

TITLE: MOLECULAR CHARACTERIZATION OF COLISTIN-RESISTANT CLINICAL ISOLATES OF *ACINETOBACTER BAUMANNII*

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ABSTRACT:

Carbapenem-resistant *Acinetobacter baumannii* is considered a public health problem limiting the treatment options. Colistin is currently the last-line therapeutic option for the treatment of nosocomial infections caused by multidrug-resistant (MDR) Gram-negative bacteria. Thus, the lack of therapeutic alternatives for infections caused by MDR *A. baumannii* has led to the increased use of the colistin. Unfortunately, resistance to colistin has been reported in strains of *A. baumannii*. Due to the potential magnitude of the problem, the molecular characterization of colistin-resistant strains is essential. The aim of this study was to perform the molecular characterization of colistin-resistant clinical strains of *A. baumannii* by Whole-Genome Sequencing (WGS). The analyses were made using different bioinformatic tools and in house scripts. Colistin MIC determination was performed by the broth microdilution method. Four colistin-resistant *A. baumannii* strains were characterized through the detection *mcr* and carbapenemase-encoding genes, mutations in *pmrAB*, *lpxC*, *lpxA* and *lpxD* genes, Multilocus Sequence Typing (MLST), and genes involved in biofilm production. The isolates had a MIC for colistin of 4 µg/mL (n=2) and 64 µg/mL (n=2). The following carbapenemase-encoding genes were detected: *blaOXA-23* (n=3), *blaOXA-65* (n=2), *blaOXA-69* (n=1) and *blaOXA-253* (n=1). Amino acid substitutions in PmrAB, LpxC and LpxD were present in all strains, however T187P and P170L substitution in PmrB were found only in strains with MICs 64 µg/mL. No *mcr* gene was detected. The Pasteur MLST scheme showed that the strains belonged to the international high-risk clones ST1 (clonal complex, CC1), ST79 (CC79) and ST25 (CC25). All strains carried biofilm associated genes, such as *bfmS/R*, *csuABC* and *pgaBCD*. Colistin-resistant *A. baumannii* is alarming. The results suggest that colistin resistance may be associated with multiple mutations in *pmrAB* and *lpxC* and *lpxD* genes. Strains belonging to high-risk clones are considered a serious threat to public health worldwide. Prudent antimicrobial administration and stringent infection control measures need to be implemented in order to minimize the spread of these strains.

Keywords: whole-genome sequencing; *Acinetobacter baumannii*; colistin resistance; Healthcare-Associated Infections (HAIs).

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