Journal of Antimicrobial Chemotherapy

J Antimicrob Chemother
doi:10.1093/jac/dky435

Wide dissemination of colistin-resistant *Escherichia coli* with the mobile resistance gene *mcr* in healthy residents in Vietnam

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Sir,

The importance of colistin in treating life-threatening infections caused by MDR bacteria is increasing. In this regard, dissemination of bacteria harbouring the mobile colistin resistance gene (*mcr*) in food animals has been highlighted, owing to the abundant usage of colistin in the agricultural sector in developing countries.[1] Although the prevalence of colistin-resistant bacteria in healthy human residents in these countries is unclear, a high prevalence of MDR bacteria in the faecal microbiota of residents in Vietnam and surrounding nations was recently revealed.[2] Therefore, here we examined the occurrence of dissemination of colistin-resistant bacteria harbouring *mcr* in the faecal microbiota of healthy residents of a representative Vietnamese village.

The study was conducted at Nguyen Xa village, Thai Binh province, Vietnam, from November 2017 to February 2018. The village, a representative rural community in Vietnam, had 7730 residents in 2008 households in 2015. A total of 98 healthy participants from 36 households were enrolled. The characteristics of the participants are summarized in Table 1.

One stool specimen was obtained from each participant using a transport swab with Cary–Blair transport medium (Eiken Chemical, Tokyo, Japan). Specimens were inoculated on selective agar medium (CHROMagar™ COL-APSE, CHROMagar, Paris, France) for isolation of colistin-resistant Gram-negative bacteria. The resulting Enterobacteriaceae-like colonies were isolated and characterized further for bacterial identification, antibiotic susceptibility, resistance genes and relevance between isolates, as described previously.[3–5]

The study was approved by the Ethics Committees of Osaka University (yakujin 29-8) and Thai Binh University of Medicine and Pharmacy (no. 773.1). All participants provided written informed consent. For any participant younger than 18 years, written informed consent was obtained from the respective parents.

As shown in Table 1, most of the stool specimens were culture positive on a selective-medium plate (CHROMagar™ COL-APSE). Among these colonies, colistin-resistant *Escherichia coli* (CR-E) that exhibited MICs of colistin between 8 and 16 mg/L were detected in 69 out of 98 specimens tested. The proportion of households that had members carrying CR-E was also quite high at 80.6% (29 positive, out of 36 households tested). Furthermore, almost all colistin-resistant isolates possessed *mcr-1* and/or *mcr-3*, except one that did not contain *mcr-1* to *-5*, as determined by PCR.

PFGE analysis of CR-E isolates showed that, within a household, the members of five households carried a similar strain, but between households there were no similar strains (Figure S1, available as Supplementary data at *JAC* Online).

Resistance profiles of CR-E to other antibiotics varied between 0 and 11, out of the 14 antibiotics tested (ampicillin, cefoxitin, cefotaxime, ceftazidime, meropenem, streptomycin, kanamycin, gentamicin, ciprofloxacin, nalidixic acid, tetracycline, chloramphenicol, fosfomycin and trimethoprim/sulfamethoxazole). The average number of antibiotics to which isolates were resistant was 5.6. The rate of MDR, defined as resistance to at least one antibiotic drug in three or more antibiotic classes,[6] of CR-E isolates was determined to be 92.8% (64/69). There were no carbapenem- or fosfomycin-resistant CR-E isolates (Table S1).

In contrast to the studies conducted on colistin-resistant bacteria in food animals, there have been only limited studies on the prevalence of colistin-resistant bacteria with *mcr* in healthy individuals. However, one recent study focused on *mcr-1*-carrying bacteria in the faecal samples of chicken farmers in Vietnam.[7] This study reported that 25% of farmers were colonized with *mcr-1*-carrying bacteria that grew on non-selective medium. However, this protocol may have the potential to lose CR-E strains owing to the abundant susceptible bacteria in stool specimens. As a result, it is difficult to obtain the true prevalence of colistin-resistant bacteria in stool specimens. In the current study, we utilized the selective medium, CHROMagar™ COL-APSE, for identifying colistin-resistant bacteria. The advantage of this method lies in its ability to detect the presence of colistin-resistant bacteria, regardless of their number.

The results of this study revealed a surprisingly high dissemination of CR-E harbouring *mcr* in the faecal microbiota of residents of a rural community in Vietnam. In particular, it was remarkable from a public health point of view, since most participating households had CR-E carriers.

Colistin is one of the most commonly used antibiotics in chickens and pigs in Vietnam.[8,9] The amount of colistin used per kg of live animal per week is as high as 14 mg for chickens and 57 mg for pigs.[9] Such a high amount of colistin consumption by animals in Vietnam may facilitate the wide dissemination of CR-E in residents of rural communities. To the best of our knowledge, this is the first

Table 1. Characteristics of participant residents and CR-E in their stool specimens

No. of households	Range of participants per household	Average number of participants per household	Total number of participants	Age range (years)	Median age (years)	Number of males
36	1–6	2.7	98	2–81	46	44 (44.9%)

Number of specimens tested (one per participant)	Number of positive culture specimens on CHROMagar™ COL-APSE	Number of *E. coli* isolates that grew on CHROMagar™ COL-APSE	Number of colistin-resistant *E. coli* isolates (MIC >2 mg/L)	Number of *mcr*-positive *E. coli* isolates	*mcr* status		
					mcr-1	*mcr-3*	*mcr-1/3*
98	88 (89.8%)	83 (84.7%)	69 (70.4%)	68	64	3	1

report of an extremely high prevalence of CR-E in residents and households.

Concordance between CR-E isolates was assessed by PFGE. The results showed that an expansion of specific clones was not observed at this high prevalence of CR-E. However, since more than 95% of CR-E isolates had *mcr-1*, the horizontal transfer of *mcr-1* among bacteria, under colistin abuse in the agricultural sector, and dissemination of these bacteria in humans via food, seems reasonable.

Acknowledgements

We thank Akiko Ookura for her technical assistance.

Funding

This work was supported by the Japan Agency for Medical Research and Development/Japan International Cooperation Agency as part of the Science and Technology Research Partnership for Sustainable Development, and the Ministry of Education, Culture, Sports, Science and Technology, Japan/Japan Society for the Promotion of Science KAKENHI (grant number 17H01687).

Transparency declarations

None to declare.

Supplementary data

Figure S1 and Table S1 are available as Supplementary data at *JAC* Online.

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