

# Molecular Epidemiology of Bloodstream Infection-causing *Acinetobacter baumannii* from Five Tertiary Hospitals in Beijing, China

Ling Guo<sup>1</sup>, Chunmei Bao<sup>2</sup>, Jie Liu<sup>3</sup>, Xiuhong Hao<sup>4</sup>, Jingui Cao<sup>5</sup>, Liyan Ye<sup>1</sup> and Jiyong Yang<sup>1\*</sup>

<sup>1</sup>Department of Microbiology, Chinese PLA General Hospital, Beijing, 100853, China

<sup>2</sup>Clinical Diagnostic Center, 302nd Hospital of China, 100039, China

<sup>3</sup>Department of Laboratory, PLA Army General Hospital, Beijing, 100700, China

<sup>4</sup>Clinical Laboratory, Navy General Hospital, PLA, Beijing, 100048, China

<sup>5</sup>Department of Infection Control, Air Force General Hospital, PLA, Beijing, 100142, China

*Acinetobacter baumannii* has emerged as a pathogen that is commonly involved in various nosocomial infections and sometimes community-acquired infections over the last decade. Nosocomial *A. baumannii* infections mainly include ventilator-pneumonia (VAP), bloodstream infections (BSI), meningitis, and wound infections. Epidemiological studies indicate the mortality rates of *A. baumannii* infections have increased from 10 to 43% in intensive care units (ICUs) and from 7.8 to 23% outside ICUs. Multidrug-resistant (MDR) *A. baumannii* bacteremia usually leads to an even higher mortality [2, 3].

Another main reasons to study *A. baumannii* is its ability to acquire the resistance determinants that caused the emergence of MDR strains and the spread of the pathogen [4]. During the past decade, the terms 'pan-drug resistance', 'extensively drug resistance', and 'MDR' have commonly been applied to *A. baumannii* to described the phenotypes of resistance to all, to all but one or two, and to three or more classes of potentially effective antimicrobial agents, respectively [5, 6]. In recent years, the increasing trend of carbapenem resistance in bacteria has become a great concern because it dramatically limits the range of therapeutic alternatives [7, 8]. The most common mechanism of carbapenem resistance in *Acinetobacter* spp. is the production of carbapenem-hydrolyzing class

The aims of the present study were: (i) to identify the clonal relationship of *A. baumannii* strains associated with BSI from Beijing hospitals; (ii) to investigate the susceptibility rates among these strains; and (iii) to identify the carbapenem-hydrolyzing genes carried by these strains. In this study, we collected 97 clinical *A. baumannii* isolates from patients with nosocomial bloodstream infection from five tertiary hospitals in Beijing, China. All *A. baumannii* isolates were identified by VITEK MALDI-TOF Mass Spectroscopy or VITEKGN identification card (BioMérieux). Antimicrobial susceptibilities were determined by VITEKGN09 cards (BioMérieux) and the results were interpreted according to the CLSI interpretative criteria. Their genetic relationship was analyzed by pulsed-field gel electrophoresis (PFGE) according to the previously described methods [12]. Sequence type (ST) was evaluated by multi loci sequence typing (MLST) following the guidance of Pasteur Institute's MLST method. A multiplex PCR was used to screen the class D carbapenemase genes including *bla*<sub>OXA-51</sub>-like, *bla*<sub>OXA-23</sub>-like, *bla*<sub>OXA-40</sub>-like, and *bla*<sub>OXA-58</sub>-like genes [13]. The presence of other resistance determinants, including *bla*<sub>SIM</sub>, *bla*<sub>AIM</sub>, *bla*<sub>IMP</sub>, *bla*<sub>VIM</sub>, *bla*<sub>SIM</sub>, and *bla*<sub>NDM</sub>, was detected by several multiplex PCR using specific primers as reported previously [14].

