

LETTER TO THE EDITOR

Open Access



Presence of plasmid-mediated quinolone resistance (PMQR) genes in non-typhoidal *Salmonella* strains with reduced susceptibility to fluoroquinolones isolated from human salmonellosis in Gyeonggi-do, South Korea from 2016 to 2019

Sohyun Lee^{1†}, Nanjoo Park^{1,2†}, Sujung Yun¹, Eunseon Hur¹, Jiwon Song¹, Hanna Lee¹, Yongsug Kim¹ and Sangryeol Ryu^{2*} 

Abstract

Non-typhoidal salmonellosis remains a pressing public health problem worldwide. Quinolones, particularly fluoroquinolones, are widely used to treat various infections, including non-typhoidal salmonellosis, which can be a serious illness. The emergence of fluoroquinolone-resistant *Salmonella* has resulted in treatment failure and high mortality rates. In this study, we estimated the presence of plasmid-mediated quinolone resistance (PMQR) genes in *Salmonella enterica* isolated from human salmonellosis patients in South Korea from 2016 to 2019. We evaluated the association of these genes with fluoroquinolone susceptibility. Antimicrobial susceptibility tests for *Salmonella* isolates were performed using the Vitek II system, and the minimum inhibitory concentrations (MIC) of ciprofloxacin and levofloxacin were determined using the E-test method. Plasmid-mediated quinolone resistance (PMQR) genes were detected by PCR amplification and quinolone resistance-determining regions (QRDRs) of the *gyrA* and *parC* genes were analyzed following Sanger sequencing of the PCR products. Thirty-four *Salmonella* strains with reduced susceptibility to fluoroquinolones (ciprofloxacin MIC \geq 0.125 μ g/mL and levofloxacin MIC \geq 0.25 μ g/mL) were selected from 208 human clinical *Salmonella* isolates. Among them, 22 *Salmonella* strains harbored one PMQR gene (*qnrA*, *qnrB*, or *qnrS*), and three *Salmonella* strains carried two PMQR genes (*qnrS* and *aac(6')-Ib-cr* or *qnrA* and *qnrB*). *qnrS* was the most common PMQR gene. Serotyping revealed that *Salmonella* 4,[5]12:i:- (32.4%, 11/34) and *Salmonella* Typhimurium (29.4%, 10/34) were the two most predominant serovars, and Multi-locus sequence typing (MLST) showed that ST19 and ST34 were the most frequent sequence types. In conclusion, *qnr* gene-positive *Salmonella* 4,[5],12:i:- and *Salmonella* Typhimurium were the main serovars responsible for reduced susceptibility to fluoroquinolones. Therefore, our findings suggest that PMQR-positive *Salmonella* strains, which can be isolated from various samples including human, food, and the environment, should be carefully monitored.

*Correspondence: sangryu@snu.ac.kr

[†]Sohyun Lee and NanjooPark contributed equally to this work

² Department of Food and Animal Biotechnology, Department of Agricultural Biotechnology, Research Institute for Agriculture and Life Sciences, Center for Food and Bioconvergence, Seoul National University, Seoul 08826, South Korea

Full list of author information is available at the end of the article



© The Author(s) 2021. This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit <http://creativecommons.org/licenses/by/4.0/>. The Creative Commons Public Domain Dedication waiver (<http://creativecommons.org/publicdomain/zero/1.0/>) applies to the data made available in this article, unless otherwise stated in a credit line to the data.

