Emergence of Multidrug-resistant *Klebsiella pneumoniae* strains in a hospital in Amazonas – Brazil

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The advent of resistance to multiple antimicrobial agents in *Klebsiella pneumoniae* is a significant public health problem. We aimed to evaluate the clonal dissemination, the prevalence of resistance determinants, and the activity of drugs for 40 *K. pneumoniae* isolates from a large Brazilian hospital in Manaus-AM. Antimicrobial susceptibility was determined by Vitek2® and by broth microdilution for fosfomycin (FOS), tigecycline (TGC) and polymyxins (POL). Phenotypic and genotypic methods were employed to check for the presence of carbapenemases, extended spectrum β-lactamases and the colistin-resistance gene *mcr-1*. The isolates clonality was determined by pulsed-field gel electrophoresis and the lineage determined by multilocus sequence typing. Due to the resistance profile, the genomes of AMKP10 and AMKP5 were drafted. The 40 isolates are resistant to at least three classes of antibiotics evaluated by Vitek2®, and they were all resistant to FOS. Ten isolates (25%) were resistant to, at least, one of the three carbapenems tested (imipenem, meropenem or ertapenem), while bla_{KPC} gene was detected in nine strains (22.5%). PFGE clustered the isolates among 10 pulsotypes (A-M), 45% belonging to pulsotype A. Most of isolates possessing the $bla_{\text{KPC-2}}$ gene belonged to subtype A1. The ST was determined for representative strains of each pulsotype, and the Clonal Complex (CC) CC258 was the most prevalent, followed by CC292, CC17 and CC23. Among the KPC producer strains belonging to subtype A1, AMKP7 was resistant to TGC, AMKP4 was resistant to POL and AMKP10 was resistant to TGC and POL besides other antimicrobials tested by the automated system, being susceptible only to aminoglycosides. POL-resistant strains had no *mcr-1* gene, suggesting another mechanism of resistance. Preliminary analysis of AMKP10 and AMKP5 draft genome has demonstrated the presence of β-lactamases genes $bla_{\text{OXA-1}}$, $bla_{\text{CTX-M-8}}$, $bla_{\text{CTX-M-15}}$, bla_{TEM}, $bla_{\text{SHV-11}}$ and $bla_{\text{KPC-2}}$ (AMKP10 only), and fosfomycin-resistance gene *fos*A; AMKP10 *rps*J has no mutations, suggesting some other TGC resistance mechanism. Thus, we could determine that *K. pneumoniae* of pulsotype A, which is related to the worldwide spread CC258, is endemic in this Brazilian hospital, and subtype A1 embrace the most resistant strains. Most alarming is that all of them are multidrug-resistant (MDR) and some are resistant to FOS, TGC and POL, last resort antibiotics often used for treating infections caused by MDR Gram-negative organisms.

Keywords: multidrug-resistant (MDR), carbapenemases, PFGE, MLST, *K. pneumoniae*