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Prevalence and antibiotic resistance of *Acinetobacter baumannii* among patients in postcardiac surgery intensive care units of Rajaei Hospital, Tehran

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Abstract

Background: *Acinetobacter baumannii* is an opportunistic, aerobic, nonfermentative, Gram-negative bacterium that can cause major nosocomial infections, especially in patients hospitalized in intensive care units (ICU). Recently, *A. baumannii* strains have been resistant to a variety of antibiotics. Thus, it was aimed to evaluate the prevalence of *A. baumannii* and their resistance to the antibiotics in the patients hospitalized in postcardiac surgery ICU.

Methods: This retrospective cross sectional study was performed in Rajaei hospital between March 2014 and February 2016. *A. baumannii* strains were isolated from blood cultures, catheter cultures, sputum cultures, and wound smear cultures. Then, isolates were characterized using standard morphological, cultural, and biochemical properties according to CLSI 2016. The frequency of A. baumannii species were reported as percent.

Results: Among 27 167 patients were admitted to the ICU, 113 individuals, including 55 males and 58 females, were identified as *A. baumannii*-infected and the prevalence rate was 0.42%. The highest rates of antibiotic sensitivity were related to Meropenem 20 (17.7%) and Colistin 16 (14.1%). The shortest length of stay (LOS) for patients with *A. baumannii* in the ICU was 3 days, while the longest LOS was 98 days.

Conclusion: The findings indicated that *A. baumannii* strains isolated from postcardiac surgery ICUs had a high prevalence and were sensitive to Meropenem and Colistin. However, new molecular-based techniques are needed to monitor nosocomial infections. Therefore, the treatment of the patients may be feasible by appropriate antibiotic therapy, and infection control policies will be improved by adopting precise disinfection strategies.

Keywords: *Acinetobacter baumannii*, Nosocomial infection, Antibiotic, Resistance

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Introduction

Antibiotic resistance is a global problem threatening public health. The outcomes of the antibiotic-resistant infections are longer hospitalization, higher cost of medical health care, and increased morbidity and

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↑What is "already known" in this topic:
Acinetobacter baumannii is an aerobic, nonfermentative, Gram-negative microorganism, causing major nosocomial infections, especially in patients hospitalized in intensive care units (ICU). The prevalence of *A. baumannii* and its resistance to antibiotics may promote health conditions and save patients' lives.

→What this article adds:
The high prevalence and, on the other hand, the sensitivity of *A. baumannii* to Meropenem and Colistin are notable to treat patients in a more targeted manner and provide new disinfection approaches.

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mortality (1). *Acinetobacter baumannii* is an opportunistic, aero bic, nonfermentative, and Gram-negative bacterium that can cause major nosocomial infections in seriously ill patients with broad-spectrum antibiotics who are hospitalized in intensive care units (ICUs) (1-3). The mortality rate is variable and ranges from 17% to 63% (4). *A. baumannii* can cause bacteremia through the bloodstream, pneumonia, septic shock, ventilator-associated pneumonia, disseminated intravascular coagulation (DIC), and in patients who suffer from burns or urinary tract infections (UTI); the inappropriate selection of antibiotics leads to poor clinical outcomes and increased mortality rates (5-7).

Recently, *A. baumannii* strains have been resistant to the family of β-lactam antibiotics such as Carbapenems and have become multidrug-resistant (MDR) pathogens (8). However, Aminoglycosides, Tigecycline, Colistin (polymyxin E), Sulbactam, and Minocycline have shown limited therapeutic success (9). Since MDR-resistant *A. baumannii* isolates are frequently found in nosocomial infections in patients requiring serious health care such as postcardiac surgery ICU (10-12); thus, this study aimed to evaluate the prevalence of *A. baumannii* and their resistance to antibiotics in patients who were hospitalized in postcardiac surgery ICU.

Methods

This retrospective cross sectional study was performed in Rajaei hospital, Tehran, Iran. A total of 27 167 patients admitted to the ICU between March 2014 and February 2016 and patients who had positive culture results for (MDR) *A. baumannii* from any specimen (blood, sputum, urine, body fluid, or wound) were included in the study. The criteria for clinical isolates were based on the CDC definition for nosocomial infections (13).

