

TITLE: DETECTION OF HYPERMUTABLE IN CARAPENEM-RESISTANT PSEUDOMONAS AERUGINOSA FROM RESPIRATORY INFECTION OF CYSTIC FIBROSE PATIENTS

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ABSTRACT: *Pseudomonas aeruginosa* is commonly associated with the chronic, progressive lung disease that is the leading cause of morbidity and mortality in cystic fibrosis (CF) patients. Carbapenem-resistant (CR) and multidrug resistant (MDR), *P. aeruginosa* isolates are spread around the world, including CF patients with chronic lung disease. On the other hand, those resistant phenotypes are still infrequent among Brazilians CF patients. The adaptation of *P. aeruginosa* to the CF lung has been extensively studied during the course of infection. Hypermutable isolates (HPM) phenotype have been described in CF and related to evolutionary advantage to bacteria, higher mutation rate and higher antimicrobial resistance rates. The objective of this study was to characterize the resistance antimicrobial rates, the minimal inhibition concentration (MIC) to carbapenems and detection of HPM in *P. aeruginosa* strains isolated from CF patients assisted in two reference centers in Rio de Janeiro. The inclusion criterion adopted was: CF patients chronically colonized with *P. aeruginosa* isolates displaying non-susceptible to at least one carbapenem, according disk diffusion test (DDT). A total of 143 CR *P. aeruginosa* isolates were collected from January 2007 to December 2016 from 18 chronic CF. Using DDT against 11 antimicrobials agents, the resistance rates to carbapenems were 132 (92.3%), 84 (58.7%) and 55 (38.5%) to IPM, MEN and DOR, respectively; rates above 40% were observed to gentamicin (GEN), amikacin (AMI) and tobramycin (TOB). More than half of the isolates was classified as MDR. Additionally, the MICs showed ranges spanned 4 to 128 µg/mL, 4 to 64 µg/mL and 4 to 32 µg/mL to IPM, MEN and DOR respectively. Frequency of mutation revealed 14 isolates (24%) were HPM and was found in 9 (50%) of the 18 CF patients. We are able to demonstrate HPM isolates among CR *P. aeruginosa* isolates from CF patients from Rio de Janeiro.

KEYWORDS: *Pseudomonas aeruginosa*. Cystic fibrosis. Antimicrobial resistance. Hypermutability. Multidrug resistance.

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