Original Article

Distribution pattern of carbapenemases and solitary contribution to resistance in clinical strains of *Acinetobacter baumannii*

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Background: This study aimed to investigate the distribution pattern of carbapenemases and evaluate their solitary contribution to carbapenem resistance.

Methods: One hundred and twelve isolates of *Acinetobacter baumannii* (*A. baumannii*) isolated from the intensive care unit (ICU) of a southern China tertiary hospital were identified, and antimicrobial susceptibility tests (ASTs) of these strains were determined. Common carbapenemases were detected and the distribution pattern of carbapenemases was analyzed. Logistic regression and general linear model analyzed were performed to identify the correlation between antimicrobial susceptibility and carbapenemase genes.

Results: These 112 strains were classified into a carbapenem-resistant *A. baumannii* (CRAB) group (71.7%) and a carbapenem-susceptible *A. baumannii* (CSAB) group (28.3%). Carbapenemase genes, including $bla_{\text{OXA-51-like}}$ (100.0%), bla_{OXA-23} (93.4%), IS*Aba1*/$bla_{\text{OXA-51-like}}$ (27.5%), $bla_{\text{NDM-1}}$ (8.8%), bla_{OXA-24} (2.2%) and bla_{OXA-58} (2.2%) were detected in CRAB strains, *and* no bla_{SIM}, bla_{VIM} and bla_{IMP} gene in these 112 isolates. There was a statistically significant difference between CSAB and CRAB group in carrying $bla_{\text{OXA-23}}$ (P<0.001) and IS*Aba1*/$bla_{\text{OXA-51-like}}$ (P=0.024).

Conclusions: A pattern of $bla_{\text{OXA-51-like}}$ (100.0%), bla_{OXA-23} (93.4%), $bla_{\text{NDM-1}}$ (8.8%), bla_{OXA-24} (2.2%) and bla_{OXA-58} (2.2%) was detected in CRAB strains. $Bla_{\text{OXA-23-like}}$ and IS*Aba1*/$bla_{\text{OXA-51-like}}$ complex might be more relevant to carbapenem resistance in *A. baumannii*. Harboring $bla_{\text{OXA-23-like}}$ and IS*Aba1*/$bla_{\text{OXA-51-like}}$ complex might increase the possibility of resistance 2.16 times [risk ratio (RR): 2.16; 95% confidence interval (CI): 1.04–4.51] and 1.29 times (RR: 1.29; 95% CI: 1.07–1.56), respectively.

Keywords: *Acinetobacter baumannii* (*A. baumannii*); multidrug resistance; carbapenem; infection; imipenem

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Introduction

Acinetobacter baumannii (*A. baumannii*) is an important nosocomial pathogen. Clinically, it causes ventilator-associated pneumonia, surgical wound infection, meningitis etc., especially in immune-compromised patients (1,2). As reported in reviews dating back to the 1970s, hospital-acquired pneumonia, especial ventilator-associated pneumonia, was the most common infection caused by *A. baumannii* (3). According to data of China Bacterial Resistance Monitoring Network (CHINET), *A. baumannii* accounted for 9.08% of the total clinical pathogenic isolates and became the third most gram-negative bacteria in the

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clinical bacteria in 2019 in China.

The risk factors of *A. baumannii* infection include invasive operations, surgical treatment and immunosuppression etc. Patients with severe basic diseases in intensive care unit (ICU) commonly need a variety of invasive surgeries and the use of high-dose broad-spectrum antibiotics, which usually leads to internal microecological imbalance and high risk of *A. baumannii* infection. Infection of *A. baumannii* always means a prolonged hospital stay and high mortality. The mortality rate of *A. baumannii* infection is 7.8% to 23% in hospital and 10% to 43% in ICU (4).

The powerful resistance of *A. baumannii* has been becoming a serious public health problem. Multidrug resistant (MDR), extensively drug resistant and even pan drug resistant strains have been commonly emerging in clinical wards, especially in ICU wards. Carbapenems, such as imipenem and meropenem, either alone or in combination with other category of antibiotics, were once effective therapeutic regimens for *A. baumannii* infections. However, clinical isolates of carbapenem-resistant *A. baumannii* (CRAB) have notably increased in recent years, and data from CHINET showed that resistance rate to imipenem has increased to 73.6% and 75.1% in 2019 in China. The CRAB epidemic has become a critical infection problem.

