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Case report

First report of the plasmid-borne colistin resistance gene (*mcr-1*) in *Proteus mirabilis* isolated from a toddler in non-clinical settings

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ABSTRACT

We report the detection of a plasmid-borne mobile colistin-resistance-gene, *mcr-1*, in *Proteus mirabilis*, a known community and hospital pathogen, that was isolated from a toddler (2 years old) in the community in Lebanon. To our knowledge, this is the first report of the occurrence of *mcr-1* in human-associated *P. mirabilis* as well as *mcr-1* in humans in the Lebanese community.

Introduction

The recent discovery and global dissemination of mobile genetic elements (*mcr*) that can confer colistin (polymyxin E) resistance have jeopardized the efficacy of this last resort antibiotic and raised public health concerns [1,2]. The spread of *mcr* might be most problematic in countries with limited resources and developing antimicrobial stewardship [3]. Previously, we have described the use of colistin in medicine and agriculture and documented the prevalence of *mcr-1* in multidrug-resistant *Escherichia coli* in different matrices in Lebanon [4–6]. However, sources and transmission of *mcr* remain largely uncharacterized in Lebanon, especially in relation to the human population. Therefore, we initiated surveillance efforts in order to better understand the molecular epidemiology of *mcr* in Lebanon.

Case report

During routine screening of fecal matter collected from diapers of 2-year-old toddlers in the community, we identified whitish and irregularly shaped colonies on RAPID'E.coli 2 agar supplemented with 4 μg/ml colistin [4–6]. A colony (LB-SH32) was further purified and appeared colorless and unable to ferment lactose on MacConkey agar but had distinctive “fishy” odor. PCR analysis showed that LB-SH32 was positive for a species-specific urease gene (*ureC*) fragment, which identified the isolate as *Proteus mirabilis* [7], a Gram-negative enteric bacterium that most commonly causes urinary tract infections but may also lead to respiratory tract-, wound- and other infections. Minimum inhibitory concentration (MIC) analysis showed that LB-SH32 was highly resistant to colistin (MIC > 4096 μg/ml), indicating that the isolate was intrinsically colistin-resistant as expected for *P. mirabilis* [8]. However, the isolate was *mcr-1*-positive (*mcr-2* to *8*-negative), which was confirmed by commercial sequencing. Heat shock transformation with plasmids extracted from LB-SH32 resulted in the successful introduction of the *mcr-1* into chemically-competent *E. coli* JM109, indicating that the *mcr-1* was plasmid-borne and transmissible to other bacteria. The transformants were also resistant to colistin (MIC ≥ 8 μg/ml). Typing showed that the plasmids belonged to IncP1-alpha, which has a broad-host range, can transfer and replicate in different Gram-negative bacteria, and can transmit resistance genes [9,10]. LB-SH32 was multidrug-resistant, displaying resistance to amoxicillin-calvulanic acid, cephalexin, imipenem, gentamicin, kanamycin, streptomycin, tetracycline, and trimethoprim-sulfamethoxazole, while harboring genes encoding beta-lactamase (bla_{TEM-1}, bla_{NDM-1}, bla_{KPC}), tetracycline

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resistance (*tetA*, *B*, and *C*), sulfonamide resistance (*sul1* and *2*), Class-1 Integrons, and integrase (*int1*).

Discussion

This is the first report of 1) transmissible plasmid-borne *mcr-1* in *P. mirabilis* from humans and 2) the detection of *mcr-1* in the Lebanese population. During the peer-review assessment of this study, a manuscript reported the detection of *mcr-1* in six clinical *E. coli* isolates of human origins in Lebanon [11]. Also, as previously mentioned, our study targeted the Lebanese population at large and was conducted on the level of the community in a non-clinical setting. Because *P. mirabilis* is intrinsically colistin resistant, this pathogen is often not screened for *mcr*. However, our study shows that *P. mirabilis* can serve as reservoir for the transmission of these genes to colistin-susceptible bacteria. Therefore, the overlooked role of *P. mirabilis* might be important to further understand the epidemiology and dissemination of *mcr*.

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Declaration of Competing Interest

The authors report no conflict of interest.

Ethical Approval

None was required.

Author Statement

IIK conceived and designed the study, acquired funding, supervised and conducted the experiments, evaluated and analyzed the data, and wrote the manuscript and approved it. ZH conducted the experiments and analyzed the data.

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