

## **Epidemiology of *mcr-1*-producing *Enterobacteriaceae* clinical isolates from Argentina.**

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### *Abstract:*

**BACKGROUND:** Mobile polymyxins (colistin –COL- and polymyxin B) resistance mediated by *mcr-1* and *mcr-2* were recently described worldwide. *mcr-1* was mostly found in *E. coli* isolates recovered from raw meat, animals, but also from human samples. Recently we reported the first *E. coli* clinical isolates harboring *mcr-1* from Argentina, these isolates were genetically unrelated (1). In February 2016, the NRL issued an alert about the presence of *mcr* in clinical isolates. **AIM:** To describe the epidemiology of *mcr-1*- *Enterobacteriaceae* (ETB) clinical isolates from Argentina.

**METHODS:** COL MICs were obtained by agar dilution (EUCAST). Other drugs were evaluated by disc diffusion and agar dilution (CLSI), except tigecycline (TIG) that was interpreted as reported (2). Resistance genes were detected by standard PCR, and allele-specific PCR for *mcr-1* and *mcr-2* genes. Genetic relatedness was assessed by XbaI-PFGE. *Salmonella* spp. M1744 was used as recipient for biparental conjugation assays.

**RESULTS:** Until Dec-2016, 85 COL-resistant ETB clinical isolates (83 *E. coli*, 1 *Citrobacter amalonaticus* and 1 *Klebsiella pneumoniae*) were confirmed at the NRL as positive for *mcr-1*, and negative for *mcr-2*. These isolates were recovered from urine sample (46; 54%), blood (13; 15%) and other sites (26). Isolates were submitted from 36 hospitals located in 8 provinces and Buenos Aires City. All strains were categorized as resistant to COL (MIC<sub>50</sub>/MIC<sub>90</sub>: 8/8 mg/L). Strains were non-susceptible to (%): ampicillin (88), nalidixic acid (82), ciprofloxacin (61), third generation cephalosporins (TGC) (53), trimethoprim-sulfamethoxazole (52), minocycline (26), gentamicin (24), nitrofurantoin (only UTI, 15), carbapenem (5) and amikacin (4). All isolates were susceptible to TIG. Resistance to TGC was associated to ESBLs (p<0.0001 Fisher’s exact test) (n): CTX-M (36); SHV (1), PER (1); plasmidic-AmpC (4). Two NDM (1 *E. coli* and 1 *C. amalonaticus*) and 1 KPC (*E. coli*) producers were detected. Sixty *E. coli* were analyzed by PFGE, 7 were repeatedly non-typeable, and the remaining 53 isolates were differentiated in 53 clonal types. COL resistance was transferred by conjugation and a ca. 60 kb plasmid was observed in a subset of nine *E. coli* isolates.

**CONCLUSIONS:** The clonal diversity of *mcr-1*-producing *E. coli* isolates suggest a key role of horizontal dissemination mediated by plasmids between human isolates. Emergence of *mcr* in carbapenemase producers and ETB species other than *E. coli* is an urgent health public issue.

### *Acknowledgments/ References:*

1) Rapoport et al. 2016 AAC, 60:4412-3 ( 2) Pasteran et al. 2012 JIDC, 6:452-6

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