Several resistance mechanisms are involved in *A. baumannii* carbapenem resistance. Generally, production of carbapenemase is thought to be an effective way. Common carbapenemases include OXA-type carbapenemases (5-9) and metallo-β-lactamases (MBLs) (5,10,11). In addition, up-regulated expression of efflux pump genes (especially AdeABC pump), and down-regulated expression of porin genes may also be associated with carbapenem resistance (12-15).

Surveillance of carbapenemase harboring pattern is necessary for guiding targeted clinical medication in different geographical origin. The drug resistance of *A. baumannii* isolates in different areas is different. There were several reports about carbapenemase harboring pattern in *A. baumannii* in different areas. However, as far as we know, few studies have focused on the distribution pattern of carbapenem in southern China and the specific contribution of different carbapenems to carbapenem antibiotic resistance. This study aims to investigate the distribution pattern of carbapenemases to evaluate (using statistical methods) their solitary contribution to carbapenem resistance.

We present the following article in accordance with the MDAR reporting checklist (available at https://dx.doi.org/10.21037/apm-21-1805).

Methods

Isolation and identification of strains

In total, 125 non-repetitive strains of the *Acinetobacter calcoaceticus-Acinetobacter baumannii* complex were collected from the patients of ICU of a tertiary hospital, Shenzhen, China, from July 2018 to June 2019. The specimen source included sputum, nasal secretion samples, etc.

The collected strains were inoculated on McConkey plate, and the single colony overnight was used for identification. According to the manufacturer's guidelines, 125 isolates were identified as *Acinetobacter calcoaceticus-Acinetobacter baumannii* complex using the AutoMicrobic system Gram-Negative Identification Card on microbiology analyzer VITEK 2 system (Biomerieux, France). 112 in 125 isolates were further confirmed as *A. baumannii* by *rpoB* gene sequence analysis assays according to previous established polymerase chain reaction (PCR) conditions.

This study was approved by the Ethics Committee of the First Affiliated Hospital of Shenzhen University (ID: 20200511007). This was a retrospective study obtaining data from hospital's information system. The results of this study may benefit patients with *A. baumannii* infection and may lead to better therapeutic outcomes. The requirement for informed consent of patients in this study was waived. All procedures performed in this study involving human participants were in accordance with the Declaration of Helsinki (as revised in 2013).

Antimicrobial susceptibility test (AST)

AST of these isolates was determined by an automated broth microdilution method (gram-negative susceptibility cards) using the VITEK 2 system. Susceptibility interpretation was based on clinical breakpoint from the Clinical and Laboratory Standards Institute (CLSI 2019, 29th edition; DocumentM100). These antimicrobials included cefazolin, cefotetan, ampicillin + sulbactam, piperacillin + tazobactam, ceftriaxone, ceftazidime, cefepime, ciprofloxacin, levofloxacin, tobramycin, gentamycin, nitrofurantoin. *Escherichia coli* ATCC 25922 and *Pseudomonas aeruginosa* ATCC 27853 were used as quality control.

According to AST result, 112 strains were divided into carbapenem-susceptible *A. baumannii* (CSAB) group and

