First detection of the *mcr-1* colistin resistance gene in *Escherichia coli* from a patient with urinary tract infection in Myanmar

N. San[1], M. S. Aung[4], P. P. Thu[1], Y. Y. Myint[1], M. T. Aung[2], T. San[3], T. T. Mar[1], M. M. Lwin[1], W. W. Maw[1], M. S. Hlaing[1] and N. Kobayashi[4]

1) *Department of Microbiology, University of Medicine 2, Yangon, Myanmar,* 2) *North Okkalapa General and Teaching Hospital,* 3) *Yangon Children's Hospital, Ministry of Health and Sports, Yangon, Myanmar and* 4) *Sapporo Medical University School of Medicine, Sapporo, Japan*

Abstract

Colistin-resistance gene *mcr-1* was detected in an *Escherichia coli* sample among 442 clinical isolates collected in a tertiary-care hospital in Yangon, Myanmar, in 2018. This isolate was classified into phylogroup A–ST23 complex and harboured $bla_{CTX\text{-}M\text{-}15}$ and $bla_{TEM\text{-}1}$, associated with multiple mutations in quinolone-resistance–determining regions in *gyrA* and *parC*.

Keywords: colistin resistance, *Escherichia coli*, *mcr-1*, Myanmar, ST23 complex

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Corresponding author: M. S. Aung, Department of Hygiene, Sapporo Medical University School of Medicine, S-1 W-17, Chuo-ku, Sapporo 060-8556, Japan.

E-mail: meijisoeaung@sapmed.ac.jp

Colistin (polymyxin E) has been increasingly used worldwide as an antibiotic of last resort for infections caused by carbapenem-resistant Gram-negative bacteria. However, since the first report in China in 2016 [1], occurrence of plasmid-mediated colistin resistance gene *mcr*-1 has been described in *Enterobacteriaceae* from animals and humans in Europe, the Americas, Australia and Asia [2]. In Myanmar, *mcr*-1 has not yet been reported, although this gene has been detected in most of its neighbouring countries.

For the surveillance of carbapenem-resistant *Enterobacteriaceae,* a total of 1555 clinical isolates were collected at the North Okkalapa General Hospital, Yangon, Myanmar, from January to October 2018 (Supplementary Table S1). Among a total of 442 isolates of *Escherichia coli,* 57 isolates (12.9%) were judged to be resistant to carbapenems by the disc diffusion test and were further analysed for the presence of *mcr* genes by PCR as described previously [3]. As a result, *mcr-1* was detected in only one isolate (MMR-CR4) derived from a urine sample of a 68-year-old female inpatient with a urinary tract infection. MMR-CR4 was resistant to multiple classes of antimicrobials, including quinolone (levofloxacin), but was susceptible to fosfomycin and tigecycline (Table 1, Supplementary Table S2). This isolate was judged to be resistant to ertapenem and colistin with low minimum inhibitory concentrations, but showed susceptibility to imipenem and meropenem.

E. coli isolate MMR-CR4 was classified into phylogenetic group A, single-locus variant of sequence type (ST) 90 (ST23 complex) and *fimH* subtype 142. Presence of *mcr-1,* $bla_{CTX\text{-}M\text{-}15}$ and $bla_{TEM\text{-}1}$ was confirmed by determination of sequences (GenBank accession nos. MK405590–MK405592), although no carbapenemase gene was detected. This isolate harboured two aminoglycoside-modifying enzyme genes and two plasmid-mediated quinolone resistance genes. In the quinolone-

TABLE 1. Antimicrobial resistance and genetic traits of *Escherichia coli* isolate MMR-CR4 in Myanmar

Characteristic	Value
Resistance profile	PIP, CEZ, CTM, CTX, CPD, SAM, ATM, ETP, GEN, MIN, SXT, LVX, COL
Phylogenetic group	A
ST	ST90 SLV (ST23Cplx)[a]
Virulence factor genes[b]	*fimH, fyuA, traT, iroN, iha, astA*
β-Lactamase genes (*bla*)[c]	CTX-M-15, TEM-1
Colistin resistance gene[c]	*mcr-1*
Aminoglycoside-modifying enzyme gene[c]	*aph(3′)-IIIa, ant(4′)-Ia*
PMQR gene[c]	*qnrS, oqxAB*
Mutation in QRDR	
gyrA	S83L, D87N
parC	S80I
FimH subtype	*fimH*142

ATM, aztreonam; CFZ, cefazolin; COL, colistin; CPD, cefpodoxime; CTM, cefotiam; CTX, cefotaxime; ETP, ertapenem; GEN, gentamycin; LVX, levofloxacin; MIN, minocycline; PIP, piperacillin; PMQR, plasmid-mediated quinolone resistance; QRDR, quinolone-resistance determining region; SAM, ampicillin/sulbactam; SLV, single-locus variant; ST, sequence type; SXT, sulfamethoxazole/trimethoprim.
[a]Allelic profile of ST: 6-4-4-1-20-8-7.
[b]Negative for *PAI, papAH, kpsMTIII, ibeA, sfa/focDC, kpsMT-K1, hlyA, kpsMTII, papC, cdtB, focG, afa/draBC, cnf1, kpsMT K5, iutA, ireA, chuA, vat, hra, sat, clbB, pic, usp.*
[c]Negative for *bla* encoding SHV, NDM, IMP, VIM, KPC, SPM, SIM, GIM, GES, IMI, DIM, BIC, AIM, SME, NMC, OXA-23, OXA-24, OXA-48, OXA-51, AmpC and also for *aac-6′-aph 2″, aac-6′-Ib-cr, mcr-2, mcr-3, mcr-4, mcr-5,qnrA, qnrB, qnrC, qnrD, qepA.*

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resistance–determining region of *gyrA* and *parC,* two and one mutations were detected, respectively.

In this study, *mcr-1* was detected in *E. coli* for the first time in Myanmar, with a low prevalence among carbapenem-resistant isolates (1/57, 1.8%), which was comparable to those reported for sporadic human cases in other countries [2,4]. The isolate MMR-CR4 harboured no carbapenemase gene, but it was a carbapenem-resistant *Enterobacteriaceae* showing multiple-drug resistance. Although ST23 complex has been scarcely identified among *E. coli* harbouring *mcr-1* in humans and animals [5,6], only ST410 (ST23 complex) was described in *mcr-1*–positive clinical isolates in China [7].

We recently reported that phylogroup A/ST23 complex was a common lineage of *E. coli* in Myanmar [8] and Bangladesh [9], and some clones had carbapenemase genes such as $bla_{\text{NDM-1}}$. Furthermore, ST23 complex, represented by ST90 and ST410, was described as one of the major lineages of carbapenemase-producing *E. coli* in Europe, and the origin of a portion of isolates was suspected to be South Asian or Southeast Asian countries [10]. Accordingly, there is a concern that *mcr-1*–positive, ST23 complex *E. coli* will acquire the carbapenemase gene, becoming an extremely drug-resistant clone. In addition, MMR-CR4 had multiple mutations in quinolone-resistance–determining regions in *gyrA* and *parC,* as identified in Austria [11], thus suggesting its selective increase with the use of quinolones. Despite its low prevalence, the presence of *mcr-1* in a clinical isolate in Myanmar should be noted as sign of spread of multidrug resistance in *Enterobateriaceae*.

Conflict of Interest

None declared.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.nmni.2019.100550.

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