

LETTERS TO THE EDITOR

Know Thy Self, Know Thy Enemy: A Current Survey and a Forecast for KPC-Producing *Klebsiella pneumoniae* Resistance Among Inpatients in Southern Brazil

To the Editor—In recent years, the most prevalent organisms isolated from inpatients in Brazilian hospitals have had a carbapenem-resistant profile; they are mostly *Klebsiella pneumoniae* carbapenemase (KPC) producers.^{1,2} One report suggests that >80% of nosocomial infections due to carbapenem-resistant Enterobacteriaceae are attributable to KPC-producing *Klebsiella pneumoniae* (KPC-*Kp*), especially in more critical care settings such as intensive care units (ICUs).^{1,3} Their presence and persistence in these environments are correlated with a clinical decline of infected patients that, despite treatment with antimicrobial drugs, are seldom eradicated from the clinical site of infection or colonization because the bulk of therapeutic options are increasingly scarce.

KPC-producing organisms are often resistant to a broad range of antibiotics beyond the β -lactams. In fact, the plasmids that carry the KPC gene may also contain genes encoding enzymes or other mechanisms, often resulting in reduced susceptibility to distinct antimicrobial classes such as fluoroquinolones and aminoglycosides among others. Many treatments of KPC infections have employed tigecycline, polymyxins (polymyxin B or colistin), or also a combination of these. Varying outcomes have been reported.⁴

Therefore, establishing the resistance profile for these isolates is crucially important not only for monitoring but also for implementing infection control measures and for better management of antibiotic therapy. A survey of KPC-*Kp* isolates from hospitalized patients was performed to provide an indicator of the prevalence of resistance to 4 potential antimicrobial agents widely used for the treatment of KPC-producing organism.

Enterobacterial isolates were recovered from inpatients between January 1 and December 26, 2016, at a tertiary hospital in Porto Alegre, Southern Brazil. Biochemical tests using a MicroScan automated system (Beckman Coulter, Brea, CA) were used to identify enterobacterial species and to determine the susceptibility profiles to amikacin (AK), fosfomicin (FOT), and tigecycline (TGC), and polymyxin B (PMB) was confirmed using E-test (AB Biodisk, Solna, Sweden). Selected *Klebsiella pneumoniae* isolates confirmed with reduced susceptibility to any carbapenem agent were then tested using a synergistic test applying phenyl-boronic acid to detect KPC (isolates included in this study). No attempt was made to select

the KPC-*Kp* isolates based on their first or subsequent recovery because we aimed to detect a possible development of resistance, although KPC-*Kp* might have been recovered more than once over this period from the same patient.

A total of 440 isolates were identified as KPC-*Kp* during the study period. According to antimicrobial susceptibility testing results, PMB was the least active antibiotic against the panel of isolates (ie, 161 of the 440 isolates [36.6%] were resistant) followed by far by FOT (44 isolates [10%] were resistant), AK (17 isolates [3.9%] were resistant), and TGC (10 isolates [2.3%] were resistant). A minor proportion of isolates displayed intermediate susceptibility to TGC (26 isolates [5.9%] were resistant) and AK (11 isolates [2.5%] were resistant). A little more than half of the KPC-*Kp* isolates (227 isolates [51.6%]) presented a “multisusceptible” profile, indicating susceptibility to the 4 antimicrobial agents tested in this survey. The remaining 213 isolates were resistant to at least 1 tested antimicrobial agent, and outstanding single resistance to PMB (115 of these 213 isolates [54%]) was the most prevalent resistance profile among the KPC-*Kp* isolates (Figure 1). Despite this drastic scenario, only 1 isolate was resistant to all 4 antibiotics tested.

Admittedly, there was no cross resistance among the antibiotics tested. Notably, however, the PMB-resistant phenotype, including a single resistance or associated with other agent(s), was the most prevalent phenotype among KPC-*Kp* isolates identified in this study (54% for single resistance and 75.7% for associated resistance).

