Infection and Drug Resistance

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ORIGINAL RESEARCH

Occurrence of *mcr* Positive Strains and Molecular Characteristics of Two *mcr-1* Positive *Salmonella typhimurium* and *Escherichia coli* from a Chinese Women's and Children's Hospital

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Background: The purpose of this study was to evaluate the prevalence of mobile colistin resistance genes (*mcr*) in Gram-negative bacteria and to analyze the molecular characteristics of *mcr-1* positive *Salmonella typhimurium strain* 75 and *Escherichia coli strain* 107 from the Quanzhou Women's and Children's Hospital in China.

Methods: The genes *mcr-1* through *mcr-9* were screened via multiplex PCR. Antibiotic susceptibility was detected using a GN11 card with the VITEK-2 compact automated system. Whole genomes were sequenced using PacBio's single molecule real-time (SMRT) technology.

Results: In this study, *mcr-1* was detected in only four strains, with a positivity rate of 0.65% (4/616). All the four strains were resistant to more than three different kinds of antibiotics. The *mcr-1* positive *S. typhimurium* strain 75 harbored IncHI2 plasmid, which carried *mcr-1* gene, while the *mcr-1* positive *E. coli* strain 107 contained four plasmids including one *mcr-1* harboring IncHI2 plasmid, one IncFII plasmid and two IncI1-I (Alpha) plasmids. Mobile elements carrying *mcr-1* in the 75_plasmid and 107_plasmid-1 were located in the IS1086(ISA*pl1*)-IS30A(*ISApl1*)-*mcr-1-hp* and IS1086(ISA*pl1*)-*mcr*-1-*hp* regions, respectively. Tn6010 carrying drug efflux pump genes was found in 75_plasmid, while cn_31611_IS26 carrying multi-drug resistance (MDR) genes were found in 107_plasmid-1.

Conclusion: This study found that *mcr-1* was prevalent at a low frequency in the Quanzhou Women's and Children's Hospital. A similar genetic pattern of *mcr-1* transmission was found in both *E. coli* and *S. typhimurium*.

Keywords: *mcr-1*, *Salmonella typhimurium*, *Escherichia coli*, molecular characteristics

Introduction

Polymyxin is highly active against most gram-negative bacteria. However, its nephrotoxicity and neurotoxicity strongly obstruct further application in the treatment of typical patients.[1] The rapid increase of multi-drug resistant (MDR) Gram-negative and the lack of new antibiotics have led to a revival of the clinical use of polymyxin, which is recognized as a last-resort antibiotic for numerous MDR bacterial infections.[2,3] Intrinsic resistance to polymyxin originates from the functional expression or mutation of chromosomal genes in *Neisseria meningitidis* or *Pseudomonas aeruginosa*.[4,5]

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Since the appearance of the first plasmid-mediated mobile colistin resistance gene (*mcr-1*) in Enterobacteriaceae,[6] this transmissible gene has been found worldwide in various gram-negative bacteria, including *E. coli, Klebsiella pneumoniae, Klebsiella oxytoca, Salmonella enterica*, and *Enterobacter* species from animal, meat, food product, environmental, and human sources.[7,8] More worrisome is the presence of *mcr-1* in Enterobacteriaceae with carbapenem resistance genes, such as bla_{NDM} and bla_{KPC}, which could seriously compromise the treatment of infections caused by these extremely drug-resistant pathogens.[9] *Salmonella enterica serovar Typhimurium* belonged to one of the most important serotypes of *Salmonella enterica*.[10] The multidrug-resistant *Salmonella enterica* serovar *Typhimurium* isolate has a high potential to disseminate the *mcr-1* gene and further challenge clinical treatment.[11,12] Meanwhile, eight new *mcr* homologues (*mcr-2* to *mcr-9*) have been identified in Enterobacteriaceae.[13] *E. coli* was identified as containing both *mcr-1* and *mcr-3.19* on a hybrid plasmid, which suggests that the evolution of *mcr* genes among various plasmids is being driven by mobile elements.[14] The phosphoethanolamine (PEA) transferase encoded by *mcr* can catalyse the attachment of PEA to lipopolysaccharide (LPS)-Lipid A, resulting in resistance to polymyxin.[15] Polymyxin resistance has attracted clinical and public health attention.[16] The purpose of this study was to evaluate the prevalence of *mcr* genes in gram-negative bacteria in the Quanzhou Women's and Children's Hospital and to analyse the molecular characteristics of *mcr-1*-positive *S. typhimurium* strain 75 and *E. coli* strain 107.

