Clinical characteristics of 1,260 patients during an outbreak of carbapenem-resistant *Acinetobacter* spp. in Porto Alegre, Brazil

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ABSTRACT

BACKGROUND: Over the last decade, *Acinetobacter baumannii* has been an important cause of nosocomial infections worldwide.

AIM: To assess clinical and epidemiological characteristics of patients during a large citywide outbreak of carbapenem-resistant *A. baumannii* (CRAB).

METHODS: Retrospective cross-sectional study that evaluated the information obtained from the official notification system for CRAB within the Municipal Health Department, Porto Alegre, Brazil, in the period of July 1st, 2007 to December 31st, 2008.

RESULTS: A total of 1,260 CRAB from infection (608 [48.3%]) or colonization (652 [51.7%]) were reported in 18 hospitals. Most patients (53.5%) were hospitalized at intensive care units and have been exposed to invasive procedures, but 757 (60.7%) patients had no underlying comorbidity reported. A total of 1,143 (90.7%) patients received some antimicrobial 90 days before CRAB detection and 36.4% received a carbapenem. Data on the outcome were available for 618 (49.0%) patients and 54.3% of them died. Infection was significantly more common in patients admitted to public hospitals; with trauma, with exposure to antibiotics in the previous 90 days, and in patients submitted to invasive procedures.

CONCLUSION: This study suggests that in the context of an outbreak, baseline comorbidities and previous carbapenem exposure may be less important risk factors for CRAB infection/colonization.

Keywords: Carbapenem; multidrug-resistance; Acinetobacter baumannii; Infection control.

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Acinetobacter baumanii has been an important cause of infection among hospitalized patients in many countries (1). These opportunistic pathogens are responsible for ventilator-associated pneumonia, bacteremia, surgical wound, and urinary tract infections particularly in patients admitted to intensive care units (ICUs) (1).

In Brazil, carbapenem-resistant *Acinetobacter baumannii-calcoaceticus* complex (CRAB has been described since 1993 (2), and it is now an endemic pathogen acknowledged as a major cause of nosocomial infections (3). CRAB has been described mainly in severely ill patients with previous antimicrobial use, especially carbapenem (1). Porto Alegre is the capital of Rio Grande do Sul, the southernmost Brazilian state. It has 1.4 million inhabitants and more than 7,000 hospital beds including public and private hospitals. In early 2007, a large outbreak of CRAB affecting all hospitals from this city was observed. The microbiological characteristics and molecular epidemiology of this outbreak have been detailed elsewhere (3). The objective of this study was to describe clinical and epidemiological characteristics of patients colonized or infected by CRAB during this citywide outbreak.

METHODS

From July 1st, 2007 to December 31st, 2008, all cases of CRAB reported to the Local Health Department (LHD) from a total of 18 hospitals were analyzed. Cases were defined as any patient who presented CRAB isolates after 48 hours of hospital admission, and were classified as an infection or colonization in accordance with NHSN criteria (4). Only the first notification of each patient was considered in this study.

Data were collected by a member of the infection control committee of each institution, who was trained to complete a notification form sheet. The infection control services of each institution received written guidelines for correct completion of the notification form. The notification system provided information on demographic, clinical findings, and outcomes of patients from whom a CRAB had been recovered. The notification was completed and forwarded via mail or email to LHD. The Clinical and epidemiological data investigated were those described in Table 1. Data analysis was performed with all valid cases (cases for which data were available). The prevalence ratio was calculated by univariate analysis to describe colonized or infected patients.

Bacterial identification was performed at each hospital using an automated identification system and/or standard phenotypic reference methods in the microbiology laboratories. In this study we will consider the identification to the genus level (*Acinetobacter* spp.) although most laboratories identified the bacteria as *A. baumannii-calcoaceticus* complex level. The antimicrobial susceptibility tests were performed and interpreted according to the Clinical and Laboratory Standards Institute (CLSI) (5).