Isolation, characterization, and susceptibility assessment: The specimens collected were blood cultures, catheters, sputum, wound smear, etc. Isolation of the bacteria was done by culturing on either selective agar media (Blood Agar, MacConkey agar, and Chocolate Agar) or enriched media (Thioglycolate) at 37°C for 24 to 48 hours (14). Methylene blue and Gram staining, oxidase test, and other differential biochemical tests were also done (15). Clinical isolates underwent species determination, and antibiotic susceptibility testing was performed by Vitek-2 system (bioMérieux, Marcy l'Etoile, France) by means of IDGN and N090 panels.

Antimicrobial susceptibility was determined using the disk diffusion technique, in accordance with the criteria established by the Clinical and Laboratory Standards Institute (CLSI) 2016 (16). The E-test method was used to assess the antimicrobial susceptibility of *A. baumannii* isolates (17). *A. baumannii* was considered MDR if it was resistant to routinely used antibiotics (including Penicillin, Cephalosporins, Fluoroquinolones, Aminoglycosides, or Trimethoprim-sulfamethoxazole) but susceptible to Carbapenems (18).

The demographic characteristics of the patients were obtained from clinical records. This information included gender, age, clinical diagnosis, the use of medical devices, comorbidities, reason for ICU admission, organ dysfunction at ICU admission, ICU length of stay (LOS), and consciousness level. Patients with evidence of any concurrent bacterial infection and children were excluded from this study. All analyses were performed using SPSS, version 20 (SPSS Inc., Chicago, Illinois, USA). All tests were 2-tailed. The normality of the data was evaluated by Kolmogorov–Smirnov test, and $p<0.05$ was considered to be statistically significant (19).

Results

Among 27 167 patients admitted to ICU, 113 individuals (55 males and 58 females) were identified as MDR *A. baumannii* infected, with the prevalence rate of 0.42%. Mean admission time before the diagnosis of MDR *A. baumannii* for different wards of the ICU was determined (Fig. 1).

The shortest LOS for patients with (MDR) *A.*

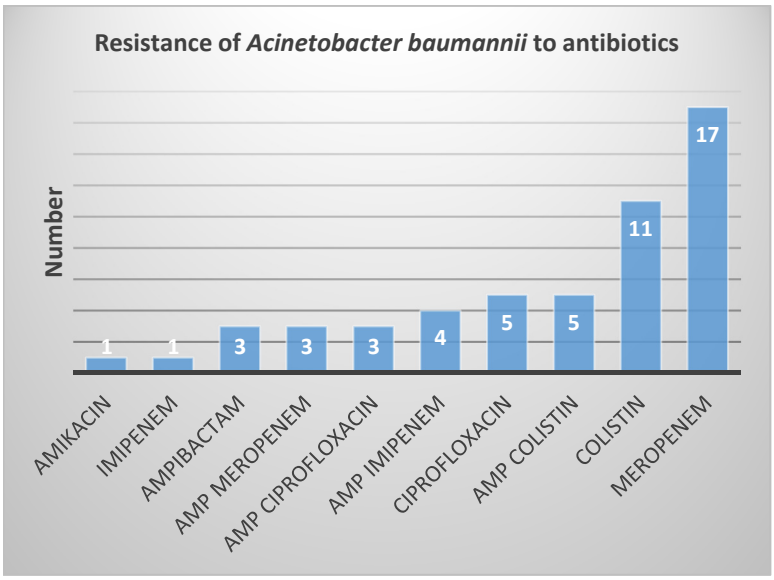

Fig. 1. The resistance frequency of *Acinetobacter baumannii* to antibiotics is shown

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baumannii in the ICU was 3 days, while the longest LOS was 98 days. The largest percentage of patients aged 60-70 years (22.1%), and a small percentage of patients aged 10-20 years (0.9%). Underlying diseases of the patients with MDR *A. baumannii* analyzed were (CABG [coronary artery bypass grafting], congenital heart disease, AVR [aortic valve replacement surgery], MVR [mitral valve replacement surgery], TVR [tricuspid valve replacement surgery], and PA [pulmonary artery] banding).

Of 23 patients with CABG, blood culture (n=12, 52.2%) had the highest frequency, of 19 patients with congenital heart disease (CHD), blood culture (n=13, 68.4%) had the highest frequency, and the lowest frequency belonged to urine culture (n=0, 0.0%). Among 113 patients with MDR *A. baumannii,* 4 individuals associated with AVR showed a positive blood culture. Of 16 patients with MVR, sputum culture (n=8, 50%) had the highest frequency and the lowest frequency was belonged to CVC (central venus catheter culture) (n=0, 0.00%). Among female patients, the highest frequency was related to blood culture (n=28, 50.9%) and sputum culture (n=27, 49.1), respectively. However, urine culture and CVC had the lowest frequencies, respectively. Among male patients, the highest frequency was related to sputum culture (n=26, 44.8).

