

TITLE: A 17 YEAR-RETROSPECTIVE STUDY (2000 - 2017) OF CARBAPENEM-HYDROLYZING CLASS D B-LACTAMASES (CHDL) ENCODING GENES AMONG *ACINETOBACTER* SPP. (ASP) IN A BRAZILIAN TEACHING HOSPITAL

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ABSTRACT:

Asp is an important pathogen detected in Brazilian hospitals. High carbapenem resistance rates have been observed among Asp mainly due to spread of the CHDLs-producing clones. In the last years, we have been noticed a change in the epidemiology of CHDL-producing Asp in some Brazilian regions with the emergence and spread of OXA-72. The aim of this work was to perform a 17-year retrospective study focusing on the evaluation of the frequency of CHDL recovered from patients hospitalized at a tertiary teaching hospital located in the city of São Paulo, Brazil. We selected 533 Asp isolates with a decrease of carbapenem susceptibility previously identified by Phoenix[®] BD automated system. All isolates were subcultured on MacConkey agar plates supplemented with imipenem (1 µg/mL), and screened for CHDLs encoding genes by multiplex PCR. MICs were determined by BrCAST/EUCAST broth microdilution. Most Asp isolates analyzed (97%) were positive for at least one CHDL-encoding gene. All isolates were positive for *bla*_{OXA-51}-like. *bla*_{OXA-23}-like was the most frequent gene (49%), followed by, *bla*_{OXA-24/40}-like (28%), and *bla*_{OXA-143}-like (6%). Detection of two CHDLs encoding genes was also observed such as *bla*_{OXA-23}-like/*bla*_{OXA-24/40}-like genes (6%), and *bla*_{OXA-23}-like/*bla*_{OXA-143}-like genes (1%). Although isolates harboring *bla*_{OXA-23}-like have been detected since 2002, the highest frequency of these isolates was observed between 2005-2011, varying from 53% in 2005 to 85% in 2010. However, a decrease in the frequency of *bla*_{OXA-23}-like was accompanied by a significant increase of *bla*_{OXA-24/40}-like in the next six years. The frequency of isolates harboring *bla*_{OXA-24/40}-like varied from 41% to 63% between the years 2012 and 2017. The Asp isolates harboring *bla*_{OXA-24/40}-like were mostly recovered from bloodstream (67%) followed by respiratory tract (16%) infections. At

least one Asp isolate harboring *bla*_{OXA-24/40}-like per year was selected for MIC determination (n=24/177). Among them, all Asp isolates were resistant to imipenem (MIC₉₀: >64 µg/mL), meropenem (MIC₉₀: >64 µg/mL), ceftriaxone (MIC₉₀: >512 µg/mL), ceftazidime (MIC₉₀: >512 µg/mL), cefepime (MIC₉₀: >512 µg/mL), and gentamicin (MIC₉₀: 32 µg/mL). Tobramycin was the most active aminoglycoside tested. Our study corroborates the findings of previous studies confirming a change in the CHDL epidemiology among Asp in our hospital since 2012. *bla*_{OXA-24/40}-like has become the most frequent CHDL detected in the last five years.

Keywords: CHDLs, *Acinetobacter* spp., carbapenem resistance

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