TITLE: INFLUENCE OF MULTIDRUG RESISTANCE ON THE FITNESS OF *PSEUDOMONAS AERUGINOSA.*

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ABSTRACT:

The ability of *Pseudomonas aeruginosa* to develop antimicrobial resistance is associated with high mortality rates in hospitals. Emergence of multidrug resistant (MDR) isolates, including carbapenem resistant, is a great challenge for antimicrobial therapy. MDR isolates accumulate resistance mechanisms and this metabolic burden usually causes decreasing in bacterial fitness. The capacity of *P. aeruginosa* to persist in several environments such as hospitals and to cause infections, is related to its fitness cost and virulence. This study aimed to assess the competition between clinical isolates with different antimicrobial susceptibility pattern, virulence, biofilm forming capacity and clonal relatedness, to verify which isolate would prevail over the other. Three *P. aeruginosa* isolates collected from patients and environment in a Burn Center (BC), were selected for this study (isolates 3, 26 and 31). MIC values for imipenem and meropenem, were obtained by agar dilution method. The individual growth of each isolate was assessed until late log phase through a growth curve. Each of the two MDR isolates, 3 and 31, were grown in co-culture with a non-MDR isolate 26, so that to determine the competition index (CI) *in vitro.* Both MDR isolates were resistant to imipenem and meropenem (MIC=8µg/mL), while the non-MDR isolate was susceptible (MIC=0.5µg/mL). The non-MDR isolate 26 had a faster growth than the others. The CI for isolates 3 x 26 was 0.0056, which corresponds to an outstanding decrease in fitness. These isolates belonged to the same clonal type (A), although isolate 26 was biofilm former and displayed *exoS* gene, while isolate 3 did not present any of these virulence factors. Then, we believed the biofilm formation capacity associated with low resistance of isolate 26 may favor the persistence of this one in the environment in relation to its competitor. The other competitive pair 31 x 26, which evaluated isolates of distinct clones, C and A respectively, also showed a low CI=0.0796. The clonal type C was found in this BC after clone A. MDR isolates had low CI values when compared *in vitro* with non-MDR isolate, which suggests that this last one predominates in the environment in relation to the others two evaluated in this work. In addition, isolate 26 has belonged to the most widespread clonal type in that BC. These data contribute with the concept that the accumulation of resistance mechanisms may be directly related to the fitness cost in *P. aeruginosa*.

Keywords: bacterial fitness, multidrug resistance, *P. aeruginosa.*

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