Table 1 Primer sequences and amplicon size

Target genes	Primer sequence
rpoB	F: GAGTCTAATGGCGGTGGTTC
	R: ATTGCTTCATCTGCTGGTTG
OXA type carbapenemases	
$bla_{OXA-23-like}$	F: GAATATGTGCCAGCCTCTAC
	R: GCATTACCGAAACCAATACG
$bla_{OXA-24-like}$	F: TGGGTGGAGCAAGCTAATGG
	R: ACGAATAGAACCAGACATTCCTTCT
$bla_{OXA-51-like}$	F: TAATGCTTTGATCGGCCTTG
	R: TGGATTGCACTTCATCTTGG
$bla_{OXA-58-like}$	F: GACAATTACACCTATACAAGAAG
	R: AAACCCACATACCAACCC
ISAba1/bla_{OXA-51}	F: CACGAATGCAGAAGTTG
	R: CTTCTGTGGTGGTTGGC
MBLs type carbapenemases	
bla_{IMP}	F: GGAATAGAGTGGCTTAAYTC
	R: TCGGTTTAAYAAAACAACCACC
bla_{NDM-1}	F: GGTTTGGCGATCTGGTTTTC
	R: CGGAATGGCTCATCACGATC
bla_{NDM-1}	F: GAGTATTCAACATTTCCGTGTC
	R: TAATCAGTGAGGCACCTATCTC
bla_{SIM}	F: TACAAGGGATTCGGCATCG
	R: TAATGGCCTGTTCCCATGTG
bla_{VIM}	F: GATGGTGTTTGGTCGCATA
	R: CGAATGCGCAGCACCAG
AdeABC efflux pump	
adeB	F: GCAGAGCGTACTCGGAATGT
	R: CCACTGAAACCCCATCCCAA

MBLs, metallo-β-lactamases.

CRAB group.

Detection of carbapenemase gene

Common carbapenemase genes of *A. baumannii*, including $bla_{OXA-51-like}$, $bla_{OXA-23-like}$, $bla_{OXA-24-like}$, $bla_{OXA-58-like}$, bla_{SIM}, bla_{VIM}, bla_{IMP}, bla_{NDM-1} and IS*Aba1*/$bla_{OXA-51-like}$ were detected according to previously established PCR conditions (13,16,17). All PCR primers used in this study were listed in *Table 1*. Four *A. baumannii* strains, ab606, ab608, ab609, and SZE, were used as positive quality control strains.

Statistical analysis

Stata/SE 15.1 (StataCorp LLC, TX, USA) was used for data entry and statistical analysis. All tests were two-tailed, and a P value ≤0.05 was considered statistically significant. Sample demographic and disease characteristic were compared using Pearson's chi-square test. AST and harboring of resistance genes were compared between the CSAB and CRAB group using Fisher-Exact test. Logistic Regression was used to assess the relations between harboring of resistance gene and antimicrobial susceptibility result. General regression model was used to make multivariate regression analysis of resistance genes and antimicrobial susceptibility results to calculate the risk ratio (RR).

Results

Clinical characteristics of A. baumannii strains

As summarized in *Table 2*, a total of 112 patients were included in this study, including 70 males (62.5%) and 42 females (37.5%). Seventy-eight (69.6%) patients were over 60 years old and 32 (28.6%) were between 16 to 59 years old. The causes of ICU admission were respiratory distress in 37 cases (33.0%), poor general condition in 27 cases (24.1%), trauma in 29 cases (25.9%), and other causes in 19 cases (17.0%).

AST

AST results of 112 *A. baumannii* strains are summarized in *Figure 1*. Of the 112 isolates, 21 strains (18.8%) were in CSAB group and 91 strains (81.2%) in CRAB group. CRAB strains showed almost 100% resistant to cephalosporins (ceftriaxone, ceftazidime, cefepime), over 70% resistant to quinolones (ciprofloxacin, levofloxacin) and aminoglycosides (tobramycin, gentamicin). In this study, there was evidence that the combination preparation such as sulbactam and cefoperazone was a reasonable choice for the treatment of CRAB infection.

Distribution of carbapenemase

As shown in *Table 3*, bla_{SIM}, bla_{VIM} and bla_{IMP} genes were not detected in any of the 112 isolates, and $bla_{OXA-51-like}$

gene was found in all 112 (100.0%) isolates. The positive rate of $bla_{\text{OXA-23-like}}$ was 93.4% in CRAB group, and 19% in CSAB group. Compared with CSAB, CRAB strains showed a statistically significant increasing distribution of $bla_{\text{OXA-23-like}}$ (P<0.001) and IS*Aba1*/$bla_{OXA\text{-}51\text{-}like}$ (P=0.024), respectively. $Bla_{\text{OXA-24-like}}$ and $bla_{\text{OXA-58-like}}$ were found in 2.2% strains, which belonged to CRAB group, and $bla_{NDM\text{-}1}$ gene was detected in 8.8% strains. No bla_{SIM}, bla_{VIM} and bla_{IMP} genes were detected in these isolates.

