PHENOTYPIC AND MOLECULAR CHARACTERIZATION OF THE *PROVIDENCIA STUARTII* HARBORING *BLA*$_{NDM}$ FROM CLINICAL SAMPLES

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Abstract

Providencia stuartii is a Gram-negative bacillus widely distributed in the environment, and is currently considered an emerging human microbial pathogen associated with nosocomial infections. *P. stuartii* has a highly dynamic genome, which contributes to its resistance to antimicrobials. The aim of this study was to analyze the antimicrobial susceptibility profile of *P. stuartii* strains isolated from clinical samples and to conduct a molecular characterization. Thirteen (13) *P. stuartii* strains were isolated from blood cultures samples of patients in an intensive care unit. The presence of the *bla*$_{NDM}$ gene was determined by PCR analysis. In addition, the minimum inhibitory concentrations (MICs) of antimicrobials were determined using the VITEK and manual methods. The genome for *P. stuartii* PS1 strain harboring *bla*$_{NDM-1}$ were sequenced with Illumina MiSeq, and preassembled genomic DNA sequences were annotated using Prokka software. A complementary analysis of the genome was performed using *Rapid Annotation Subsystem Technology* (*RAST*). Among the thirteen (13) of *P. stuartii* strains analyzed, 11 carriers of the *bla*$_{NDM}$ gene and showed resistance to meropenem and imipenem. The MIC values ranged from 4-128 µg/mL. A partial genomic characterization for *P. stuartii* PS2 strain (resistant for 64 µg/mL, carbapenemic) using *RAST* indicated a wide range of genes related to drug efflux pumps and biocidal agents. A total of 73 genes were related to antimicrobial resistance and toxic compounds. The genetic systems were characterized, such as the multiple drug extrusion (*MATE)*, family-division-nodulation (*RND)*, and the major facilitator *superfamily (MFS)*. Partial genomic analysis of the *P. stuartii* PS2 strain confirmed the presence of the *bla*$_{NDM-1}$ and *bla*$_{TEM}$ genes and other genes for β-lactamase resistance. In addition, genetic systems for producing and releasing siderophores associated with iron uptake and other genes coding for heme ring and heme receptors and transporters were identified. About 40 genes were identified and expressed proteins for uptake and metabolism of iron. The mobilome analysis of the PS2 strain showed a high concentration of insertion sequences associated with mobile genetic elements, and prophages inserted into the genomes, suggesting the existence of a flexible genome. These *P. stuartii* strains were highly diverse for antimicrobial resistance which may lead to a difficulty for therapies for infections caused by this bacterium.

Keywords: Providencia stuartii, genomic sequencing, mobilome, resistance genes, virulence