Patients in 2 age-groups (younger than 10 years and 40-50 years) had the highest frequency of BC. Patients in 2 age-groups (30-40 and 40-50 years) had the highest frequency of CVC. Patients in 3 age-groups (less than 10 years, 60-70 years, and 70-80 years) had CVC infection. Patients in 2 age-groups (20-30 and 50-60 years) showed signs of CAC (central artery catheter culture) infection. Among female patients, the highest frequency was related to CVC infection (n=58, 9.1%). Among male patients, the highest frequency was related to CVC infection (n=2, 3.4%). Also, 10 (18.2%) deaths were observed among 55 male patients, and 13 (22.4%) deaths were reported among 58 female patients. Among age groups, the highest frequency of death was related to 30-40 and 70-80 age groups. The highest rates of antibiotic sensitivity were related to Meropenem 20 (17.7%) and Colistin 16 (14.1%) (Table 1).

Discussion

Infections due to *A. baumannii* and the development of MDR species are a major global problem threatening the public health (10). Management of MDR Acinetobacter spp. is of high importance for the treatment of different infections. Acinetobacter has natural antibiotic resistance and survives in hospitals and persist on different surfaces due to its ability to natural resistance genes. There are several possible or definite mechanisms by which this resistance occurs: (1) antimicrobial-inactivating enzymes; (2) decreased availability of bacterial targets, owing to reduced outer membrane permeability which occurs by the loss or decreased expression of porins and overexpression of multidrug efflux pumps; and (3) new mutations that alter cellular functions or the targets (changes in penicillin-binding proteins). A mix of these mechanisms may be found in the same bacterium (20, 21). This study evaluated the prevalence, antibiotic susceptibility, and the outcomes of the patients with MDR-*A. baumannii* in postcardiac surgery ICUs of Rajaei hospital. In this regard, in this study, it was observed that the prevalence rate of MDR- *A. baumannii* was 28.3% and the highest rates of antibiotic sensitivity were related to Meropenem and Colistin.

Nosocomial infection is referred to as an infection that has occurred within 72 hours, 3 days of discharge, or a 30-day period after the surgery (22). About 30% of these infections are caused by Gram-negative bacteria and these statistics reach to 70% in ICU-hospitalized patients (6, 23). The incidence of nosocomial infections due to the MDR Gram-negative organisms, including *Pseudomonas aeruginosa*, *A. bumanni* (24), and positive germs such as methicillin-resistant *Staphylococcus aureus* (25), have increased dramatically in recent years. Castilho et al reported that the prevalence of MDR *A. baumannii* was elevated among isolates from the patients in 5 ICUs in Brazil. They also declared that most of *A. baumannii* isolates showed resistance to beta-lactam antimicrobial agents, particularly, carbapenems and third and fourthgeneration Cephalosporins. In addition, 91.1% of the strains were MDR (26). However, the prevalence

Table 1. The resistance frequency of *Acinetobacter baumannii* to antibiotics and time of consumption

Antibiotic	First round consumption	Total consumption within 6 months
Amikacin	1	5
Ampicillin amikacin	0	2
Ampibactam	3	11
Ampicillin ampibactam	0	1
Meropenem	17	44
Ampicillin Meropenem	3	9
Imipenem	1	4
Ampicillin Imipenem	4	10
Gentamicin	0	1
Ampicillin gentamicin	0	1
Cotrimoxazole	0	5
Ampicillin Cotrimoxazole	0	1
Ciprofloxacin	5	26
Amp ciprofloxacin	3	11
Colistin	11	63
Ampicillin Colistin	5	18
Tazocin	0	2
Ampicillin Tazocin	0	3