Table 2 Sample demographic and disease characteristic

Characteristics	Number	%
Age		
≤15	2	1.8
16–59	32	28.6
≥60	78	69.6
Gender		
Female	42	37.5
Male	70	62.5
Reason of ICU admission		
Respiratory distress	37	33.0
Poor general condition	27	24.1
Trauma	29	25.9
Others	19	17.0

ICU, intensive care unit.

Univariate logistic analysis and multivariate regression analysis for carbapenem resistance

As presented in *Table 4*, $bla_{\text{OXA-23-like}}$, $bla_{\text{OXA-24-like}}$, IS*Aba1*/$bla_{\text{OXA-51-like}}$, and *adeB* were included to perform the univariate logistic and multivariate regression analyses. Two variables, $bla_{\text{OXA-24-like}}$ and $bla_{\text{OXA-58-like}}$, were dropped automatically by Stata/SE statistical software.

Based on the result of multivariate regression analysis, carrying $bla_{\text{OXA-23-like}}$ and IS*Aba1*/$bla_{\text{OXA-51-like}}$ might increase the possibility of carbapenem resistance by 2.16 times [adjusted RR =2.16; 95% confidence interval (CI): 1.04–4.51] and 1.29 times (adjusted RR =1.29; 95% CI: 1.07–1.56), respectively.

Discussion

A. baumannii is an important nosocomial pathogen, which can cause ventilator-associated pneumonia, surgical wound infection, meningitis etc. *A. baumannii* can enter the bloodstream and cause bacteremia, which may further develop into sepsis. *A. baumannii* infection leads to a high clinical mortality. In this decade, an increasing number of

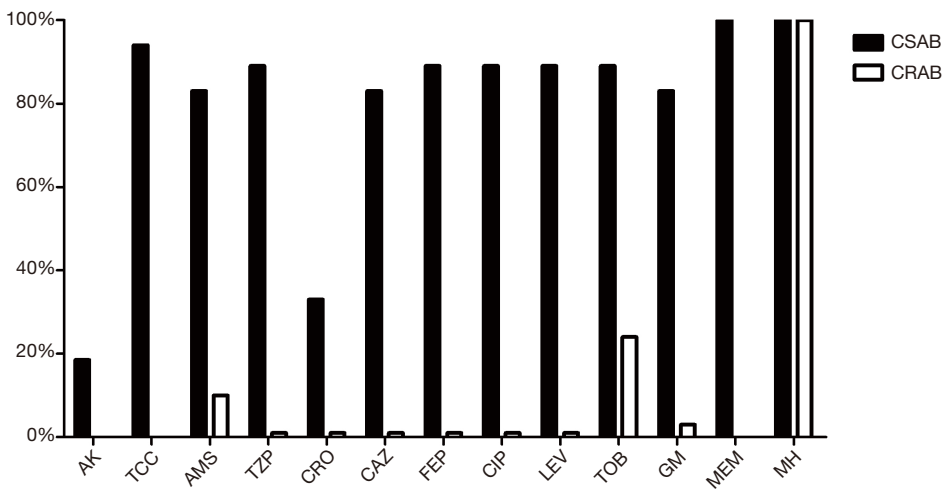

Figure 1 Percentage of antibiotic sensitivity of CSAB and CRAB strains. CSAB, carbapenem-susceptible *A. baumannii*; CRAB, carbapenem-resistant *A. baumannii*; *A. baumannii*, *Acinetobacter baumannii*; AK, amikacin; TCC, ticarcillin-clavulanic acid; AMS, ampicillin-sulbactam; TZP, piperacillin-tazobactam; CRO, ceftriaxone; CAZ, ceftazidime; FEP, cefepime; CIP, ciprofloxacin; LEV, levofloxacin; TOB, tobramycin; GM, gentamicin; MEM, meropenem; MH, minocycline.