Methods

Bacterial Strains

A total of 616 clinical gram-negative isolates were collected at the Quanzhou Women's and Children's Hospital from January 2018 to April 2019. The specimens were derived from 218 stool, 142 sputum, 102 throat swab, 68 blood, 35 urine, 35 pus, 10 alveolar lavage fluid, 2 cerebrospinal fluid, 2 ascites, and 2 endotracheal intubation tube segment samples. The study was conducted in accordance with the Declaration of Helsinki, and ethical permission for this study was approved by the Quanzhou Women's and Children's Hospital ethics committee (2017 Ethical Review No. 11). Guardians provided informed consent on behalf of the minors. Strains were identified using the GN card with the VITEK-2 compact automated system (bioMérieux).

DNA Extraction

The DNA extraction procedure was performed according to previously reported methods.[17] After the strain was recovered overnight on LB agar plates, a single colony was picked and resuspended in 100 μL of double distilled water. The suspension was heated at 100°C for 10 min and centrifuged at 5000 rpm for 10 min. DNA was quantified using a UV spectrophotometer, and 1 μL of the supernatant was collected for PCR.

mcr Gene Detection

mcr genes (*mcr-1–9*) were screened by multiplex PCR using primers as previously described.[10] Multiplex PCR reagents were purchased from Nanjing Vazyme Biotechnology Co., Ltd. PCR was conducted by an ABI 7500 instrument, and PCR products were visualised by observing their position after DNA electrophoresis. The PCR products were sent to Fuzhou Boshang Biological Co., Ltd for Sanger sequencing and the sequences were aligned by NCBI BLAST.

Antibiotic Susceptibility Testing

The minimum inhibitory concentration (MIC) of antibiotics was detected using a GN11 card using the VITEK-2 compact automated system (bioMérieux). Antibiotics tested included ampicillin (AMP), ampicillin/sulbactam (SAM), piperacillin/tazobactam (TZP), cefazolin (CZO), cefotetan (CTT), ceftazidime (CAZ), ceftriaxone (CRO), cefepime (FEP), aztreonam (ATM), ertapenem (ETP), imipenem (IMP), amikacin (AMK), gentamicin (KAN), tobramycin (TOB), ciprofloxacin (CIP), levofloxacin (LEV), nitrofurantoin (NIT), and trimethoprim/sulfamethoxazole (SXT). Interpretation of the results was based on the guidelines published by the Clinical and Laboratory Standards Institute (CLSI).[18] The MIC of colistin (COL) purchased from Shanghai Jizhi Biochemical Technology Co., Ltd. was determined using a broth microdilution method. Briefly, the COL diluted in multiples was added to a sterilized 96-well polystyrene plate, 100 μL bacterial suspension diluted 1:1000 with MH broth was added into each well and OD_{600} was determined after it was incubated at 35°C for 20h. ≥4μg/mL was interpreted as resistance in according to the European Committee on Antimicrobial Susceptibility Testing (EUCAST) breakpoint standard.[19] *E. coli* ATCC8739 and

S. typhimurium ATCC14028 were selected as quality control strains.

Whole Genome Sequencing (WGS)

S. typhimurium strain 75 and *E. coli* strain 107 (MIC of COL ≥8 μg/mL) were selected for whole genome sequencing. DNA extraction was carried out according to the instructions of the bacterial genomic DNA extraction kit (TIANGEN Biochemical Technology Co., Ltd). Genomes were sequenced using PacBio's SMRT third-generation sequencing technology, using the HGAP 4 process from PacBio's official analysis software SMRT Link (V6.0.0.47841) for de novo genome assembly. Library construction and sequencing was performed by Tianjin Biochip Bio Co., Ltd. Multilocus sequence typing (MLST), plasmid type, plasmid MLST, antibiotic resistance genes/chromosomal point mutations, and mobile genetic elements were analysed using MLST 2.0, PlasmidFinder 2.1, pMLST 2.0, ResFinder 4.1, and MobileElementFinder, respectively.[20–23] Circular imaging and comparisons between multiple plasmids were conducted using the BLAST ring image generator (BRIG).[24]

