

**TITLE:** LOW PREVALENCE OF THE *MCR-1* GENE AMONG CARBAPENEMASE PRODUCING CLINICAL ISOLATES OF ENTEROBACTERIALES

**AUTHORS:** ÁVILA, H.<sup>1,3</sup>; WINK, P.L.<sup>1,2</sup>; DALMOLIN, T.V.<sup>1,2</sup>; LIMA-MORALES, D.<sup>1</sup>; BARTH, A.L.<sup>1,2,3</sup>

**INSTITUTION:**1. LABORATÓRIO DE PESQUISA EM RESISTÊNCIA BACTERIANA (LABRESIS), CENTRO DE PESQUISA EXPERIMENTAL, HOSPITAL DE CLÍNICAS DE PORTO ALEGRE (HCPA), PORTO ALEGRE, RS (R. Ramiro Barcelos, 2350, 2º andar, CEP 90035-903, Porto Alegre-RS, Brazil); 2. PROGRAMA DE PÓS-GRADUAÇÃO EM CIÊNCIAS FARMACÊUTICAS (PPGCF), FACULDADE DE FARMÁCIA, UFRGS, PORTO ALEGRE, RS (Av. Ipiranga, 2752, 1º andar, CEP 90610-000, Porto Alegre-RS, Brazil); 3. DEPARTAMENTO DE ANÁLISES, FACULDADE DE FARMÁCIA, UFRGS, PORTO ALEGRE, RS (Av. Ipiranga, 2752, CEP 90610-000, Porto Alegre-RS, Brazil)

**ABSTRACT:**

Polymyxins are the last resort for the treatment of infections caused by Carbapenem Resistant Enterobacterales (CRE). In November 2015, polymyxin resistance mediated by the gene *mcr-1* was described and the acquisition of this gene by CRE is of particular concern as it would lead to multidrug resistance isolates, which can cause untreatable infections. The aim of the present study was to evaluate the prevalence of carbapenemase/*mcr-1* co-producers in *Enterobacterales* among clinical isolates in southern Brazil during a 5 years period. The “Laboratório de Pesquisa em Resistência Bacteriana – LABRESIS” has received 6524 isolates reported as non-susceptible to carbapenems from April 2013 to May/2018. All these isolates were submitted to RT-PCR HRM with primers for *bla*<sub>KPC</sub>, *bla*<sub>NDM</sub>, *bla*<sub>OXA-48-like</sub>, *bla*<sub>GES</sub>, *bla*<sub>IMP</sub> and *bla*<sub>VIM</sub>. A total of 4778 (73.24%) proved to present carbapenemase gene(s). All carbapenemase positive isolates were evaluated for the presence of the *mcr-1* gene by pooling 10 isolates together and submitting them to DNA extraction and conventional PCR, with specific primers for the *mcr-1* gene. All isolates from a pool with *mcr-1* positive result were re-tested individually by the same conventional PCR in order to identify the isolate(s), which presented the gene. Individual isolates positive for the *mcr-1* gene were tested for carbapenem and polymyxin susceptibility by broth microdilution. We found only 5 isolates, which presented the *mcr-1* gene and a carbapenemase gene. All co-producers presented the *mcr-1/bla*<sub>KPC</sub> genes. Two co-producers (*K. pneumoniae* 3111F and *E. coli* 3431F) were obtained in 2014; one co-producer (*E. coli* 5798F) was obtained in 2016 and the other two co-producers (*K. pneumoniae* 6701F and *E. coli* 6699F) were identified in 2018. All co-producers were recovered from rectal swabs, with exception of *E. coli* 6699F which was recovered from ascites fluid. The MIC for meropenem was: 256mg/L for *K. pneumoniae* 3111F and *E. coli* 6699F; 128mg/L for *K. pneumoniae* 6701F; 8 mg/L for *E. coli* 5798F; and 32mg/L for *E. coli* 3431F. The MIC for polymyxin was 4 mg/L for all isolates, with exception to *K. pneumoniae* 6701F, which was 0.25 mg/L. The prevalence of the *mcr-1* gene is very low (0.1%) among carbapenemase positive clinical of *Enterobacterales*. However, the detection of two isolates in 2018 co-producing *bla*<sub>KPC</sub>/*mcr-1* genes is a warning for a possible increase of the prevalence of this isolates in the coming years.

**Keywords:** Carbapenemase; *mcr-1*; Polymyxin; Resistance Genes

**Development Agencies:** CNPq, CAPES, FINEP/HCPA, INPRA (Instituto Nacional de Pesquisa em Resistência Antimicrobiana)