Molecular Epidemiology of KPC-2 Producing Klebsiella pneumoniae

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**Short Communication**

Abstract

We describe the molecular epidemiology of the KPC-2 K. pneumoniae among public hospitals in the Amazon State, Brazil. A total of 4.4% (5/113) of the K. pneumoniae isolates were identified as KPC-producing and CTX-M-109 beta-lactamase. Further, MultiLocus Sequence Typing identified three clones STs11, 40 and 2230. To the best of our knowledge, the present study demonstrates for the very first time, detection of the multidrug resistant K. pneumoniae (KPC-2), ST2230 clone, in Brazil.

Keywords: ST2230; CTX-M-109; Carbapenem Resistance; Antimicrobial; Multi Resistant

Text

Nosocomial infections caused by carbapenemase-producing bacteria has increased worldwide and have become a serious public health threat [1]. Infections resulting from this pathogen may lead to a serious life-threatening illness [2] and are characterized by a resistant phenotypic profile to monobactams, carbapenems, broad spectrum cephalosporins, fluoroquinolones and aminoglycosides [2-4]. These bacteria pose a significant risk for hospitalized patients, particularly for neonates, immune-compromised, diabetics or patients with alcohol-associated disorders or bloodstream infections, as well as those receiving advanced medical care [2,3]. The antibiotic therapies available to treat these infections are restricted to tigecycline, polymyxins and occasionally aminoglycosides [3,5]. A number of KPC variants have been described among which the KPC-2 and -3 are the most prevalent [3,5]. In this study, we described the molecular epidemiology of five KPC-producing K. pneumoniae among public hospitals in the Amazon region. In the year 2015, a total of 133 clinical samples of K. pneumoniae were obtained from inpatients from two public hospitals in Manaus-Brazil. The biochemical identification and susceptibility test of these isolates were performed by VITEK-2 automated system protocols (bioMérieux, France). The screening detection for Extended-Spectrum Β-Lactamase (ESBL) and for carbapenemase production were performed according to CLSI (2015) recommendations [6]. Plasmid DNA was extracted with the use of PureLink™ Quick Plasmid Miniprep Kit (INVITROGEN, CARLSBAD, CA, USA). Further, molecular analysis was performed by Polymerase Chain Reactions (PCRs). PCR amplifications for bla_{CTX-M} gene were performed according to Villegas, et al. [7]. For carbapenemase production (bla_{KPC}), we designed one pair of primers (bla_{KPC}FW-5´-ATGTCACTGTATCGCCGTC-3´) and (bla_{KPC}RV-5´-TTACTGCCCGTTGACGCC-3´). For bla_{NDM} production gene, we designed another pair of primers (bla_{NDM}FW-5´-GCCCAATATTATGCACCCGG-3´); (bla_{NDM}RV-5´-CGCAGCTTGTCGGCCAT-3´). The sequencing of the bla_{KPC} and bla_{NDM} amplicons were performed at ABI 3130 sequencer, (Applied Biosystems, Foster City, CA). These sequences were analyzed with a software geneious V.10.0.10. Multilocus Sequence Typing was performed according to Institut Pasteur’s MLST scheme (http://bigd.web.pasteur.fr/ ) and for bla_{CTX-M} gene, the blastn was made (http://blast.ncbi.nlm.nih.gov/Blast.cgi ). The total of the 113 isolates of the K. pneumoniae were obtained from different biological sites such as urine 44.2% (50/113), blood 30% (34/113), tracheal aspirate 20.3% (23/113), wound 1.76% (2/113) and fecal 0.88% (1/113). The susceptibility test of them showed resistance of 100% to ceftriaxone and cefepime; 69.9%
KPC-2, a key pathogen set for global nosocomial dominance. Positive patients, should be
isolated from inpatients at the same general hospital. These may affect vulnerable patients [13]. The ST11 and ST340 clones contributing to the local dissemination of these clones, which health professionals and their flow between different hospitals; the horizontal transfer of antibiotic resistance, acting also as an isolate from hospital environment and play an important role in healthcare settings [12,13]. The spread of the antibiotic resistance genes maybe be associated with the dissemination of clones, and health care settings caused by K. pneumoniae [8]. Concerned with this problem, the World Health Organization (WHO) developed a global priority pathogens list, in which K. pneumoniae is at the priority one (critical) (http://www.who.int/medicines/publications/global-priority-list-antibiotic-resistant-bacteria/en/). The endemic dissemination of the carbapenemase variant KPC-2 and KPC-3, has been reported in the USA (5.7%), Italy (89.5%), Canada (89.3%), and China (63%) [9-12]. The ST258 clone, predominant in European countries, has contributed significantly to the worldwide distribution of the carbapenemase resistance [4]. In Asia, there are different clones such as ST392 and ST395, which also harbor the blaKPC gene, whereas in Brazil, different STs such as ST437, ST340 and ST942, harboring the KPC-2 variant, have been described and isolated from different healthcare settings [12,13]. The spread of the antibiotic resistance genes maybe be associated with the dissemination of clones, and other factors such as plasmids, and transposons – i.e. Horizontal Gene Transfer (HGT) - between bacteria [4,14,15]. Furthermore, the capacity of the K. pneumoniae to colonize medical equipment and to survive for long periods of time, at extreme temperature in the environment, explains why this pathogen can also be isolated from hospital environment and play an important role in the horizontal transfer of antibiotic resistance, acting also as an efficient donor and receptor [4,13,16-19]. The events observed in the present study, suggest that asymptomatic carriers, such as health professionals and their flow between different hospitals; patient or other people who move through hospitals, may be contributing to the local dissemination of these clones, which may affect vulnerable patients [13]. The ST1 and ST340 clones were isolated from inpatients at the same general hospital. These clones were observed in different states of Brazil such as Ceará, Pernambuco, Rio de Janeiro, Piauí, Alagoas and Federal District [13]. To date, only one clone (ST841) was described in Manaus, Amazonas [13]. The ST2230 clone, that has been described before in China, was isolated from a blood sample of a newborn from a maternity hospital, being the first description in the city and in Brazil, and possibly representing an important fact, once it is associated with multidrug resistance. Pereira, et al. detected resistant clones to carbapenems, amikacin, ticarcylene and colistin [13]. In the present study, the clones were sensitive to colistin and to amikacin. Since the KPC-producing bacteria present a resistance profile to different classes of antibiotics, such as monobactams, carbapenems and broad spectrum cephalosporins, the last therapeutic options that remain is polymyxin B, colistin and fosfomycin [3,13,19]. A serious prophylactic action in the health centers with focus on control measure of the environment, contact precautions, hand hygiene, early identification of asymptomatic carriers, antimicrobial stewardship and the implementation of the infection control guideline, are obligatory to prevent, control or at least to reduce the risks of dissemination of these virulent clones [20]. Preventive measures are necessary to avoid the dissemination of these highly pathogenic clones among hospitals and KPC producing K. pneumoniae positive patients, should be isolated and treated according standard guidelines.

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References


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