Nucleotide Sequence

The complete sequences of 75_chromosome, 75_plasmid, 107_chromosome, 107_plasmid-1, 107_plasmid-2, 107_plasmid-3, 107_plasmid-4 were deposited in GenBank under the accession numbers CP075372, CP075373, CP075374, CP075375, CP075376, CP075377, CP075378, respectively, which will be made public on May 24, 2021.

Results

mcr Gene Screening and Drug Susceptibility results of *mcr*-Positive Strains

The *mcr-1* gene was only detected in four strains, with a positivity rate of 0.65% (4/616). Two *S. typhimurium* strains and one *E. coli* strain were found in the gastrointestinal tract of three different patients, and one *E. coli* strain was found in the urine of a single patient. The age of the patients ranged between 1.3 and 2.7 years. All four patients recovered after treatment. Additional clinical data of the four patients with *mcr-1*-positive *S. typhimurium* or *E. coli* infections are shown in Table 1. Drug susceptibility results indicated that the *S. typhimurium* strain 74, *S. typhimurium* strain 75, *E. coli* strain 107, and *E. coli* strain 332 were multi-resistant, and their profiles appear in Table 2.

Genetic Characteristics of Strains and Plasmids Bearing *mcr-1*

The genome of the *S. typhimurium* strain 75, which belongs to the ST34 strain type, consisted of a 4.88 Mb chromosome which contained no mutations of the *acrB, parC* and *16S_rrsD* genes. It also contained a circular 0.24 Mb *mcr-1*-positive 75_plasmid encoding the IncHI2 replication protein as well as drug resistance genes such as *oqxA, oqxB, FosA3, mcr-1, aac(3)-IV, aadA8b, aadA2, aadA1, sul2, sul3, sul1, dfrA12, cmlA1, floR*, and *blaCTX-M-14* (Table 3). The genome of the *E. coli* strain 107 belonged to an unknown strain type and consisted of a 4.88 Mb chromosome with mutations such as parC:p.S80I, parE:p.S458A, gyrA:p.S83L, and gyrA:p.D87N. It also contained four plasmids, identified here as 107_plasmid 1–4. 107_plasmid-1 is 0.27 Mb, circular, *mcr-1* positive, and encodes the IncHI2 replication protein, as well as the drug resistance genes *dfrA27, sul2, sul1, aph(3')-Ia, aph(4)-Ia, aadA16, aac(3)-IV, fosA3, mph(A), ARR-3, floR, blaCTX-M-14*, and *qacE*. 107_plasmid-2 is an IncFII type plasmid and carries the drug resistance genes *rmtB, blaTEM-214, blaTEM-141, blaCTX-M-55, blaTEM-206*, and *blaTEM-1B*. Both 107_plasmid-3 and −4 encode the IncI1-I(Alpha) replication protein (Table 3).

A BLAST search indicated that the 75_plasmid showed an overall query coverage (97–99%) and nucleotide similarity (99.98%) to several plasmids, such as pGDP37-4 (GenBank no. MK673548.1), pS438 (CP061125.1), and pSH16G0648 (MH522418.1). In addition, the size and backbone structure of these plasmids were quite similar

Table 1 Clinical Data of Four Patients Isolated *E. coli* or *S. typhimurium* with *mcr-1* Positive

No	Isolates	Gender	Age	Diseases	Hospitalized Days	Antibiotics Used	Outcomes
74	Sty	Female	1.3	Salmonella enteritis	0*	Ceftazidine	Get better
75	Sty	Female	1.6	Salmonella enteritis	8	Cefotaxime	Get better
107	*E. coli*	Male	1.3	Infectious diarrhea	9	CRO and metronidazole	Get better
332	*E. coli*	Female	2.7	Urinary Tract Infection	7	NIT	Get better

Note: *Outpatient.

