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Factors influencing survival in patients with multidrug-resistant *Acinetobacter baumannii* infection

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A B S T R A C T

Multidrug-resistant (MDR) *Acinetobacter baumannii* (Acb) is a rapidly emerging pathogen in healthcare settings. The aim of this study was to evaluate the predictors of poor outcome in patients with MDR Acb. This is the first report documenting factors influencing survival in patients with MDR Acb in this tertiary hospital. This study is a prospective of the hospital epidemiology database. A total of 73 patients with 84 Acb isolates were obtained between August 2009 and October 2010 in this hospital. In the present study, the 30-day mortality rate was 39.7%. Of 84 Acb isolates, 50 (59%) were MDR, nine (11%) were pan-resistant, and 25 (30%) were non-MDR. The non-MDR isolates were used as the control group. The factors significantly associated with multidrug resistance included previous surgeries, presence of comorbidity (renal disease), use of more than two devices, parenteral nutrition, and inappropriate antimicrobial therapy. Significant predictors of 30-day mortality in the univariate analysis included pneumonia, diabetes mellitus, renal disease, use of more than two devices, and inappropriate antimicrobial therapy administered within two days of the onset of infection. The factors associated with mortality in patients with MDR Acb infection in this study were: age ≥ 60 years, pneumonia, diabetes mellitus, renal disease, use of more than two invasive procedures, and inappropriate antimicrobial therapy. Vigilance is needed to prevent outbreaks of this opportunistic and deadly pathogen.

Introduction

Acinetobacter baumannii (Acb), found ubiquitously in the environment, is an aerobic Gram-negative rod which is a non-fermenter of glucose.[1] Multidrug-resistant (MDR) Acb is a rapidly emerging pathogen in healthcare settings. Carbapenems are often used as last resort antibiotics to treat MDR gram-negative bacteria infections.[2] The aim of this study was to evaluate predictors of poor outcome in patients infected with MDR Acb.

Methods

Setting

This research was approved by the Microbiology Laboratory and by the Ethics Committee on Human Research of the Universidade Federal de Uberlândia (Opinion No. 479/09). The university hospital is a 530-bed teaching tertiary safety net hospital. The intensive care unit has 30 beds and combines general medical unit and a semi-closed surgical unit.

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Study design

This study was a prospective study of the hospital epidemiology database and included 84 isolates of Acb from 73 patients for the period of August 2009 to October 2010. Patients with more than one isolate were counted only once. Documented patient demographics and potential risk factors included diagnosis, duration of hospitalization, intensive care unit (ICU) stay, patient location, age, gender, race, previous hospitalization, previous surgeries, previous antibiotic use, any kind of medical intervention, such as the need for mechanical ventilation, central vascular catheters, tracheostomy, and parenteral nutrition, and the patients' medical histories, including underlying malignancy, diabetes mellitus, renal disease, acquired immunodeficiency syndrome (AIDS), and chronic obstructive lung disease. The source of the Acb isolates was also noted.

Identification and characterization of MRD Acb

Identification of *Acinetobacter* and susceptibility testing was performed using Vitek 2. Testing was carried on according to the manufacturer's specifications for this instrument, and was done in accordance with the Clinical and Laboratory Standards Institute[3] recommended practices.

An isolate was deemed pan-resistant if it was resistant to all commonly tested antibiotics except colistin. MDR Acb isolates were defined as those resistant to more than three classes of antibiotics.

Appropriate therapy was defined as one or more agents active against the Acb complex, given with adequate dosage and route of administration, not later than 24h after the culture was obtained.

Statistical analysis

Patients were stratified into two groups according to multidrug resistance. Continuous variables were expressed as mean ± standard deviation, and categorical variables were expressed as a percentage of the total number of patients analyzed. The chi-square test with Yates's correction or Fisher's exact test were used for categorical variables. A p-value less than 0.05 was considered statistically significant. All statistical analyses were performed with the Statistical Package for Social Sciences, version 17 (SPSS Inc. – Chicago, IL, USA).

Results

A total of 73 patients were studied and 84 Acb isolates were obtained between August 2009 and October 2010 in the tertiary hospital. These infections were endemic. The mean age of the patients was 57.8 years, and 49 (67.1%) patients were male. Twenty three (31.5%) patients underwent surgeries. The most frequent comorbidity was renal disease in 22/73 (30.1%), followed by malignancy in 10/73 (13.7%), and diabetes mellitus in 8/73 (10.9%). Forty seven patients (64.4%) required more than two devices; mechanical ventilation in 45 patients (61.6%); central vascular catheters in 44 patients (60.3%); tracheostomy in 25 patients (34.2%); and parenteral nutrition in 25 patients (34.2%). Empiric antimicrobial therapy was administered in 58 (79.1%) patients. The rate of inappropriate antimicrobial therapy was 41.1%. The 30-day mortality rate was 39.7%. Patient characteristics, underlying conditions, and disease-related characteristics are listed in Table 1.