RESULTS

A total of 1,260 documented CRAB cases were reported from patients attending hospitals during the study period. The majority of patients were male (59.5%), older than 50 years (54.34 ± 22.35 years), with hospital admission at the Brazilian Public Unified Health System (85.2%), and without hospitalization in the previous 90 days (Table 1). The specimens were mostly (78.2%) obtained from the lower respiratory tract or from the skin or rectal swabs as surveillance culture. More than 70% of patients with CRAB had been submitted to an invasive procedure although most of them had no underlying disease. A total of 1,143 patients received some antimicrobial within the last 90 days before CRAB detection. The antimicrobial most widely used was penicillin (748; 65.6%), followed by carbapenems (415; 36.4%), quinolones (340; 29.7%), and cephalosporins (313; 27.4%). Outcome data were available for 639 patients at the moment of data collection (Table 1).

We were able to establish that 625 patients were colonized and 626 were infected by CRAB, according to the NHS. Considering different hospital units, we found that most patients at ICUs (61.0%) were infected, while in clinical units most patients (63.6%) were colonized by CRAB.

The prevalence ratio (PR) of infection was statistically significant for patients that were hospitalized in public hospitals (PR = 1.504; CI 95% = 1.342-1.686); had trauma (PR = 1.465; CI 95% = 1.283-1.673), and used antibiotic in the previous 90 days (PR = 1.957; IC 95% = 1.419-2.698). Moreover, the PR of infection was statistically significant for all invasive procedures described (Table 2).

Table 1: Clinical Characteristics of Patients colonized/infected by CRAb.

Variable	Valid cases (100%)	n (%)
Sex		
Male	1251	745 (59.5)
Female		506 (40.5)
Type of Hospital Admission	1246	
Public Health System		1062 (85.2)
Private		184 (14.8)
Hospitalization in previous 90 days	1255	353 (28.1)
Isolation Site	1258	
Lower respiratory tract		508 (40.4)
Surveillance culture[1]		476 (37.8)
Blood		123 (9.8)
Urine		106 (8.4)
CSF		6 (0.5)
Wound		39 (3.1)
Invasive Procedure	1251	
MV[2]		757 (60.5)
SV[3]		945 (75.5)
CVC[4]		918 (73.3)
Surgery		625 (50.4)
Underlying Disease	1248	
Heart disease		488 (39.1)
Chronic kidney disease		345 (27.6)
Chronic lung disease		258 (20.7)
Diabetes		256 (20.5)
Cerebrovascular disease		208 (16.7)
Imunossupression		171 (13.7)
Trauma		111 (8.8)
No underlying Disease		757 (60.5)
Use of antibiotic in previous 90 days	1137	
Penicilin		748 (65.8)
Carbapenem		415 (36.5)
Quinolone		340 (29.9)
Cephalosporin		313 (27.5)
Aminoglycoside		176 (15.4)
Polymyxin		43 (3.78)
Tetracycline		13 (1.14)
Outcomes	1085	
Crude Mortality		347 (31.2)
Hospital discharge		292 (26.9)
Not defined		446 (41.1)

[1]Skin or rectal swabs; [2]MV – mechanical ventilation; [3]UC- urinary catheter; [4]CVC – central venous catheter.
CSF: Cerebrospinal Fluid; MV: mechanical ventilation; UC: urinary catheter; CVC: central venous catheter.

Table 2: Prevalence ratio associated with infection or colonization of patients with CRAb.