Table 2 MIC of *mcr-1* Positive *S. typhimurium* and *E. coli* Strains

No	COL	AMP	SAM	TZP	CZO	CTT	CAZ	CRO	FEP	ATM	ETP	IMP	AMK	KAN	TOB	CIP	LEV	NIT	SXT
74	4(R)	≥32(R)	≥32(R)	≤4(S)	≥64(R)	4(R)[a]	4(S)	≥64(R)	32(R)	4(S)	≤0.5(S)	≤1(S)	8(R)[a]	≥16(R)	≥16(R)	≤0.25(S)	≤0.25(S)	64(I)	≥320(R)
75	16(R)	≥32(R)	≥32(R)	≤4(S)	≥64(R)	4(R)[a]	4(S)	≥64(R)	32(R)	8(I)	≤0.5(S)	≤1(S)	2(R)[a]	≥16(R)	≥16(R)	≤0.25(S)	≤0.25(S)	64(I)	≥320(R)
107*	8(R)	≥32(R)	≥32(R)	8(S)	≥64(R)	≤4(S)	16(R)	≥64(R)	32(R)	≥64(R)	≤0.5(S)	≤1(S)	≥64(R)	≥16(R)	≥16(R)	≥4(R)	≥8(R)	64(I)	≥320(R)
332*	4(R)	≥32(R)	≥32(R)	≤4(S)	≥64(R)	≤4(S)	≥64(R)	≥64(R)	≥64(R)	≥64(R)	≤0.5(S)	≤1(S)	≤2(S)	≤1(S)	≤1(S)	≤0.25(S)	≤0.25(S)	≤16(S)	≤20(S)

Note: *ESBL positive; [a]the drug susceptibility results have been calibrated as drug resistance in accordance to CLSI.

Abbreviations: S, sensitive; I, intermediary; R, resistant.

(Figure 1A). The 107_plasmid-1 showed an overall query coverage (96%) and nucleotide similarity (99.95–99.99%) to several plasmids, such as pWF5-29 (GenBank no. MG385063.1), pXGE1mcr (KY990887.1), and pLD22-1-MCR1 (CP047877.1). The size and backbone structure of these plasmids were also quite similar (Figure 1B). Further research shows that a 102,172–103,380 region sequence structure encoding hypothetical protein (hp) was inserted in 75_plasmid, and a 251,336–253,752 region sequence structure encoding hp, y4hO, and y4hP was inserted 107_plasmid-1 (Figure 1). Mobile elements carrying *mcr-1* sequences of the IS1086(ISA*pl1*)-IS30A (*ISApl1*)-*mcr-1-hp* and IS1086(ISA*pl1*)-*mcr-1-hp* regions were identified in the 75_plasmid and 107_plasmid-1, respectively (Figure 1). MobileElementFinder analysis showed that the 72,498–79,343 region of the 75_plasmid belonged to a composite transposon of Tn6010, while the 251,336–253,752 and 77,044–108,655 regions of the 107_plasmid-1 belonged to the IS682 and cn_31611_IS26 regions, respectively.

Discussions

In this study, the *mcr-1* gene was detected in only four strains, with a positivity rate of 0.65% (4/616), which was similar to the 0.62% rate reported by Rong Fan et al.[25] This indicated that there was no detection of any *mcr* types other than *mcr-1* in Quanzhou. CRO was used to treat diarrhoea infection in patient #107 but bacterial resistance may have led to treatment failure, resulting in prolonged hospital stay (10 days).

mcr-1 was found to frequently coexist with other drug resistance genes (ie genes responsible for resistance to carbapenems[26,27] and extended-spectrum β-lactam drugs),[28,29] indicating the possibility of the emergence of bacteria with MDR.[30] Drug susceptibility results of this study indicated that all the four strains were resistant to more than three different groups of drugs. All *mcr-1*-positive strains were resistant to COL. It was previously reported that *mcr-1* appeared in carbapenem-resistant Enterobacteriaceae.[31] Fortunately, we found that the four strains were sensitive to ETP and IMP. Further analysis showed that the *S. typhimurium* strain 75 and *E. coli* strain 107 were susceptible to carbapenem, and this was consistent with the absence of carbapenem-resistant genes in both the strains.