The sites of Acb isolation in patients were blood stream and vascular catheters in 33 (39.3%), respiratory tract in 27 (32.1%), and urinary tract in 15 (17.8%).

Of the 84 Acb isolates, 50 (59%) were MDR, nine (11%) were pan-resistant, and 25 (30%) were non-MDR. Using the non-MDR isolates as the control group, the risk factors for the acquisition of MDR Acb were calculated (Table 2). The factors significantly associated with multidrug resistance included previous surgery, presence of comorbidity (renal disease), use of more than two devices, parenteral nutrition, and inappropriate antimicrobial therapy.

Significant predictors of 30-day mortality in the univariate analysis included patients with pneumonia, diabetes mellitus, renal disease, use of more than two devices, and inappropriate antimicrobial therapy administered within two days of infection onset (Table 3).

Table 1 - Patient characteristics, underlying conditions and disease-related characteristics in patients with *Acinetobacter baumannii* (Acb) infections from August 2009 to October 2010 at the Hospital das Clínicas, Universidade Federal de Uberlândia, MG, Brazil

Characteristics	Patients n = 73 (%)
Age, years median years (minimum-maximum)	57.8 (0-94)
Gender (male)	49 (67.1)
Duration of hospital stay before Acb infection median days (minimum-maximum)	49.5 (1-224)
Admission	
Clinic	49 (67.1)
Surgical	7 (9.6)
Trauma	17 (23.3)
Admitted to intensive care unit	25 (34.2)
Any surgical procedure	23 (31.5)
Comorbidity	
Diabetes mellitus	8 (10.9)
Renal disease	22 (30.1)
Malignancy	10 (13.7)
Acquired immunodeficiency syndrome	2 (2.7)
Chronic obstrutive lung disease	2 (2.7)
Invasive procedures	
More than two	47 (64.4)
Central venous catheter	44 (60.3)
Mechanical ventilation	45 (61.6)
Tracheostomy	25 (34.2)
Parenteral nutrition	25 (34.2)
Empiric antimicrobial therapy	58 (79.4)
Inappropriate antimicrobial therapy	30 (41.1)
Total mortality (30 days after infection)	29 (39.7)

Acb, *Acinetobacter baumannii*.

Table 2 - Risk factors for 73 multi-resistant Acb isolates

Characteristics	Acb MDR n = 49(%)	Acb-non-MDR n = 24(%)	p*	OR (95% CI)
Age, years median years (minimum-maximum)	62 (18-93)	46 (2m-84)		NA
Gender (male)	31 (63.3)	17 (70.8)	014	0.71 (0.22-2,28)
Duration of hospital stay before Acb infection median days (minimum-maximum)	55 (1-224)	36 (1-112)		NA
Presence in intensive care unit	15 (30.6)	10 (41.7)	0.45	0.62 (0.2-1,92)
Comorbidity				
Diabetes mellitus	5 (10.2)	3 (12.5)	1.00	0.8 (0.14-4,71)
Acute renal failure	15 (30.6)	7 (29.2)	0.02	1.07 (0.33-3,57)
Malignancy	8 (16.3)	2 (8.3)	0.48	2.15 (0.37-16.1)
Acquired immunodeficiency syndrome	2 (4.1)	0	1.00	Indefinite
Chronic obstrutive lung disease	1 (2.1)	1 (4.2)	1.00	0.48 (0.01-18.51)
Invasive procedures				
More than two	38 (77.6)	9 (37.5)	0.001	5.76 (1.76-19.4)
Central venous catheter	31 (63.3)	13 (54.2)	0.62	1,46 (0.48-4.41)
Mechanical ventilation	32 (65.3)	13 (54.2)	0.50	1.59 (0.53-4.85)
Tracheostomy	19 (38.8)	6 (25)	0.36	1.9 (0.57-6.52)
Parenteral nutrition	17 (34.7)	8 (33.3)	0.02	1.06 (0.34-3.39)
Empiric antimicrobial therapy	40 (81.3)	18 (75)	0.54	1.48 (0.39-5.52)
Inappropriate antimicrobial therapy	20 (40.8)	10 (41.7)	0.03	0.97 (0.32-2.92)
Total mortality (30 days after infection)	21 (42.9)	8 (33.3)	0.28	1.50 (0.48-4.72)

Acb, *Acinetobacter baumannii*; Acb MDR, multidrug resistant *Acinetobacter baumannii*; Acb-non-MDR, non-multidrug resistant *Acinetobacter baumannii*; OR, odds ratio; 95% CI, confidence interval; NA, non applicable; *p ≤ 0,05.