Because therapeutics against gram-negative bacilli are scarce and the emergence of this resistance mechanism is a concern, all available options that still show some degree of susceptibility should be strictly monitored. Among the antibiotics evaluated in this survey, PMB has been more widely used than the others. FOT, despite its emergence resistance among KPC-*Kp*,⁵ still showed a low resistance rate; however, its application has been restricted to treating lower urinary tract infections. In addition, despite the current low resistance rates presented to AK and TGC, only in some specific site-related infections has their effectiveness been proven. Thus, as previously shown, the high rate of PMB-resistance seems to be independently associated with its use in clinical practice.^{2,6}

KPC production is a major clinical and public health problem in Brazil because it has been increasingly reported and poses a challenge to antimicrobial therapy. This survey described the emergence of KPC-*Kp* with a PMB-resistance phenotype as a major disseminated pattern in a tertiary-care hospital in Southern Brazil. Failure to reduce the rates of PMB-resistant isolates is worrisome because it may lead to an endemic presence of this phenotype. Measures to control the spread of KPC-mediated resistances, especially those driven by prior exposition as appears to occur with PMB in this study, are urgently needed.

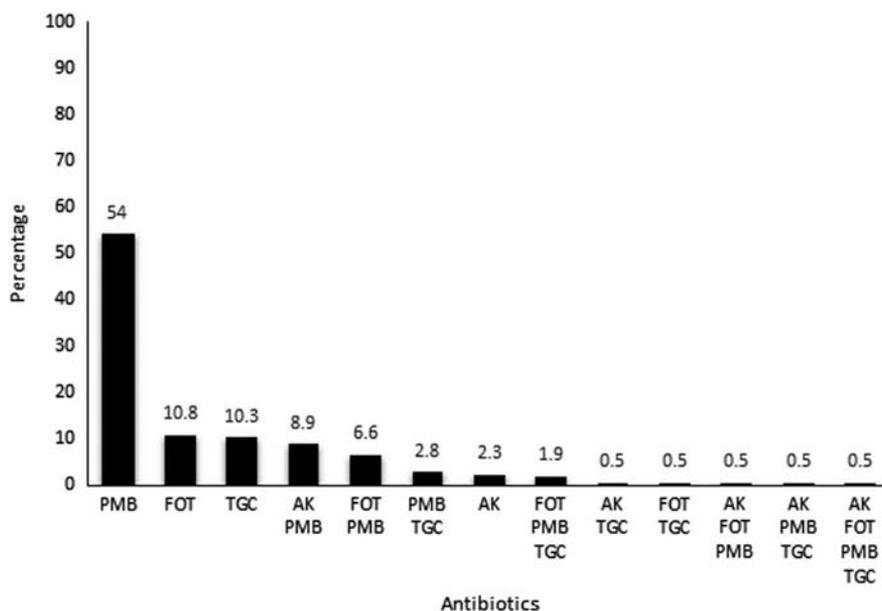


FIGURE 1. Percentage distribution of antimicrobial resistance patterns of KPC-*Kp* from inpatients during the study period.

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Reliability of Surveillance for Ventilator-Associated Events and Pneumonia; Methodological and Statistical Issues

To the Editor— I was interested to read the paper by Kerlin et al¹ published in the February 2017 issue of the *Infection Control and Hospital Epidemiology*.¹ The authors compared interrater reliabilities for ventilator-associated event (VAE) surveillance, traditional ventilator-associated pneumonia (VAP) surveillance, and clinical diagnosis of VAP by intensivists.¹ In total, 150 charts from intensive care units (ICUs) within 5 hospitals, including all VAEs and traditionally defined VAPs identified during the primary study and randomly selected charts of patients without VAEs or VAPs, were selected for review.¹ All charts independently reviewed by 2 research assistants (RAs) for VAEs, 2 hospital infection preventionists (IPs) for traditionally defined VAP, and 2 intensivists for any episodes of pulmonary deterioration.¹

Based on their results, in total, 93–96 VAEs were identified by RAs; 31–49 VAPs were identified by IPs, and 29–35 VAPs