The *S. typhimurium* monophasic pandemic sequence ST34 clone has attracted global attention because of its rapidly increasing resistance to MDR. This clone was

Table 3 Phenotypic and Molecular Features of *mcr-1* Positive *S. typhimurium* Strain 75 and *E. coli* Strain 107

Chromosome/ Plasmid	Size (MB)	MLST	Plasmid Type	pMLST	Resistance Genes	Chromosomal Point Mutations
75_chromosome	4.88	34	–	–	*aph(3")-Ib, aph(6)-Id, aac(6')-Iaa, sul2, blaTEM-1B, tet(B)*	*acrB, parC* and *16S_rrsD* found without known mutations
75_plasmid	0.24	-	IncHI2	3	*oqxA, oqxB, FosA3, mcr-1, aac(3)-IV; aadA8b, aadA2, aadA1, sul2, sul3, sul1, dfrA12, cmlA1; floR, blaCTX-M-14*	-
107_chromosome	4.8	Unknown	-	-	No found	parC:p.S80I, parE:p.S458A, gyrA:p.S83L, gyrA:p.D87N
107_plasmid-1	0.27	-	IncHI2	3	*dfrA27, sul2, sul1, aph(3')-Ia, aph(4)-Ia, aadA16, aac(3)-IV, mcr-1, fosA3, mph(A), ARR-3, floR, blaCTX-M-14, qacE*	-
107_plasmid-2	0.07	-	IncFII	F2:A-:B-	*rmtB, blaTEM-214, blaTEM-141, blaTEM-1B, blaCTX-M-55, blaTEM-206, blaTEM-1B*	-
107_plasmid-3	0.09	-	IncI1-I(Alpha)	154	No found	-
107_plasmid-4	0.09	-	IncI1-I(Alpha)	154	No found	-

Note: - annotated as not determined.

Abbreviations: *aph(3")-Ib*, aminoglycoside O-phosphotransferase APH(3")-Ib gene; *aph(6)-Id*, aminoglycoside O-phosphotransferase APH(6)-Id gene; *aac(6')-Iaa*, aminoglycoside 6′-N-acetyltransferase; *sul2*, sulfonamide-resistant dihydropteroate synthase Sul2 gene; *blaTEM-1B*, BlaTEM-1b beta-lactamase; *tet(B)*, tetracycline efflux MFS transporter Tet(B) gene; *oqxA*, multidrug efflux RND transporter periplasmic adaptor subunit OqxA gene; *oqxB*, multidrug efflux RND transporter permease subunit OqxB gene; *FosA3*, fosfomycin resistance glutathione transferase FosA3; *mcr-1*, MCR-1 family phosphoethanolamine–lipid A transferase gene; *aac(3)-IV*, AAC(3)-IV family aminoglycoside N-acetyltransferase gene; *aadA8b*, AadA8b aminoglycoside (3")adenylyltransferase; *aadA2*, ANT(3")-Ia family aminoglycoside nucleotidyltransferase AadA2 gene; *aadA1*, ANT(3")-Ia family aminoglycoside nucleotidyltransferase AadA1 gene; *sul3*, sulfonamide-resistant dihydropteroate synthase Sul3 gene; *sul1*, sulfonamide-resistant dihydropteroate synthase Sul1 gene; *dfrA12*, trimethoprim-resistant dihydrofolate reductase DfrA12 gene; *cmlA1*, chloramphenicol efflux MFS transporter CmlA1 gene; *floR*, chloramphenicol/florfenicol efflux MFS transporter FloR gene; *blaCTX-M-14*, class A extended-spectrum beta-lactamase CTX-M-14; *dfrA27*, trimethoprim-resistant dihydrofolate reductase DfrA27 gene; *aph(3')-Ia*, aminoglycoside O-phosphotransferase APH(3')-Ia gene; *aph(4)-Ia*, aminoglycoside O-phosphotransferase APH(4)-Ia gene; *aadA16*, ANT(3")-Ia family aminoglycoside nucleotidyltransferase AadA16 gene; *aac(3)-IV*, AAC(3)-IV family aminoglycoside N-acetyltransferase gene; *mph(A)*, Mph(A) family macrolide 2′-phosphotransferase gene; *ARR-3*, NAD(+)–rifampin ADP-ribosyltransferase Arr-3 gene; *qacE*, quaternary ammonium compound-resistance protein; *rmtB*, RmtB family 16S rRNA (guanine (1405)-N(7)-methyltransferase gene; *blaCTX-M-55*, class A extended-spectrum beta-lactamase CTX-M-55; *acrB*, multidrug efflux pump RND permease AcrB; *parC*, topoisomerase IV; DNA gyrase; *parE*, DNA topoisomerase IV subunit B; *gyrA*, DNA gyrase (subunit A).

