resistance elements and spread via a few international clones. Many isolates are resistant to all antimicrobials except colistin, and some infections are untreatable with existing agents. Novel approaches including combinations of agents and extended infusion times may be required to optimize therapy. Appropriate use of antimicrobials and infection-control measures are critical to minimize antimicrobial resistance.

Keyword: Infections , *Acinetobacter baumannii* , ICU