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Letter to the Editor

Carbapenemase KPC-2 in ESBL-producing *Enterobacteriaceae* from two clinics from Villavicencio, Colombia

Dear Editor,

The emergence of ertapenem resistance in *Klebsiella pneumoniae*, related to the production of carbapenemases such as KPC enzymes is worrisome because it decreases current antimicrobial drugs available for the treatment of these microorganisms. In Colombia KPC-2 producing organisms have been reported and are frequently resistant to multiple plasmid-mediated antibiotic classes.¹ Thirteen broad-spectrum cephalosporins-resistant isolates of the family *Enterobacteriaceae* (11 *K. pneumoniae* and 2 *Escherichia coli*) were collected from two private tertiary care clinics in Villavicencio between October 2008 and September 2009. The isolates were screened by PCR assay for *bla*_{TEM}, *-SHV*, *-CTX-M-1*, *-CTX-M-2*, *-CTX-M-8*, *-CTX-M-9*, *-PER-2*, *-CMY-2* and *bla*_{KPC} genes. Sequencing of the amplified fragments identified CTX-M-12 (13/13) as the most frequent enzyme in the clinical isolates evaluated, followed by SHV-12 (7/13), TEM-1 (4/13), KPC-2 (3/13), CTX-M-8 (1/13), and SHV-5 (1/13). One of the 11 *K. pneumoniae* isolates carried two CTX-M type genes and one SHV-type gene concomitantly. Three KPC-producer *K. pneumoniae* isolates also encoded for expression of *bla*_{CTX-M-12} gene and *bla*_{SHV-12} concomitantly. Two *E. coli* isolates were carrying *bla*_{CTX-M1} like gene. The combination of two CTX-M type genes found in one isolate of *K. pneumoniae* is of interest because the *bla*_{CTX-M-8} gene is commonly plasmid-harbored and does not show resistance to non-β-lactams antibiotics (aminoglycosides, fluoroquinolones and trimethoprim-sulfamethoxazole). These resistance genes are encoded by plasmid, with the exception of tetracycline that expressed resistance with MICs of >8 mg/L. The nucleotide sequencing of three isolates positive for KPC genes showed 100% *bla*_{KPC-2} (accession number AY034847) similarity. The fact that some *K. pneumoniae* isolates harbor multiple ESBL genes in combination with the carbapenemase KPC-2 encoding gene is important as this isolates were susceptible *in vitro* to all carbapenems with Microscan Neg Combo Panel Type 50 (Dade Behring, CA, USA). Susceptibility interpreted according to CLSI standards² could increase the likelihood of therapeutic failures whether ertapenem is used to treat urinary tract infections or blood stream infections because *in vivo*

carbapenemase could hydrolyze ertapenem.^{3,4} Although reported ertapenem susceptibility could in fact be false susceptibility because of the higher breakpoint at MicroScan panel type 50 systems. The use of other panels like MicroScan urinary reference could prevent unnecessary reporting of false negative results by using lower breakpoints according to CLSI standards. Despite ertapenem resistance carbapenems, such as doripenem, have been proposed to treat infections caused by KPC-producing isolates for its ability to achieve bacteriostatic activity.⁵ The PFGE of ESBL-producing *K. pneumoniae* isolates showed two clusters of 84% and 94% similarity, respectively. Isolates from cluster 1 expressed ESBL type CTX-M-12 and KPC-2, and cluster 2 isolates expressed ESBL type CTX-M-12, SHV-12 and KPC-2. Antimicrobial phenotype for cluster 1 isolates expressed resistance to non-β-lactam antibiotics, i.e., to almost all aminoglycosides (MICs for gentamicin of ≥8 mg/L), fluoroquinolones (MICs of ciprofloxacin >2 mg/L), and the combination of sulfamethoxazole and trimethoprim. The exception was tetracycline that showed susceptibility, MICs <4 mg/L. Cluster 2 isolates expressed resistance to all non-β-lactam antibiotics. Emergence KPC enzymes is worrisome due to therapeutic failures when ertapenem is used. However, possible false susceptibility results to ertapenem can occur in clinical microbiology laboratories when reference breakpoints from automated systems, such as MicroScan, are used.

Conflicts of interest

The authors declare no conflicts of interest.

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