associated with resistant-pattern ASSuT (AMP, streptomycin, sulfamethoxazole, and tetracycline).[32] The ST34 phenotype-associated drug resistance genes *blaTEM-1B, aph(3")-Ib, aph(6)-Id, sul2*, and *tet(B)* were also found in *S. typhimurium* strain 75. It may be that unknown mutations in *acrB, parC*, and *16S_rrsD* do not confer quinolone resistance, which was consistent with the sensitivity of this strain to CIP and LEV. The detection of ST34 strains carrying the *mcr-1* gene in diarrhoea suggests that the Chinese children were suffering from the disease caused by this pathogen.[33,34] The presence of the COL resistance genes (*mcr-1, mcr-3*, and *mcr-5*) combined with the MDR phenotype in ST34 had spread across different countries, with most *mcr-1* genes from the ST34 isolates detected in the plasmid type IncHI2, followed by IncI2 and IncX4.[35] The *mcr-1*-positive 75_plasmid was circular and encodes the IncHI2 replication protein. Several genes encoding components involved in antitoxin systems as well as colicin, tellurite, and heavy metal tolerance likely play critical roles in the environmental stability of IncHI2 plasmids in the ST34 clone.[36] Therefore, the ST34 strain is more likely to acquire *mcr*-bearing plasmids. All strains harbouring the *mcr-1* gene were reported to carry the MDR plasmid. The 75_plasmid also contained drug resistance genes, which mediated the emergence of MDR. Here, we reported for the first time that *mcr-1* and *aadA8b* coexist in the IncHI2 plasmid of the ST34 strain. This finding was important because this genetic