Keywords: *Salmonella*, Quinolone resistance, Plasmid-mediated quinolone resistance, PMQR

Background

Salmonellosis is a disease caused by *Salmonella* that usually produces acute onset of fever, abdominal pain, diarrhea, and vomiting. Antimicrobial therapy is not recommended in healthy individuals with mild or moderate infection [1]. This is due to the use of antimicrobials may not shorten the duration of clinical symptoms, but is rather a risk for prolonged *Salmonella* infection [2]. However, high-risk groups including infants, the elderly, and immunocompromised patients may require antimicrobial therapy [1]. Quinolones, particularly fluoroquinolones (e.g., ciprofloxacin and levofloxacin), are a critically important antimicrobial class, and invasive *Salmonella* infections in adults are commonly treated with quinolones. However, because quinolones are frequently used in human and veterinary medicine, resistance to this antimicrobial class has evolved among *Salmonella* strains [3]. Fluoroquinolone resistance is mostly associated with chromosomal mutations in the bacterial genes encoding targeted enzymes, DNA gyrase and topoisomerase IV (quinolone resistance determining region, QRDR). However, fluoroquinolone resistance can also be acquired by plasmid encoded genes (plasmid-mediated quinolone resistance, PMQR). There are several well-known PMQR gene groups, including *qnr* families (*qnrA*, *qnrB*, *qnrC*, *qnrD*, *qnrE*, *qnrS*, and *qnrVC*), antibiotic efflux pump-coding genes (*qepA* and *oqxAB*), antibiotic modification enzyme gene (*aac(6)-Ib-cr*), and a newly described phosphorylase gene (*crpP*) [4]. According to previous studies, the *qnr*, *aac(6)-Ib-cr*, and *qepA* genes are commonly detected in South Korea; therefore, we chose these genes to investigate in this study [5, 6]. The Qnr is a pentapeptide repeat protein that protects DNA gyrase and topoisomerase IV by inhibiting quinolone [7, 8]. The *aac(6)-Ib-cr* gene encodes aminoglycoside acetyltransferase that simultaneously induces resistance against aminoglycoside and fluoroquinolone [9]. PMQR facilitates the spread of quinolone resistance, leading to the emergence of high quinolone resistance, making infections difficult to treat [10]. Therefore, the presence of PMQR genes in *Salmonella* strains with reduced susceptibility to fluoroquinolones indicates that continuous monitoring and clinical attention are required. Although PMQR genes confer reduced susceptibility of bacteria to fluoroquinolones, their influence on nalidixic acid susceptibility is minor [11]. The United States National Antimicrobial Resistance Monitoring System (NARMS) has indicated the presence of PMQR genes among *Salmonella* and other enteric bacteria isolated from humans,

retail meat, and food animals in the United States. Additionally, NARMS recently reported an increase in the proportion of ciprofloxacin-non-susceptible strains lacking nalidixic acid resistance [12]. In Canada, a relatively high prevalence of PMQR genes has been reported in human isolates of non-typhoidal *Salmonella* with resistance and reduced susceptibility to fluoroquinolones [13]. Likewise, PMQR gene-positive *Salmonella* 4,[5],12:i:- were recently isolated from pigs, chickens, humans, geese, and cats in China [14]. In this study, we aim to estimate the presence of the plasmid-mediated quinolone resistance genes and their association with fluoroquinolone susceptibility in non-typhoidal *Salmonella* isolates from human clinical samples in South Korea from 2016 to 2019.

Methods

Thirty-four nontyphoidal *Salmonella* strains with intermediate resistance to quinolone or fluoroquinolone were selected and evaluated from 208 human clinical *Salmonella* strains. The strains were isolated from fecal samples of diarrhea patients in Gyeonggi-do, South Korea, by the Research Institute of Health & Environment from 2016 to 2019 (see Additional file 1). The rectal swab samples were plated on *Salmonella-Shigella* (SS) agar (Oxoid, Basingstoke, UK) and incubated at 37 °C for 18 to 24 h. Isolates with typical *Salmonella* phenotypes were confirmed using the Vitek II system with a GN card (bioMérieux Inc., Marcy l'Etoile, France). *Salmonella* serotyping was done according to the White-Kauffmann-Le Minor scheme using slide agglutination test (O antigen) and tube agglutination test (H antigen) with antisera. The isolates were serotyped using the somatic (O) (provided from Korea Disease Control and Prevention Agency, KDCA) and flagella (H) antisera (Difco, Detroit, MI, USA). The absence of *hin* gene in the monophasic variant of *Salmonella* Typhimurium was confirmed by PCR. Antimicrobial susceptibility tests were performed using the Vitek II system with the AST-N169 card (bioMérieux Inc.) according to the manufacturer's instructions. The minimum inhibitory concentrations (MIC) of ciprofloxacin and levofloxacin were determined using the E-test method (bioMérieux Inc.). Quinolone and fluoroquinolone MIC values were confirmed according to CLSI guidelines [15]. In *Salmonella*, a ciprofloxacin MIC of 0.12–0.5 µg/mL is defined as intermediate and MIC ≥ 1 µg/mL is defined as resistant, while a levofloxacin MIC of 0.25–1 µg/mL is defined as intermediate and MIC ≥ 2 µg/mL is defined as resistant. Additionally,