Table 3 Distribution pattern of carbapenemases

Gene	CRAB (n=91)		CSAB (n=21)		P value	Prevalence rate (%)
	N	Prevalence rate (%)	N	Prevalence rate (%)		
$bla_{OXA\text{-}51\text{-}like}$	91	100.0	21	100.0	–	100.0
$bla_{OXA\text{-}23\text{-}like}$	85	93.4	4	19.0	<0.001	79.5
$bla_{OXA\text{-}24\text{-}like}$	2	2.2	0	0.0	–	1.8
$bla_{OXA\text{-}58\text{-}like}$	2	2.2	0	0.0	–	1.8
IS*Aba1*/$bla_{OXA\text{-}51\text{-}like}$	25	27.5	1	4.8	0.024	23.2
$bla_{NDM\text{-}1}$	8	8.8	0	0.0	0.348	7.1
bla_{SIM}	0	0.0	0	0.0	–	0.0
bla_{VIM}	0	0.0	0	0.0	–	0.0
bla_{IMP}	0	0.0	0	0.0	–	0.0

CRAB strains. CSAB, carbapenem-susceptible *A. baumannii*; CRAB, carbapenem-resistant *A. baumannii; A. baumannii, Acinetobacter baumannii*.

Table 4 Univariate logistic and multivariate regression analyses for carbapenem resistance

Variables	Carbapenem resistance					
	Univariate logistic analysis			Multivariate regression analysis		
	OR	P value	95% CI	RR	P value	95% CI
$bla_{OXA\text{-}23\text{-}like}$	7.62	<0.01	2.28–25.48	2.16	0.03	1.04–4.51
IS*Aba1*/$bla_{OXA\text{-}51\text{-}like}$	12.49	0.01	1.58–98.39	1.29	0.01	1.07–1.56

OR, odds ratio; CI, confidence interval; RR, risk ratio.

pan-drug resistant isolates have been reported globally. This indicated that *A. baumannii* strains with powerful resistance ability have been becoming a serious problem for clinical infection control. As reported, relevant mechanisms to carbapenem resistance include enzyme-hydrolyzing, overproduction of efflux pump, changing of outer membrane and biofilm formation (16-18). Monitoring molecular characteristic is necessary for taking effective measures to control clinical infection. In view of the complex mechanism of drug resistance, it is difficult to evaluate the contribution of different carbapenem enzymes. In this study, we found carrying $bla_{OXA\text{-}23\text{-}like}$ and IS*Aba1*/$bla_{OXA\text{-}51\text{-}like}$ might increase the possibility of carbapenem resistance by 2.16 times (adjusted RR=2.16; 95% CI: 1.04–4.51) and 1.29 times (adjusted RR=1.29; 95% CI: 1.07–1.56), respectively. Compared with CSAB strains, CRAB strains showed a statistically significant increasing distribution of $bla_{OXA\text{-}23\text{-}like}$ (P<0.001) and IS*Aba1*/$bla_{OXA\text{-}51\text{-}like}$ (P=0.024).

Elderly patients with underlying diseases, highly selective antibiotics and mechanical ventilation, are an important population for nosocomial infection of *A baumannii*. In this study, we found 69.9% of *A. baumannii* infected patients were ≥60 years old, and most of them had fundamental illness. We also found that 62.5% of infected patients were male and had an extended period of hospitalization, which was consistent with the report of Wisplinghoff *et al.* (19).

Carbapenem was once regarded as main antibacterial drug for *A. baumannii* infection (20), but the susceptibility has decreased in the recent years. In this study, 81.3% of *A. baumannii* isolates were CRAB, which was consistent with the report in Thailand (21). The resistance rate of ceftazidime and other third generation cephalosporins was over 75%, and that of solitary quinolones or aminoglycosides was basically over 60%.

Clinically, a combination of different category of antibiotic is common option for CRAB infection (22). The combination of cefoperazone and sulbactam showed a good

performance in treating infection of CRAB. Tigecycline and polymyxin are other drugs commonly used in CRAB infection. Nevertheless, the effect of tigecycline remains controversial. Some research concluded that tigecycline was be effective, but other clinical research regarded tigecycline might be associated with higher in-hospital mortality and lower microbial eradication rate (23,24).