Discussion

Infections caused by Acb are of great concern worldwide. This is the first report documenting factors influencing survival in patients with MDR Acb infection in this hospital. Although many studies across the world on Acb have been reported, most have involved populations with both monomicrobial and polymicrobial infections. In the present study, only patients with monomicrobial infection were selected. Acb is usually considered a healthcare-associated pathogen, and reports on the incidence of nosocomial Acb outbreaks has been increasing.[4] Several investigators have found an association of MDR Acb with co-morbidities.[5] The lethality rate due to Acb is high, ranging from 22% to 59%.[6,7] In the present study, the 30-day mortality rate was 39.7%. The significant factors for MDR Acb infection were any surgical procedure, acute renal failure, more than two invasive procedures, parenteral nutrition, and inappropriate antimicrobial therapy. These findings are consistent with other reports, but this is the first prospective study in this hospital to provide detailed epidemiological characteristics and outcomes of patients with Acb infections.

Several studies have demonstrated that the severity of the underlying diseases, ventilator-associated pneumonia, or wound infection can be sources of bacteremia and that long-term ventilator support, recent surgery, carbapenem resistance, and inappropriate use of antibacterial agents are associated with poor outcome in *Acinetobacter* bacteremia.[8,9] Although the available evidence suggests a significant effect on patient outcome in terms of prolonged hospital stay and duration of mechanical ventilation, the attributable mortality of MDR infections remains arguable.[10,11] In the present study, bacteremia, surgical procedure, malignancy, central venous catheter, mechanical ventilation, parenteral nutrition, and empiric antimicrobial therapy were not significantly associated with 30-day mortality. Univariate analysis showed that pneumonia, diabetes mellitus, renal disease, use of more than two devices, and inappropriate antimicrobial therapy administered within two days of infection onset were associated with increased mortality. The impact of inappropriate antimicrobial therapy and antibiotic resistant strains are not negligible and should, therefore, be verified by further prospective and randomized studies.

Table 3 - Univariate analysis of predictive factors of mortality in patients with *Acinetobacter baumannii* infection during the period of August 2009 to October 2010

Predictive factors	Mortality/total (%)	Univariate analysis p* (OR)
Age (years)		
≥ 60	21/40	0.02* (3.45)
< 60	8/33	
Bacteremia		
MDR	12/21	0,62 (1.87)
Non-MDR	5/12	
Pneumonia		
MDR	11/23	0.002* (Indefinite)
Non-MDR	0/14	
Surgical procedure		
Yes	5/23	0.06 (0.3)
No	24/50	
Diabetes mellitus		
Yes	6/8	0.05* (5.48)
No	23/65	
Renal disease		
Yes	15/22	0.002* (5.66)
No	14/51	
Malignancy		
Yes	2/10	0.29 (0.33)
No	27/63	
Use more than two invasive procedures		
Yes	12/47	0.002* (0.18)
No	17/26	
Central venous catheter		
Yes	21/44	0.13 (2.4)
No	8/29	
Mechanical ventilation		
Yes	19/45	0.75 (1.32)
No	10/28	
Parenteral nutrition		
Yes	9/25	0.82 (0.79)
No	20/48	
Empiric antimicrobial therapy		
Yes	22/58	0.74 (0.70)
No	7/15	
Inappropriate antimicrobial therapy		
Yes	22/30	0.0000032* (14.14)
No	7/43	

MDR, multidrug-resistant; OR, odds ratio; *p ≤ 0,05.

Conclusion

The factors associated with mortality in patients with MDR Acb infection in this study were age ≥ 60 years, pneumonia, diabetes mellitus, renal disease, use of more than two invasive procedures, and inappropriate antimicrobial therapy. Acb has emerged as an important nosocomial pathogen and infections due to MDR strains have been difficult to control, especially in intensive care units. Vigilance is needed to prevent outbreaks of this opportunistic and deadly pathogen.

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Conflict of interest

All authors declare to have no conflict of interest.

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