Variable	n	Infected n (%)	Colonized n (%)	Prevalence ratio (CI 95%)[1]	p-value
Sex					
Male	745	386 (51.8)	359 (48.2)	0.915 (0.816-1.027)	0.128
Female	506	240 (47.4)	266 (52.6)		
Health System					
Public	1062	495 (46.6)	567 (53.6)	1.504 (1.342-1.686)	< 0.001
Private	184	129 (70.1)	55 (29.9)		
Hospitalization in previous 90 days	353	198 (56.1)	155 (43.9)	1.176 (1.048-1.319)	0.008
Invasive Procedure					
Surgery	625	345 (55.2)	280 (44.8)	1.227 (1.097-1.373)	<0.001
CVC[3]	918	535 (58.3)	383 (41.7)	2.111 (1.756-2.538)	<0.001
SV[4]	945	536 (56.7)	409 (43.3)	1.912 (1.592-2.296)	<0.001
MV[5]	757	455 (60.1)	302 (39.9)	1.728 (1.510-1.978)	<0.001
Underlying Disease					
Chronic lung disease	258	136 (52.7)	122 (47.3)	1.055 (0.925-1.204)	0.430
Heart disease	488	228 (46.7)	260 (53.3)	0.882 (0.785-0.990)	0.032
Trauma	111	79 (71.2)	32 (28.8)	1.465 (1.283-1.673)	<0.001
Diabetes	256	113 (44.1)	143 (55.9)	0.846 (0.780-0.983)	0.022
Imunossupression	171	100 (58.5)	71 (41.5)	1.188 (1.033-1.367)	0.024
Chronic kidney disease	345	194 (56.2)	151 (43.8)	1.162 (1.036-1.304)	0.013
Cerebrovascular disease	208	118 (56.7)	90 (43.3)	1.151 (1.007-1.316)	0.05
Use of antibiotic in previous 90 days	1137	599 (52.7)	538 (47.3)	1.957 (1.419-2.698)	<0.001
Outcomes					
Crude Mortality	347	114 (32.8)	233 (67.2)	1.751 (1.463-2.096)	<0.001

[1] CI – Confidence interval; [2]CVC – central venous catheter; [3]UC – urinary catheter ; [5] MV – mechanical ventilation.

DISCUSSION

Our study provides clinical information on a large number of patients, increasing the chances to detect distinct characteristics potentially associated with CRAB, which could not be detected in previous studies owing to the lower number of patients assessed. Actually, to the best of our knowledge this was the largest study assessing clinical characteristics of patients with CRAB.

In fact, our results corroborate the findings of previous studies which showed that most cases occur in patients submitted to invasive procedures at ICUs and who have been previously exposed to an antimicrobial agent (7,8). Indeed, approximately 60% of patients were under mechanical ventilation, a recognized risk factor for A. *baumannii* (1), around 75% of them had a central venous catheter and/or a urinary catheter, and half of them had been previously submitted to a surgical procedure. Although we have not assessed any severity of illness score, based on the findings above, we may infer that most patients were at least moderately, if not severely, ill when CRAB has been recovered, which is also an important factor associated with these organisms, despite the carbapenem susceptibility profile (8,9,10). However, it is of note that around 60% of patients had no comorbidity documented, what is in contrast to other studies which reported that at least another disease is usually documented (7,8). The high proportion of patients with no underlying disease might be a particular characteristic associated with large and uncontrolled CRAB dissemination. Importantly, in this study trauma was associated with CRAB infection as already reported in soldiers at war (11).

Additionally, it is interesting that only one-third of patients have received a carbapenem in the last 90 days, which is a main, if not the major, risk factor for CRAB infection/colonization, according to other studies (8,9,10).

The risk factors observed for CRAB infections were actually those associated with nosocomial infections. A large number of patients analyzed in our study provided useful information regarding the relation between infection and colonization, which allows us to consider that any 'clinical adverse characteristic' may increase the risk for infection by these organisms.

Most cases in our city could be associated to the overcrowding of the health services and the reduced staff for patient assistance in many institutions. This may facilitate horizontal transmission, as occurred in this large outbreak, and was already demonstrated through the molecular analysis of the isolates (3). Although private hospitals were also involved in the outbreak, most patients originated from public hospitals, where such conditions may be exacerbated. Probably, poor adhesion to the infection control measures may also explain (10,12) at least partially, the spreading of CRAB through many hospitals. In summary, this large study strengthens the evidence that ICU hospitalization, invasive procedures, use of previous antimicrobial treatment, and trauma are factors associated with CRAB infection. However, it suggests that in the context of a large outbreak, comorbidities may be less important risk factors for CRAB infection.

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