Strong resistance of *A. baumannii* is due to its genomic plasticity. Under selective pressure of antibiotics, *A. baumannii* can acquire resistance through two ways: (I) integration of resistance determinants by horizontal transfer of mobile elements (25); and (II) regulation intrinsic resistance mechanisms, including up-regulation of some intrinsic hydrolases and efflux pumps, down-regulation of membrane permeability, formation of biofilm (1,2,26-29).

Carbapenemases are β-lactamases that confer resistance to carbapenem, penicillin and cephalosporin. According to the Ambler classification system, common carbapenemases in *A. baumannii* include B class (MBLs) and D class (OXA-type carbapenemases). The former includes bla_{SIM}, bla_{VIM}, bla_{IMP}, and bla_{NDM}. The latter includes $bla_{OXA-51-like}$, $bla_{OXA-23-like}$, $bla_{OXA-24-like}$, and $bla_{OXA-58-like}$. $Bla_{OXA-23-like}$ gene cluster (encoding OXA-23, OXA-27 and OXA-49) has been shown to contribute to carbapenem resistance. $Bla_{OXA-24-like}$ is another OXA type carbapenemase gene cluster, which encodes OXA-24, -25, -26, and -40.

The strains of different geographical origin had different carbapenemase harboring patterns. Koirala *et al.* found bla_{OXA-23} (52%) and bla_{OXA-40} (28%) were the most frequent genes among carbapenem non-susceptible isolates in Illinois (USA) (30). Indian scholar observed 97.7% of CRAB harboring $bla_{OXA-23-like}$ gene, bla_{NDM-1} (29.1%) and $bla_{OXA-58-like}$ (3.5%) in India (31). And in Thailand, a pattern of bla_{OXA-23} (82.6%), bla_{NDM-1} (9.1%), bla_{OXA-24} (0.3%) and bla_{OXA-58} (6.5%) was reported (21). In this study, we found a pattern of $bla_{OXA-51-like}$ (100.0%), bla_{OXA-23} (93.4%), bla_{NDM-1} (8.8%), bla_{OXA-24} (2.2%) and bla_{OXA-58} (2.2%) in CRAB strains. And the harboring of $bla_{OXA-23-like}$ increased the possibility of *A. baumannii* carbapenem resistance by 2.16 times (adjusted RR =2.16; 95% CI: 1.04–4.51) in these strains.

The chromosomal gene $bla_{OXA-51-like}$ is intrinsic in *A. baumannii*. Harboring $bla_{OXA-51-like}$ gene alone can hardly cause carbapenem resistance. IS*Aba1*/$bla_{OXA-51-like}$ complex is $bla_{OXA-51-like}$ with an additional genetic element IS*Aba1* upstream insertion. This structure can result in overexpression of OXA-51-like enzyme and confers resistance to carbapenems. Notably, in this study we detected 27.5% isolates carrying IS*Aba1*/$bla_{OXA-51-like}$, which belonged to CRAB group, and no IS*Aba1*/$bla_{OXA-51-like}$ complex was found in the CSAB strains. Also, the presence of IS*Aba1*/$bla_{OXA-51-like}$ complex was significantly associated with resistance of carbapenem (adjusted RR =1.29; 95% CI: 1.07–1.56), which indicated that IS*Aba1*/$bla_{OXA-51-like}$ could play an important role in carbapenem resistance.

Furthermore, over-expression of AdeABC efflux pump was associated with carbapenem resistance. In this study, we found no significant difference in carrying *adeB* gene between CRAB group and CSAB group (P=0.51>0.05). This result may be because our study only involved the detection of pump gene, but did not discuss the expression of this gene. We will conduct further research on the contribution of overproduction of different efflux pumps in the future.

A. baumannii drug resistance has been increasing in these years, which has brought severe challenge to clinical treatment. To reverse this situation, on the one hand, the use of antibiotics outside the indications should be strictly controlled and antibiotics should be selected according to the results of AST. On the other hand, we should strengthen the surveillance of distribution pattern of drug resistance genes to prevent or delay the emergence of drug-resistant strains.

