TITLE: ENDEMIC CARBAPENEM-RESISTANT *Klebsiella pneumoniae* STRAINS REVEAL A CANDIDATE FOR THE PANDRUG-RESISTANT STATUS IN A HOSPITAL IN AMAZONAS

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ABSTRACT

High dissemination rate of multidrug resistant Carbapenem-resistant *K. pneumoniae* (CRKP) has been a problem in Brazilian hospitals, narrowing the treatment options to the use of tigecycline (TIG) and colistin (COL). Our objective was to evaluate susceptibility profile, phenotypic and genotypic carbapenemase (Carb) detection, and to compare the clonality of clinical isolates of *K. pneumoniae* of a hospital in Manaus. For this purpose, we used the antibiogram and the detection test of beta-lactamases by Vitek2, Modified Hodge Test (MHT), tests with inhibitors and potentiator (IPT) to detect Carbs, minimum inhibitory concentration (MIC) in mg/L of TIG and polymixin B (POL) determination by broth microdilution (CLSI 2014) to CRKP, typing by Pulsed-Field Gel Electrophoresis (PFGE). *bla*$_{NDM}$ *bla*$_{KPC}$, *bla*$_{VIM}$, *bla*$_{IMP}$, *bla*$_{SPM}$ and *bla*$_{OXA-48}$ genes were investigated. Forty-one *K. pneumoniae* were analysed. Among these, 10 (24 %) were resistant to at least one of the 3 carbapenems and were phenotypically screened. MHT revealed 6 out 10 CRKP as positive. However, by IPT, 9 out 10 CRKP had positive characteristics, being 5 possible producers of metallo-beta lactamase and *K. pneumoniae* carbapenemase and other 4 possible OXA-48. Nevertheless, only 3 isolates were positive to *bla*$_{KPC}$. PFGE shared all isolates in 10 pulsotypes (A-J). Pulsotype B clustered 20 out 41 isolates in 11 subtypes (B1 - B11). Subtype B3 comprised 8 isolates, of which 5 were CRKP, but only 2 were *blaKPC*. Among the other CRKP, 2 were of subtype B11 as well as 1 isolate of each of the following subtypes: B2, I2 and J1. Among the CRKP, 1 was intermediate (MIC=4) and 3 were highly resistant (MIC>256) to TIG. Two isolates were COL (MIC>=16) and to POL (MIC=8 and >16) resistant. The isolate AMKP4 was COL resistant and AMKP10 was TIG and COL resistant. Both were susceptible to amikacin and gentamycin. Taking all together, pulsotype B seems endemic to the hospital, but different carpabenem resistance mechanisms (CRM) were involved. Seven CRKP were negative for genes tested. Therefore, plasmid transference harboring different Carb genes could explain why even isolates of the same subtype have distinct CRM and this will be further evaluated. In conclusion, among all, *K. pneumoniae* AMKP10 is a CRKP resistant to the two last-resort antibiotics and for this strain, only the amynoglycosides matter. Unfortunately, *K. pneumoniae* AMKP10 revealed a worrisome panorama as a true candidate for the pandrug-resistant status.

Keywords: Multiresistant, Carbapenemases, PFGE, Colistin, Tigecycline

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