a nalidixic acid MIC ≥ 32 $\mu\text{g/mL}$ is defined as resistant, and there is no intermediate category. Total DNA was extracted from overnight cultures of *Salmonella* isolates using the Nextractor NX-48 system and NX-48 bacterial DNA kits (Genolution Inc., Seoul, Korea). PMQR genes (*qnrA*, *qnrB*, *qnrS*, *aac(6')-Ib-cr*, and *qepA*) were detected by PCR amplification using primers described in previous studies [16–18]. The QRDR region of the *gyrA* and *parC* genes was each PCR-amplified using previously described primers [19]. PCR products were purified and Sanger sequenced by Macrogen Inc, Korea. The nucleotide sequences of QRDRs in *gyrA* and *parC* genes were compared with the counterpart sequences of quinolone-susceptible reference strain *Salmonella* Typhimurium LT2 (GenBank Accession number AE006468) using BLAST. Seven housekeeping genes (*aroC*, *dnaN*, *hemD*, *hisD*, *purE*, *sucA*, and *thrA*) were amplified using previously reported MLST primers (see Additional file 2). PCR products were sequenced by Macrogen (South Korea). Each isolate's sequence type (ST) was assigned according to the PubMLST website. Phylogenetic analyses of the isolates using MLST-based clusters were conducted with BioNumerics software (Applied Maths, Sint-Martens-Latem, Belgium). The correlation between PMQR genes and MIC values was analyzed by Fisher's exact test using GraphPad Prism software v.5 (GraphPad Software Inc., La Jolla, CA). A P-value < 0.05 was considered to indicate statistical significance.

Results and discussion

Thirty-four *Salmonella* strains with reduced susceptibility to fluoroquinolones were identified from Gyeonggi-do, South Korea, from 2016 to 2019. *Salmonella* 4,[5],12:i:- (32.4%, 11/34) and *Salmonella* Typhimurium (29.4%, 10/34) were the predominant serovars. Isolated *Salmonella* serovars showing intermediate resistance to quinolones, particularly fluoroquinolones, were presented in Table 1. In the last two decades, *Salmonella* 4,[5],12:i:- has rapidly emerged worldwide [14]. In South Korea, the first foodborne outbreak of *Salmonella* 4,[5],12:i:- was reported in 2008 [20]; the same serovar, which exhibits nalidixic acid resistance, was isolated from pigs and chickens in South Korea [21]. Similarly, most *Salmonella* 4,[5],12:i:- isolates from chickens, geese, and cats in China were resistant to nalidixic acid (52.5%) [14]. Isolates of enrofloxacin-resistant *Salmonella* 4,[5],12:i:- from swine in the United States have also been reported [22].

All 34 isolates (100%) showed reduced susceptibility to levofloxacin, 32 isolates (94.1%) showed reduced susceptibility to ciprofloxacin, and 27 isolates (79.4%) were also resistant to nalidixic acid. We obtained seven

non-typhoidal *Salmonella* isolates that showed reduced susceptibility to fluoroquinolones and susceptibility to nalidixic acid. Resistance to nalidixic acid could be related to reduced susceptibility to fluoroquinolones because it typically required chromosomal mutations in the quinolone resistance-determining region (QRDR) or acquisitions of PMQR genes (Table 1). Reduced susceptibility to fluoroquinolones without nalidixic acid resistance indicated PMQR presence [10], and the US NARMS has found higher percentages of isolates with reduced susceptibility to ciprofloxacin than nalidixic acid resistance since 2005 [12].