Limitations

This study had several limitations. Firstly, the source of the strains was only from one hospital, and collection was conducted over a short period of time. Secondly, the regulation of efflux pump gene expression was not discussed in this study. This study only focused on the common drug resistance mechanism of *A. baumannii*, and did not involve other mechanisms, such as the low production of outer membrane protein affecting membrane permeability and the over production of efflux pump.

Conclusions

A pattern of $bla_{OXA-51-like}$ (100.0%), bla_{OXA-23} (93.4%), bla_{NDM-1} (8.8%), bla_{OXA-24} (2.2%) and bla_{OXA-58} (2.2%) was detected in CRAB strains, and $bla_{OXA-23-like}$ and IS*Aba1*/$bla_{OXA-51-like}$ complex might be more relevant to carbapenem resistance in *A. baumannii*. We also evaluated their solitary contribution to carbapenem resistance by statistical methods. These findings could help to develop effective regimens and prevention strategies for controlling *A.*

baumannii infections.

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Footnote

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. This study was approved by the Ethics Committee of the First Affiliated Hospital of Shenzhen University (ID: 20200511007). This was a retrospective study obtaining data from hospital's information system. The requirement for informed consent of patients in this study was waived. All procedures performed in this study involving human participants were in accordance with the Declaration of Helsinki (as revised in 2013).

References

1. Antunes LC, Visca P, Towner KJ, et al. Acinetobacter baumannii: evolution of a global pathogen. Pathog Dis 2014;71:292-301.
2. Harding CM, Hennon SW, Feldman MF. Uncovering the mechanisms of Acinetobacter baumannii virulence. Nat Rev Microbiol 2018;16:91-102.
3. Roca I, Espinal P, Vila-Farrés X, et al. The Acinetobacter baumannii oxymoron: commensal hospital dweller turned pan-drug-resistant menace. Front Microbiol 2012;3:148.
4. Falagas ME, Bliziotis IA, Siempos II, et al. Attributable mortality of Acinetobacter baumannii infections in critically ill patients: a systematic review of matched cohort and case-control studies. Crit Care 2006;10:R48.
5. Rodríguez CH, Nastro M, Famiglietti A. Carbapenemases in Acinetobacter baumannii. Review of their dissemination in Latin America. Rev Argent Microbiol 2018;50:327-33.
6. Mendes RE, Bell JM, Turnidge JD, et al. Emergence and widespread dissemination of OXA-23, -24/40 and -58 carbapenemases among Acinetobacter spp. in Asia-Pacific nations: report from the SENTRY Surveillance Program. J Antimicrob Chemother 2009;63:55-9.
7. Karampatakis T, Tsergouli K, Politi L, et al. Polyclonal predominance of concurrently producing OXA-23 and OXA-58 carbapenem-resistant Acinetobacter baumannii strains in a pediatric intensive care unit. Mol Biol Rep 2019;46:3497-500.
8. Opazo A, Domínguez M, Bello H, et al. OXA-type carbapenemases in Acinetobacter baumannii in South America. J Infect Dev Ctries 2012;6:311-6.
9. Nigro S, Hall RM, et al. Distribution of the blaOXA-23-containing transposons Tn2006 and Tn2008 in Australian carbapenem-resistant Acinetobacter baumannii isolates. J Antimicrob Chemother 2015;70:2409-11.
10. Routray A, Lavanya P, Soniya R, et al. Multiplex PCR for genes encoding prevalent OXA and NDM-1 carbapenemases in Acinetobacter. J Pharm Res 2013;7:324-6.
11. Maamar E, Alonso CA, Ferjani S, et al. NDM-1- and OXA-23-producing Acinetobacter baumannii isolated from intensive care unit patients in Tunisia. Int J Antimicrob Agents 2018;52:910-5.
12. Yang YS, Chen HY, Hsu WJ, et al. Overexpression of AdeABC efflux pump associated with tigecycline resistance in clinical Acinetobacter nosocomialis isolates. Clin Microbiol Infect 2019;25:512.e1-6.

