First Description of mcr-1-Mediated Colistin Resistance in Human Infections Caused by Escherichia coli in Latin America

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Yi-Yun Liu and colleagues recently reported the emergence of plasmid-mediated colistin resistance in China, raising great concern around the world (1–5). The mcr-1 gene was originally detected in commensal Escherichia coli from pigs but was immediately associated with other Enterobacteriaceae species of farm animal, meat, and human origins (1–5). A previous study reported short-term intestinal colonization in travelers to South America, suggesting the presence of the mcr-1 gene in the region (4). In this report, we describe the detection of mcr-1 in E. coli isolates causing human infections in Argentina.

A selection of 87 colistin-resistant clinical isolates submitted to the National Reference Laboratory in Antimicrobial Resistance (NRLAR) from 2008 to January 2016 were screened for mcr-1 by PCR and Sanger sequencing. The collection included 28 E. coli isolates, 19 Klebsiella pneumoniae isolates, 36 isolates of other members of the family Enterobacteriaceae, and 4 isolates of nonfermenter Gram-negative bacilli. The mcr-1 gene was detected in nine E. coli isolates recovered from nine patients admitted to six hospitals in three cities (Table 1). The average age of the patients was 68.5 (range, 53 to 93) years, and six of them were male. In five patients, mcr-1-positive E. coli isolates were associated with severe infections (Table 1). All nine E. coli isolates were genetically unrelated, as assessed by XbaI pulsed-field gel electrophoresis. mcr-1-mediated colistin resistance was successfully transferred by conjugation to a laboratory Salmonella strain; no other resistance was cotransferred. Four of the nine E. coli isolates coproduced different CTX-M variants (Table 1).

Given reports indicating discrepancies in the determination of the MICs of polymyxins (6), we assessed phenotypic methodologies used to detect mcr-1-mediated colistin resistance, i.e., agar dilution according to CLSI guidelines and Etest (bioMérieux), Vitek2C (bioMérieux), the BD Phoenix System (Becton Dickinson), and Sensititre (TREK Diagnostic Systems), by following the manufacturers’ recommendations. Colistin MICs were interpreted according to EUCAST (resistance, >2 µg/ml). The nine mcr-1-positive E. coli isolates were resistant to colistin by all of the MIC methodologies; the MICs ranged from 4 to 16 µg/ml (Table 1). For the remaining 78 mcr-1-negative, colistin-resistant E. coli isolates, the colistin MICs ranged from 8 to >64 µg/ml (agar dilution; data not shown). The polymyxin B MICs determined by agar dilution mimic those of colistin (8 to 16 µg/ml). Although the disk diffusion method (10-µg colistin disk) is not standardized for polymyxins, all nine E. coli isolates carrying the mcr-1 gene displayed colistin inhibition zones of ≤11 mm. Nevertheless, molecular detection is the gold standard for mcr-1 identification.

These isolates represent the first confirmed Latin American mcr-1-positive clinical isolates, highlighting the widespread potential of this mechanism. Until now, mcr-1-positive isolates have been found sporadically in humans and associated with invasive and noninvasive diseases (5). However, in our country, mcr-1-positive E. coli isolates were found mostly in invasive infections, suggesting fitness for the hospital environment. The isolates harboring the mcr-1 gene were genetically unrelated, and the mechanism was horizontally transferable. The available MIC measurement methodologies consistently detected mcr-1-positive E. coli isolates. Since 2010, the epidemiology of our country has changed drastically, especially driven by the dissemination of K. pneumoniae carbapenemase-producing K. pneumoniae ST258, other members of the family Enterobacteriaceae (7), and also extremely drug-resistant Acinetobacter baumannii. This situation was caused by the massive use of polymyxins as part of double- or triple-combination therapy schemes for severe infections. According to the National Surveillance on Antimicrobial Resistance conducted by the WHONET-Argentina Network (90 laboratories), colistin resistance in E. coli increased from (total number of E. coli isolates) 0.4% in 2012 (n = 13,221), to 0.8% in 2014 (n = 18,244) (P < 0.001). During 2015, the National Strategy for the Control of Antimicrobial Resistance was implemented in our country. However, the current information about antimicrobial resistance in veterinary medicine, animal production, and food production is scarce. At the NRLAR, we issued a regional alert on 2 February 2016, warning about the emergence of mcr-1-mediated colistin resistance in clinical isolates from Argentina, and released guidelines for active surveillance by health care providers. By 9 March 2016, 10 additional colistin-resistant E. coli isolates from six new hospitals had been submitted to the NRLAR and confirmed as mcr-1 positive. The finding of mcr-1 in E. coli clinical isolates is probably the tip of the iceberg that is a big hidden health issue in South America.

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REFERENCES