PMQR genes were detected in 25 (73.5%) out of 34 *Salmonella* isolates, including one (2.9%) isolate positive for *qnrA*, two (5.9%) isolates positive for *qnrB*, 23 (67.6%) positive for *qnrS*, and two (5.9%) positive for *acc(6')-Ib-cr* (Table 1). The correlation between PMQR genes and MIC values was statistically insignificant. According to previous studies, the *qnr* gene family was predominantly detected in *Salmonella* strains isolated from travelers. Most of the strains carrying the *qnrS* gene showed reduced susceptibility to ciprofloxacin [21]. The *qnrS* gene was mostly harbored by *Salmonella* 4,[5],12:i:- and *Salmonella* Typhimurium [23, 24]. The *qepA* gene was not detected in any isolate. According to a study on PMQR gene prevalence in clinical *Enterobacteriaceae* isolates from South Korea, *qnrB* was the most frequently observed PMQR gene before 2000, whereas *qnrS*, *aac(6')-Ib-cr*, and *qepA* emerged after 2000 [25]. Although most PMQR-positive isolates possessed only one gene, two *Salmonella* Saintpaul isolates were positive for *qnrS* and *acc(6')-Ib-cr* and one *Salmonella* Carno isolate was positive for *qnrA* and *qnrB*. Among the PMQR gene-positive *Salmonella* isolates from patients and turkey meat, *Salmonella* Saintpaul carrying one *qnrS1* gene was reported in the Netherlands and Denmark [26, 27]. *Salmonella* Carno is a rare serotype, and this serovar has not been extensively studied.

To estimate genetic correlations, multi-locus sequence typing (MLST) was conducted. Nine isolates of ST19 type (seven *Salmonella* Typhimurium and two *Salmonella* 4,[5],12:i:-), 9 isolates of ST34 type (nine *Salmonella* 4,[5],12:i:-), 2 isolates of ST36 type (two *Salmonella* Typhimurium), ST27 type (two *Salmonella* Saintpaul), ST13 type (one *Salmonella* Agona and one *Salmonella* Hato) and ST469 type (two *Salmonella* Rissen) were identified. ST19 and ST34 were the predominant STs in *Salmonella* Typhimurium and *Salmonella* 4,[5],12:i:-, which had high genetic diversity but were over 80% similar to each other (Fig. 1). ST19 and ST34 are more common in *Salmonella* Typhimurium STs responsible for infections worldwide [28, 29]. ST19 and ST34 prevalence in *Salmonella* 4,[5],12:i:- has

Table 1 Isolation and antibiotic resistance information for *Salmonella* isolates evaluated in this study