13. Zhang Y, Li Z, He X, et al. Overproduction of efflux pumps caused reduced susceptibility to carbapenem under consecutive imipenem-selected stress in Acinetobacter baumannii. Infect Drug Resist 2018;11:457-67.
14. Nasr P. Genetics, epidemiology, and clinical manifestations of multidrug-resistant Acinetobacter baumannii. J Hosp Infect 2020;104:4-11.
15. El-Shazly S, Dashti A, Vali L, et al. Molecular epidemiology and characterization of multiple drug-resistant (MDR) clinical isolates of Acinetobacter baumannii. Int J Infect Dis 2015;41:42-9.
16. Mentasti M, Prime K, Sands K, et al. Rapid detection of OXA-23-like, OXA-24-like, and OXA-58-like carbapenemases from Acinetobacter species by real-time PCR. J Hosp Infect 2020;105:741-6.
17. Turton JF, Ward ME, Woodford N, et al. The role of ISAba1 in expression of OXA carbapenemase genes in Acinetobacter baumannii. FEMS Microbiol Lett 2006;258:72-7.
18. Abdi SN, Ghotaslou R, Ganbarov K, et al. Acinetobacter baumannii Efflux Pumps and Antibiotic Resistance. Infect Drug Resist 2020;13:423-34.
19. Wisplinghoff H, Perbix W, Seifert H, et al. Risk factors for nosocomial bloodstream infections due to Acinetobacter baumannii: a case-control study of adult burn patients. Clin Infect Dis 1999;28:59-66.
20. Doi Y. Treatment options for carbapenem-resistant gram-negative bacterial infections. Clin Infect Dis 2019;69:S565-75.
21. Leungtongkam U, Thummeepak R, Wongprachan S, et al. Dissemination of blaOXA-23, blaOXA-24, blaOXA-58, and blaNDM-1 Genes of Acinetobacter baumannii Isolates from Four Tertiary Hospitals in Thailand. Microb Drug Resist 2018;24:55-62.
22. Viehman JA, Nguyen MH, Doi Y, et al. Treatment options for carbapenem-resistant and extensively drug-resistant Acinetobacter baumannii infections. Drugs 2014;74:1315-33.
23. Ni W, Han Y, Zhao J, et al. Tigecycline treatment experience against multidrug-resistant Acinetobacter baumannii infections: a systematic review and meta-analysis. Int J Antimicrob Agents 2016;47:107-16.
24. Mei H, Yang T, Wang J, et al. Efficacy and safety of tigecycline in treatment of pneumonia caused by MDR Acinetobacter baumannii: a systematic review and meta-analysis. J Antimicrob Chemother 2019;74:3423-31.
25. Fournier PE, Vallenet D, Barbe V, et al. Comparative genomics of multidrug resistance in Acinetobacter baumannii. PLoS Genet 2006;2:e7.
26. Siroy A, Molle V, Lemaître-Guillier C, et al. Channel formation by CarO, the carbapenem resistance-associated outer membrane protein of Acinetobacter baumannii. Antimicrob Agents Chemother 2005;49:4876-83.
27. del Mar Tomás M, Beceiro A, Pérez A, et al. Cloning and functional analysis of the gene encoding the 33- to 36-kilodalton outer membrane protein associated with carbapenem resistance in Acinetobacter baumannii. Antimicrob Agents Chemother 2005;49:5172-5.
28. Rumbo C, Gato E, López M, et al. Contribution of efflux pumps, porins, and β-lactamases to multidrug resistance in clinical isolates of Acinetobacter baumannii. Antimicrob Agents Chemother 2013;57:5247-57.
29. Bratu S, Landman D, Martin DA, et al. Correlation of antimicrobial resistance with beta-lactamases, the OmpA-like porin, and efflux pumps in clinical isolates of Acinetobacter baumannii endemic to New York City. Antimicrob Agents Chemother 2008;52:2999-3005.
30. Koirala J, Tyagi I, Guntupalli L, et al. OXA-23 and OXA-40 producing carbapenem-resistant Acinetobacter baumannii in Central Illinois. Diagn Microbiol Infect Dis 2020;97:114999.
31. Kumar S, Patil PP, Singhal L, et al. Molecular epidemiology of carbapenem-resistant Acinetobacter baumannii isolates reveals the emergence of blaOXA-23 and blaNDM-1 encoding international clones in India. Infect Genet Evol 2019;75:103986.

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