The Clinical and Molecular Characterization of Extensively Drug Resistant (XDR) *Acinetobacter baumannii* Complex from Clinical Isolates in Hospital Raja Perempuan Zainab II

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Abstract

*Acinetobacter baumannii* (*A. baumannii*) is an important cause of hospital-acquired infections. However, treating these infections is a challenge due to the isolation of multiply drug resistant strains that has limited antibiotic susceptibility. This study aims to consider the molecular characteristics of the XDR *A. baumannii*, the clinical characteristics of patients who are treated for the bacterial infection and recognize factors associated with poor treatment outcome. A cross sectional study was conducted among patients from which XDR *A. baumannii* were isolated from 1st January 2016 to 30th April 2017 in Hospital Raja Perempuan Zainab II. The isolates from non-repeat clinical samples which show extensive drug resistance pattern were collected and their species identification were confirmed using Vitek 2®. These isolates were then subjected to multiplex PCR analysis for the detection of oxacillinases resistance genes, namely *bla*<sub>OXA-51-like</sub>, *bla*<sub>OXA-23-like</sub>, *bla*<sub>OXA-24-like</sub> and *bla*<sub>OXA-58-like</sub>. Patients’ records of infective cases were reviewed for demographic data and clinical characteristics. These data were analysed using multiple logistic regression to identify variables that lead to end-of-treatment mortality among patients who were infected with XDR *A. baumannii*. XDR *A. baumannii* were isolated from 116 patients, and 65 of these cases were considered infectives and were treated for their XDR *A. baumannii* infection. All the isolates harboured the *bla*<sub>OXA-51-like</sub> gene, while the *bla*<sub>OXA-23-like</sub> were detected in all isolates but two. Most of the isolates regarded as clinically significant are from tracheal aspirate (45 samples), followed by blood (9 samples) and the remaining are from urine, tissue and pus (11 samples). Among those who are treated, the end-of-treatment mortality rate was 60.0% (39 patients). Repeat cultures after 72-hour of treatment were obtained from 31 of the infected patients, with 35.5% (11 patients) achieving microbiological eradication, 6.5% (2 patients) having microbiological noneradication while the majority (58.1%; 18 patients) having breakthrough infection. In the multivariable analysis, presence of sepsis (adjusted odds ratio (aOR) 7.93; 95% confidence interval (CI) 1.45, 43.26; *p*-value = 0.017) and presence of arterial catheter (aOR 15.53; CI 1.66, 145.71; *p*-value = 0.016) were independently associated with increased risk of end-of-treatment mortality. Conversely, longer treatment duration with polymyxin (aOR 0.71; CI 0.588, 0.856; *p*-value <0.001) was associated with decreased risk of end-of-treatment mortality. Most of the XDR *A. baumannii* isolates in this study harboured the *bla*<sub>OXA-51-like</sub> gene and the *bla*<sub>OXA-23-like</sub>. Almost half of the isolates were considered clinically significant. Among patients who are treated for XDR *Acinetobacter baumannii* infection,
presence of sepsis and presence of arterial catheter significantly increased risk of mortality. Yet, the risk for end-of-treatment mortality may be reduced with longer duration of colistin therapy.

**Keywords:** *Acinetobacter baumannii*, multidrug-resistant organisms, hospital-acquired infection, resistance genes, clinical relevance

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