

**MOLECULAR CHARACTERIZATION OF *ACINETOBACTER*
BAUMANNII INTEGRATED WITH GENOMIC RESISTANCE
ISLAND**



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Ph.D. (MEDICAL MICROBIOLOGY)

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ABSTRACT

Acinetobacter baumannii is ornamented with sophisticated antibiotic resistome ranging from a single resistance gene to genomic resistance island (GRI) and is the deadliest pathogen of 21st century to inflict debilitated patients. Local and global prevalence of MDR, PDR, and XDR *A. baumannii* are rising and city, country, and continent wise trafficking of this pathogen is evidenced and sooner this institute has to cope with this bug. Carbapenem resistant-*A. baumannii* (CRAB) has already emerged, rifampicin are the next generation antibiotic to be combined, and polymyxins are the final magic bullet. In this study, we deciphered a complete antibiotic resistome of CRABs and investigated molecular epidemiology in relation to local and global perspective. Antibiotic disk diffusion test, conventional and Multiplex Real Time PCR, whole genome pyrosequencing, hybridization, plasmid profiling, and MLST were performed to answer these objectives. All CRABs (n=111) were MDR to PDR and were rifampin resistant. Some isolates possessed *arr-2* gene (n=35), and mutations (L904S, P906R, K909N, and M1262K) were noted in *rpoB* gene in an *arr-2* negative isolate. Genetic characterization was done in 37 isolates. *bla*_{OXA-23} flanked upstream by *ISAbal* was responsible for carbapenem resistance (n=37). Whole genome pyrosequencing of Ab08-ColR was able to identify AbaR4, GRI present in European clone I (AB0057). GRI similar to pan-European clones, AbaR1, -R2, -R3, and -R5 were also elucidated (n=34). Analysis of the sequence data clarified that dephosphorylated lipid A as a possible mechanism of colistin resistance. *bla*_{TEM-1} is rare in *A. baumannii* globally, but was found in 15 isolates (40.5%) here. Molecular typing tools, like RAPD and ribotyping, could type isolates into 4 groups with discriminatory index (DI) of 0.64 and suggested that these clones were endemic to this institute since 2003/2004. Ribotype X and RAPD type I was found to spread intra-institutionally. The study of evolution of these strains were possible through MLST, which showed that some of our clones were simultaneously isolated in China, Korea, Europe, and Argentina, while others originated independently in Thailand. Ribotyping (DI=0.78) was worthwhile to interrogate endemic population and MLST seemed highly discriminatory with the fact that recombination was inevitable phenomena in *A. baumannii*. This is the first study to report the existence of international clones in Thailand and to our knowledge this is the first study to identify *bla*_{TEM-1} here and propose mechanism of colistin resistance in *A. baumannii* both in Thailand and overseas. Under these circumstances, monitoring and surveillance of institutional, intra-institutional and international clones are mandatory for proper treatment, prevention, and control.

KEY WORDS: ACINETOBACTER BAUMANNII/ INTERNATIONAL CLONE/
/GENOMIC RESISTANCE ISLAND/ANTIBIOTIC
RESISTANCE/MLST

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