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Letter to the Editor

First detection of *mcr-1* plasmid-mediated colistin-resistant *Escherichia coli* in Lebanese poultry

Sir,

The wide dissemination of multidrug-resistant Gram-negative bacteria (MDR-GNB), especially carbapenem-resistant bacteria, as common causative agents of human infections has necessitated the re-use of old antibiotics, namely colistin, which was abandoned in the past owing to its undesired nephrotoxicity in the human body [1]. Colistin belongs to the polymyxin group of polypeptide antibiotics that attack the lipopolysaccharide (LPS) and phospholipids in the outer cell membrane of GNB, leading to cellular leakage and subsequent bacterial death [1]. Resistance to colistin is mainly due to modifications to LPS and lipid A by the addition of aminoarabinose or phosphoethanolamine [1]. Prior to the end of 2015, such modifications were only due to chromosomal mutations of target genes involved in those pathways. Recently, the plasmid-mediated colistin resistance gene *mcr-1*, a member of the phosphoethanolamine transferase enzyme family in *Escherichia coli*, was reported in *E. coli* in China from pigs and meat [2]. Subsequently, *mcr-1* plasmid-mediated colistin-resistant bacteria have been detected in animals and humans across Asia, Africa, the Americas and Europe [3].

Here we report the first detection of a single *mcr-1*-positive colistin-resistant *E. coli* strain isolated from poultry in Lebanon. This isolate was recovered in Sidon on 14 August 2015 from a rectal swab obtained during a surveillance study aimed at determining the epidemiology of MDR-GNB in Lebanese poultry (unpublished data). In that study, 982 faecal swabs were collected from 49 chicken farms located in the seven districts of Lebanon. Swabs were cultured on MacConkey agar plates supplemented with cefotaxime (2 μg/mL) for the screening of MDR organisms. Identification of the isolated strain was performed using matrix-assisted laser desorption/ionisation time-of-flight mass spectrometry (MALDI-TOF/MS). Antibiotic susceptibility testing was performed by the disk diffusion method (Sanofi-Diagnostic Pasteur, Marnes-la-Coquette, France). The *E. coli* isolate showed an extend-spectrum β-lactamase (ESBL) phenotype and was resistant to penicillins, ceftazidime, cefotaxime, aztreonam, ciprofloxacin, gentamicin and trimethoprim/sulfamethoxazole and, surprisingly, was also resistant to colistin with an inhibition zone diameter of 10 mm. To confirm colistin resistance, colistin Etest strips (bioMérieux, Marcy-l'Étoile, France) and broth microdilution were used. Etest and broth microdilution revealed minimum inhibitory concentrations (MICs) of 2 μg/mL and 4 μg/mL, respectively, thus confirming colistin resistance in this isolate. Using standard PCR amplification and sequencing as described previously [3], the *mcr-1* gene was confirmed in this *E. coli* isolate. The obtained sequence was deposited in GenBank with the accession no. **MF197562**. A conjugation experiment using *E. coli* J53 as recipient was also conducted but was unsuccessful, suggesting that either *mcr-1* is located on a non-conjugative plasmid or it is chromosomally located. PCR amplification and sequencing revealed that the isolate harboured a $bla_{\text{TEM-135-like}}$ ESBL gene with a difference of six base pairs only at the extremities. Multilocus sequence typing (MLST) was performed based on seven housekeeping genes and revealed that the isolate belongs to ST515. This ST differs from those previously reported in *E. coli* isolates harbouring the *mcr-1* gene in food-producing animals. However, ST515 *mcr-1*-harbouring *E. coli* has been isolated from the blood of a male patient at an emergency department in Canada [2]. We thus suppose that this isolate could be a candidate for human infections with possible therapeutic challenges if ever transmitted and introduced into hospital and community settings.

In Lebanon, although insignificant, colistin resistance is not new in that it has been reported in clinical settings since the early 2000s. However, the mechanism of colistin resistance was not previously investigated. To the best of our knowledge, the first and only determination of colistin resistance mechanism in Lebanon was recently performed by Okdah et al., where three colistin resistant *Klebsiella pneumoniae* strains were isolated from Sahel Hospital in Beirut [4]. Colistin resistance in these isolates was mediated by inactivation of *mgrB*, *phoQ*, *pmrA* and *pmrB* genes involved in the modification of LPS in the outer cell membrane, the primary target of colistin in GNB [4]. Here we report the first detection of the *mcr-1* plasmid-mediated colistin resistance gene in Lebanon. As demonstrated by Olaitan et al., *mcr-1*-harbouring strains can be readily spread from animals to the human gut [5] and thus our finding sparks concerns over the transmission of *mcr-1* strains to the Lebanese community. Nowadays, carbapenem-resistant isolates are disseminated in clinical and community settings in Lebanon. This dissemination has necessitated the frequent use of colistin and non-β-lactam antibiotics in Lebanese hospitals [4]. Therefore, it is expected that *mcr-1*-positive strains, when transmitted from animals to humans in Lebanon, will be easily selected and further diffused into the country by the selective pressure applied by the use of colistin and other antibiotics in clinical settings. Surveillance studies addressing the current epidemiology of colistin resistance are thus warranted in Lebanon. In addition, the usage of colistin in veterinary medicine should be re-evaluated, as unpublished data have revealed its heavy use in animals in Lebanon.

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Competing interests

None declared.

Ethical approval

Not required.

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References

[1] Kempf I, Fleury MA, Drider D, Bruneau M, Sanders P, Chauvin C, et al. What do we know about resistance to colistin in *Enterobacteriaceae* in avian and pig production in Europe? Int J Antimicrob Agents 2013;42:379–83.
[2] Walkty A, Karlowsky JA, Adam HJ, Lagace-Wiens P, Baxter M, Mulvey MR, et al. Frequency of *mcr-1*-mediated colistin resistance among *Escherichia coli* clinical isolates obtained from patients in Canadian hospitals (CANWARD 2008–2015). CMAJ Open 2016;4:E641–5.
[3] Chabou S, Leangapichart T, Okdah L, Le Page S, Hadjadj L, Rolain JM. Real-time quantitative PCR assay with *Taq*Man® probe for rapid detection of *mcr-1* plasmid-mediated colistin resistance. New Microbes New Infect 2016;13:71–4.
[4] Okdah L, Leangapichart T, Hadjadj L, Olaitan AO, Al-Bayssari C, Rizk R, et al. First report of colistin-resistant *Klebsiella pneumoniae* clinical isolates in Lebanon. J Glob Antimicrob Resist 2017;9:15–6.
[5] Olaitan AO, Thongmalayvong B, Akkhavong K, Somphavong S, Paboriboune P, Khounsy S, et al. Clonal transmission of a colistin-resistant *Escherichia coli* from a domesticated pig to a human in Laos. J Antimicrob Chemother 2015;70:3402–4.

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