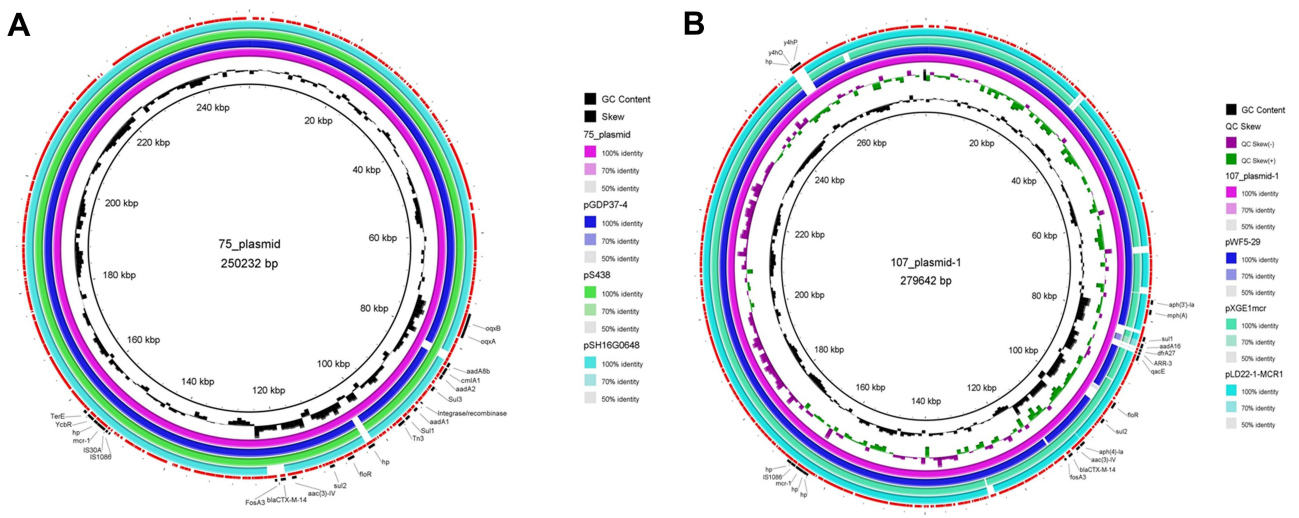

Figure 1 Circular representation of the studied plasmids. GC content and GC Skew were represented on the distance scale (in kbp) on the inner map. Each plasmid was compared to its most closely-related plasmid. The red arc around the map indicated ORFs. Certain important genes were also indicated on the ring. The hp is short for hypothetical protein. (**A**) 75_Plasmid alignment map; (**B**) 107_Plasmid-1 alignment map.

combination may increase the spread risk of aminoglycoside resistance.

The most common *mcr-1*-positive *E. coli* strain ST10 has been frequently detected in China.[37] The genetic makeup of *mcr-1*-positive *E. coli* was highly diverse.[38] Therefore, it was unsurprising that we found an unknown sequence type in the *E. coli* strain 107. The 107_chromosome of *E. coli* strain 107 in this study contained mutation types such as parC:p.S80I, parE:p.S458A, gyrA:p.S83L, gyrA:p.D87N, which confered quinolone resistance.[39] In 90% of *E. coli* cases, the *mcr-1* gene was related to IncX4, IncHI2, and IncI2 mobilizable plasmids, which spread easily worldwide.[40–42] The *mcr-1*-positive 107_plasmid-1 was circular and encoded the IncHI2 replication protein. Two *mcr-1*–bearing plasmids (IncI2 and IncHI2) were observed in the same strain.[43] The 107_plasmid-1 and 2 both carried numerous drug resistance genes, which may increase the risk of the development of pan-drug resistance.

BLASTp analysis showed that the hp inserted in the 75_plasmid was an IS4-like element ISVsa5 family transposase reported to inactivate the *mcr-1* gene by insertion in *S. typhimurium*;[44] The hp, y4hO, and y4hP that were inserted into the 107_plasmid-1 belonged respectively to IS66 transposase TnpA, TnpB, and IS66-like element ISEc23 family transposase, which were present in the other *mcr-1*-positive plasmids. MobileElementFinder analysis showed that the 72,498–79,343 region belonged to a composite transposon of Tn6010, including the efflux pump genes *oqxA* and *oqxB*. These genes were similar to those of the oqxAB-carrying plasmids pHXY0908 (from chickens) and pHK0653 (from a human patient) in *S. typhimurium*.[45] Four mobile element structures carrying *mcr-1* in Enterobacteriaceae have been reported: (1) with both ends containing the ISA*pl1* transposon Tn6330 (ISA*pl1*–*mcr*-1–orf–ISA*pl1* structure); (2) with a single upstream ISA*pl1* (ISA*pl1*–*mcr*-1–orf structure); (3) with a single downstream ISApl1 (*mcr*-1–orf–ISA*pl1* structure); (4) with sequences lacking ISA*pl1* altogether (*mcr*-1–orf structure).[46,47] Of note, the sequence region of IS1086(ISA*pl1*)-IS30A(*ISApl1*)-*mcr-1-hp* in 75_plasmid and the sequence region of IS1086(ISA*pl1*)-*mcr*-1-*hp* in 107_plasmid-1 both belonged to upstream ISA*pl1* element, which was observed in 78% of IncHI2 plasmids in *E. coli*.[40] Cn_31611_IS26 (IS6 family) included 11 drug resistance genes (*dfrA27, sul2, sul1, aph(4)-Ia, aadA16, aac(3)-IV, mcr-1, mph(A), ARR-3, floR*, and *qacE*), which may be acquired from a Tn region containing several drug resistance genes.

In conclusion, this study revealed that the *mcr-1* gene had low prevalence in the Quanzhou Women's and Children's Hospital. The same genetic strategy for *mcr-1* transmission was found in both *E. coli* and *S. typhimurium*. *mcr-1* transmission should attract the attention of the public health sector, which should adopt urgent methods such as strictly controlling the large-scale use of polymyxin in agriculture and animal husbandry to control its spread.

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Disclosure

The authors declare that they have no conflict of interest.

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