UNIVERSITI TEKNOLOGI MARA

GENETIC PROFILING OF MULTIDRUG RESISTANT *Acinetobacter baumannii* ISOLATES FROM A TERTIARY HOSPITAL IN MALAYSIA

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MSc

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AUTHOR'S DECLARATION

I declare that the work in this thesis was carried out in accordance with the regulations of Universiti Teknologi MARA. It is original and is the results of my own work, unless otherwise indicated or acknowledged as referenced work. This thesis has not been submitted to any other academic institution or non-academic institution for any degree or qualification.

I, hereby, acknowledge that I have been supplied with the Academic Rules and Regulations for Post Graduate, Universiti Teknologi MARA, regulating the conduct of my study and research.

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ABSTRACT

Acinetobacter baumannii is ubiquitous in the hospital setting and nature, which often causes pneumonia, soft tissue infection, meningitis, and urinary tract infection. The emergence of multidrug resistant (MDR) *A. baumannii* is worrisome as it limits an appropriate number of antimicrobial agents to treat these infections. In Malaysia, detailed information on molecular epidemiology and responsible antibiotic resistance mechanisms of *A. baumannii* remain scarce. In this study, various antibiotic resistance genes and their loci were investigated in association to their antibiotic susceptibility profile. Genotyping of the genes among strains and its relatedness to various sources were also investigated by Multilocus Sequence Typing (MLST). Hence, the profiling of antibiotic resistance genes with their location using both chromosomal and plasmid-mediated as well as the genetic lineage of all clinical isolates of *A. baumannii* by MLST were conducted. A total of 128 MDR *A. baumannii* isolates were collected from Microbiology Laboratory, Department of Pathology, Hospital Sungai Buloh, Selangor Malaysia from August 2017 to August 2018. The isolates were collected from patients admitted to the intensive care unit (ICU), coronary care unit (CCU), neonatal intensive care unit (NICU), high dependency ward (HDW), and general wards. The specimens include tracheal aspirate (TRAS), bronchoalveolar lavage (BAL), blood, cerebrospinal fluid (CSF), urine, sputum and others. The identification of the isolates was performed by Vitek 2 System and PCR for 16s rRNA for specific *Acinetobacter* spp. Antimicrobial susceptibility test was carried out using imipenem, ceftazidime, amikacin, gentamicin, ampicillin, ciprofloxacin and colistin. The antibiotic resistance genes; bla_{OXA-23}, bla_{OXA-24}, bla_{ADC}, bla_{VIM}, and bla_{IMP} were detected using PCR in both chromosome and plasmid. The PCR for insertion sequence IS*Aba*1 upstream bla_{OXA-23} gene was done on the chromosome only. Thirty of *A. baumannii* isolates that showed different profiles of antibiotic susceptibility pattern and band formation in PCR were subjected for MLST analysis. The isolates were frequently detected in HDW (39.84%), followed by general wards (29.69%) and ICU (28.13%). Majority of the isolates were isolated from TRAS (37.50%), blood (19.53%), BAL (13.28%), and CSF (9.37%). Most of the isolates were resistant (>90%) to ceftazidime, amikacin, gentamicin and ciprofloxacin. All isolates were resistant to ampicillin and carbapenem, however remain susceptible to colistin. Almost all isolates were identified as *A. baumannii*, except one isolate confirmed as *A. pittii* based on the DNA sequence analysis of its *rpoB* gene. The antibiotic resistance genes namely bla_{OXA-23} (99.22%), bla_{VIM} (99-100%), and bla_{ADC} (98-99%) resided in both chromosomal and plasmid DNA. The insertion sequences; IS*Aba*1 was detected upstream of the bla_{OXA-23} gene in 99.22% of the isolates. None of the isolate harbour bla_{IMP} and bla_{OXA-24} genes. Four sequence types (STs) were distinguished involving ST2 (76.67%), ST164 (10%), ST642 (10%) and ST643 (3.4%), with ST2 was prevalent in this study. The ST2 clone was circulating in all wards, while less appearance of ST642 was observed in ICU, HDW and general wards. The ST164 only circulated in general wards and HDW. The findings in this study revealed that ST2 is a predominant sequence type amongst *A. baumannii* isolates and its occurrence seem present in all sites in the hospital, suggesting spread of the MDR strain. These ST were associated with acquired bla_{OXA-23} gene indicating that the *A. baumannii* has undergone an evolution in the hospital setting. Thus, judicious use of broad-spectrum antibiotic in treating *A. baumannii* infections need to be improved, with surveillance activity regularly conducted to reduce the spread of MDR *A. baumannii*.

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TABLE OF CONTENTS