TITLE: DIVERSITY OF CARBAPENEMASES GENES AND OCCURRENCE OF HIGH RISK CLONES IN *Pseudomonas aeruginosa* ISOLATED FROM HOSPITAL UNIVERSITÁRIO DE LONDRINA

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ABSTRACT:
A limited number of *Pseudomonas aeruginosa* genotypes, known as high-risk clones, are responsible for epidemics of nosocomial infections by multidrug-resistant (MDR) or extensively drug-resistant (XDR) strains worldwide. In this study, we characterized *P. aeruginosa* isolates focusing on the diversity of carbapenemases genes and on the identification of high-risk clones. Two hundred-ten *P. aeruginosa* isolates non-susceptible to ceftazidime, imipenem and/or meropenem were isolated from various clinical specimes and identified based on phenotypic and molecular techniques. Susceptibility testing was performed by the disc diffusion method. The modified Hodge test (MHT) and Blue Carba test (BCT) were used for phenotypic determination of carbapenemases production. The isolates were screened by the triple disc synergy (TDST) for the detection of metallo-beta-lactamases. Carbapenemases genes were investigated by PCR and the amplicons were sequenced. ERIC-PCR and MLST were performed for strain typing. In this study, 54.7% and 31.9% of the isolates showed the MDR and XDR phenotype, respectively. Antimicrobial susceptibility testing revealed high resistance rates to the quinolones (77.6%), aminoglycosides (72.8%) and carbapenems (80.9% and 78.1% for imipenem and meropenem, respectively). All isolates were susceptible to the polymyxins. The carbapenemase production was observed in 30.0% and 33.3% of the isolates by the MHT and BCT, respectively. Metallo-beta-lactamases production was verified in 67 isolates. Carbapenemases encoding genes were detected in 70 isolates. The most frequent carbapenemase detected was SPM-1 in 63 isolates, followed by 3 KPC-2, 2 IMP-16, and one of each VIM variant (VIM-1 and VIM-7). The ERIC-PCR of carbapenemases producers represented 18 different genotypes. Five strains were typed by MLST and the KPC producer isolate was identified as ST235, the VIM-1 as ST230, the VIM-7 as ST1284, the IMP-16 as ST273 and the SPM-1 as ST277. The rates of carbapenemase production obtained as well as the different carbapenemase families detected ilustrates that the carbapenemase production is an important mechanism of carbapenem resistance in our institution. Furthermore, high clonal diversity among the carbapenemase producing isolates and the presence of international high risk clones constitute a concern cause, requering effective and strict measures of infection control and serious interventions on carbapenem administration.

Keywords: *Pseudomonas aeruginosa,* carbapenemases, high risk clones

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