PFGE analysis showed that 39 different types have been identified, designated types 1-39. Among them, 52 (53.6%) isolates belonged to type 1 and 45 (46.4%) belonged to other types. MLST analysis revealed that 73 stains were designated to 9 different existing STs and 24 stains belonged to new STs. The predominant ST, ST699, was found in 65

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isolates. ST63, ST64, ST68, ST338, ST359, ST396, ST667, or ST691 was only found in one isolate. eBURST analysis of the nine existing STs found in this study together with other profiles of the Institute Pasteur's MLST database showed that ST699 belongs to international CC2 [15].

*A. baumannii* is, in clinical terms, intrinsically resistant to ampicillin, amoxicillin-clavulanate, cefazolin, cefotaxime, ceftriaxone, ertapenem, trimethoprim, and fosfomycin. Antibiotics of choice for the treatment of *A. baumannii* infections include the aminoglycosides, fluoroquinolones, and carbapenems [16]. In our study, of the 97 *A. baumannii* isolates, 71 (73.2%) were resistant to amikacin, 73 (75.26%) were resistant to ciprofloxacin, and 64 (65.98%) were resistant to levofloxacin. The whole rate of imipenem susceptibility is 22.68% (22/97), and 17.02% (8/47), 73.33% (11/15), 27.27% (3/11), 0% (0/17), and 0% (0/7) among the strains isolated from the five hospitals, respectively. In the first hospital, the major ST type of the resistant isolates is ST699 (37/40), all of which can be detected with the *bla*<sub>OXA-23</sub>-like gene. The rate of imipenem susceptibility is 73.33% (11/15) in the second hospital, which is significantly higher than those of other hospitals. In addition, there were no ST699 in the isolates from this hospital and most isolates cannot be designated to specific STs except ST667 (n=1) and ST359 (ST=1). This is a hospital for infectious diseases, which might explain why the characteristics of the *A. baumannii* is different from others in terms of STs and drug resistance. In the other three hospitals, the result was similar to that in the first hospital: the main ST was ST699 and almost all the resistant can be detected with *bla*<sub>OXA-23</sub>-like gene.

**\*Corresponding Author:** Dr. Jiyong Yang, Department of Microbiology, Chinese PLA General Hospital, Beijing, 100853, China, Tel: +86 10 66936575, E-mail: yangjy301@hotmail.com

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Among the 75 isolates that resist to imipenem, resistance to carbapenems was related to *bla*<sub>OXA-23</sub>-like (n=66), both *bla*<sub>OXA-23</sub>-like and *bla*<sub>OXA-58</sub>-like (n=1), *bla*<sub>OXA-58</sub>-like (n=4), and *bla*<sub>NDM-1</sub> (n=2). No resistance genes that were described previously can be detected in the remaining two isolates.

In conclusion, we have documented the characteristics of BSI-causing *A.baumannii* isolates from five tertiary hospitals in Beijing, China. The carbapenem-resistant rate ranges from 78.32% and 91.36% among the four of five hospitals (no data could be obtained from the second hospital). There were intra-and inter-hospital outbreak spreads and ST699 belonging to international CC2 was the predominant disseminating clones. Further studies are warranted to investigate why the isolates from the second hospital are completely different from the others. The production of CHDLs, especially OXA-23, may play an important role in reducing imipenem susceptibility among the *A.baumannii* isolates. Our results are concordant with the observations that the *bla*<sub>OXA-23</sub>-like genes have disseminated in medical institutes worldwide including China [17-19]. We additionally identified two *bla*<sub>NDM-1</sub>-positive *A. baumannii* isolates. Previous studies showed that the patients with carbapenem-resistant *A. baumannii* bacteremia have higher mortality rate than those with carbapenem-susceptible *A. baumannii* bacteremia [20]. Therefore, given the high resistance rate to drugs especially carbapenems and the prevalence of high-risk clones, it is necessary to strengthen the monitoring to prevent and control the clinical infection of *A.baumannii* in nosocomial environment.

## Competing Interests

The authors declares that they have no competing interests.

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