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reported in this study was lower than the other studies, including Dorodgar et al (63.2%) (27) and Rodríguez-Baño et al (47%) (28), but it was higher than the study of Javanbakht et al (22.6%) (29). Two recent studies showed that *A. baumannii* strains were completely resistant to Meropenem (17, 27). In contrast, this study indicated that Meropenem and Colistin were the best choices for the treatment of patients in postcardiac surgery ICU. Colistin is the only therapeutic strategy for the treatment of carbapenem-resistant *A. baumannii* isolates. In a study in the USA, it was shown that the percentage of resistance to carbapenems in *A. baumannii* isolates increased from 21% in 2003–2005 to 48% in 2009–2012 (13). Several studies have shown that *A. baumannii* isolates retained their sensitivity to Colistin. In addition, the prescription of Colistin or Tigecycline, solely or in combination, has the ability to reduce the risk of mortality (30). However, *A. baumannii* has the potential to be resistant to both Colistin (31) and Tigecycline (32). Therefore, precise diagnosis using antibiogram according to up-to-date standards may prevent the development of resistant isolates and help to reduce the burden of nosocomial infections. Based on various studies, the mortality rate related to nosocomial infections due to Acinetobacter species is approximately 7.8% to 23% (27, 33). The reason for this increasing incidence of MDR strains in ICUs may be the severity of underlying conditions, the excessive use of antimicrobials, lower hygiene, and inappropriate disinfection strategies to control the infections in ICU (10). In addition, several genetic properties may contribute to antibiotic resistance such as antibiotic efflux, enzymatic inactivation (eg, AmpC and OXA-like β-lactamases) and reduced permeability of the outer membrane. Hood et al reported that antibiotic efflux effectively contributes to NaCl-induced tolerance to Levofloxacin and Amikacin, whereas different mechanisms are involved in inducing the tolerance to Imipenem and Colistin. NaCl mediates tolerance to Colistin in MDR *A. baumannii* isolates. However, this study did not evaluate the concentrations of NaCl in the specimens (34).

Ayyıldız et al indicated that 8.8% of the patients in the ICU had *A. baumannii* when they were using extracorporeal membrane oxygenation (ECMO) as a standard technique to support temporary cardiovascular and respiratory aid to the patients in ICU (35). Moreover, Lee et al showed that 7.5% of the patients were colonized with MDR *A. baumannii*. Compared to uncolonized patients, the colonized patients presented an elevated mortality rate; also, the ICU length of stay (LOS) was significantly higher in colonized patients than in uncolonized patients (36). Based on the data of this study, the shortest LOS for patients with MDR *A. baumannii* in the ICU was 3 days, while the longest LOS was 98 days.

In a study conducted by Pérez-Pedrero et al, it was concluded that the treatment with Colistin inhalation would improve the results in patients with pulmonary infections of the *A. baumannii*. They also stated that Colistin inhalation should be used as an adjuvant therapy with intravenous therapy in patients with acute respiratory infection caused by *A. baumannii* (37). In another study conducted by Chan et al on 55 patients, it was revealed that pneumonia associated with ventilator in Carbapenem-resistant *A. baumannii* can be effectively treated with second-line drugs. However, it is unclear whether combined therapy has a better effect (9). Joung et al performed a study over a period of 6 years in 116 patients with Acinetobacter-acquired pneumonia. They reported that inappropriate antimicrobial treatment for *A. baumannii* has been associated with adverse outcomes. Physicians should be aware that appropriate antibacterial therapy must be prescribed immediately to reduce the risk of adverse outcomes if *A. baumannii* is isolated from respiratory specimens of patients (38). In a study conducted by Erbay et al on 103 patients with blood-associated infections due to *A. baumannii*, the delay in receiving proper treatment resulted in poor clinical outcomes in the patients. The use of more severe empirical treatment can be considered in hospitals where *A. baumannii* isolates have high resistance (39). This study had several limitations. First, it was not possible to provide documents to describe resistance mechanisms. A better understanding of possible mechanisms may help prevention and control approaches. Second, it is hard to generalize the findings to all areas of other wards or regions. Third, this was a cross sectional study and further investigation is needed at other hospitals and wards to follow up the alterations in resistance status of this microorganism.

Conclusion

This study presented an increased prevalence of antibiotic-resistant *Acinetobacter baumannii* strains in ICU. The findings demonstrated that *A. baumannii* strains isolated from postcardiac surgery ICUs had a high prevalence and sensitivity to Meropenem and Colistin. However, more precise and accurate culture methods and molecular techniques are required to monitor nosocomial infections. Therefore, the treatment of the patients hospitalized in ICUs may be more achievable by prescribing appropriate antibiotic therapy and infection control policies by precise disinfection strategies.

Conflict of Interests

The authors declare that they have no competing interests.

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