#	Serotype	Year	ST	AST ^a .	QRDR	PMQR	MIC ^b .	
				Nalidixic acid			Ciprofloxacin	Levofloxacin
29	Typhimurium	2016	19	R	GyrA(D87Y)	–	0.125	0.25
43	Typhimurium	2017	36	S	–	<i>qnrS1</i>	0.125	0.38
44	Typhimurium	2017	36	S	–	<i>qnrS1</i>	0.125	0.38
48	Typhimurium	2017	19	S	–	<i>qnrS1</i>	0.125	0.25
63	Typhimurium	2017	19	R	GyrA(D87Y)	–	0.125	0.25
53	Typhimurium	2018	19	R	–	<i>qnrS1</i>	0.19	0.38
17	Typhimurium	2018	16	R	GyrA(S83F)	–	0.125	0.25
19	Typhimurium	2018	19	R	GyrA(D87Y)	–	0.125	0.25
20	Typhimurium	2018	19	R	–	<i>qnrS1</i>	0.25	0.5
21	Typhimurium	2018	19	R	GyrA(D87Y)	<i>qnrS1</i>	0.25	0.75
13	I 4,[5],12:i:-	2017	34	R	–	<i>qnrS1</i>	0.19	0.38
22	I 4,[5],12:i:-	2018	34	S	–	<i>qnrS1</i>	0.125	0.25
23	I 4,[5],12:i:-	2018	34	R	–	<i>qnrS1</i>	0.19	0.38
24	I 4,[5],12:i:-	2018	19	S	–	<i>qnrS1</i>	0.125	0.38
25	I 4,[5],12:i:-	2018	34	S	–	<i>qnrS1</i>	0.125	0.25
54	I 4,[5],12:i:-	2018	34	R	–	<i>qnrS1</i>	0.19	0.5
55	I 4,[5],12:i:-	2018	34	R	–	<i>qnrS1</i>	0.19	0.38
57	I 4,[5],12:i:-	2018	34	R	–	<i>qnrS1</i>	0.125	0.38
59	I 4,[5],12:i:-	2018	34	R	–	<i>qnrS1</i>	0.19	0.5
50	I 4,[5],12:i:-	2018	19	R	–	<i>qnrS1</i>	0.25	0.5
61	I 4,[5],12:i:-	2019	34	R	–	<i>qnrS1</i>	0.25	1
11	Rissen	2017	469	R	GyrA(S83Y), ParC(T57S)	–	0.125	0.5
12	Rissen	2017	469	R	GyrA(S83Y), ParC(T57S)	–	0.125	0.38
2	Saintpaul	2017	27	R	–	<i>qnrS1, aac(6)-Ib-cr</i>	0.5	0.38
3	Saintpaul	2017	27	R	–	<i>qnrS1, aac(6)-Ib-cr</i>	0.5	0.38
8	Enteritidis	2017	11	R	GyrA(D87N)	–	0.032	0.25
10	Kentucky	2017	11	R	GyrA(D87G)	–	0.047	0.25
15	Carno	2017	1992	R	ParC (T57S)	<i>qnrA, qnrB</i>	0.19	0.5
16	Agona	2017	13	R	ParC (T57S)	<i>qnrB</i>	0.125	0.5
18	Hato	2018	13	R	ParC (T57S)	<i>qnrS1</i>	0.125	0.5
32	Duesseldorf	2016	292	R	GyrA(S83F), ParC(T57S)	–	0.125	0.25
51	Braenderup	2018	311	R	ParC(T57S)	<i>qnrS2</i>	0.19	0.5
52	Derby	2018	Undetermined	S	–	<i>qnrS1</i>	0.125	0.38
62	Newport	2019	214	R	–	<i>qnrS1</i>	0.125	0.25

ST sequence typing, QRDR quinolone-resistance determining region, PMQR plasmid-mediated quinolone resistance, MIC minimum inhibitory concentration

^a Vitek II system with AST-N169 card

^b E-test method

significantly increased in Canada, and some of these STs demonstrate quinolone resistance [30]. It has been reported that ST19 is significantly associated with ciprofloxacin resistance in China [31] and that ST34 is linked to the nalidixic acid resistance in Africa [32]. *Salmonella* Agona ST13 was the most prevalent serovar isolated from chicken meat in Sri Lanka [33], and a *Salmonella* Agona strain isolated from chicken meat in China possessed a T57S substitution in ParC and carried *qnrS* [34]. *Salmonella* Rissen ST469 was isolated

from ready-to-eat mussels in Spain and pork products in Portugal [35, 36]. Moreover, ST469 was the third most predominant ST isolated from pork samples in China and nearly one-third of the ST469 isolates were resistant to ciprofloxacin [37]. However, the sequence type of one *Salmonella* Derby isolate could not be determined by MLST, suggesting the possibility that a potential novel ST of *Salmonella* Derby has emerged in South Korea.

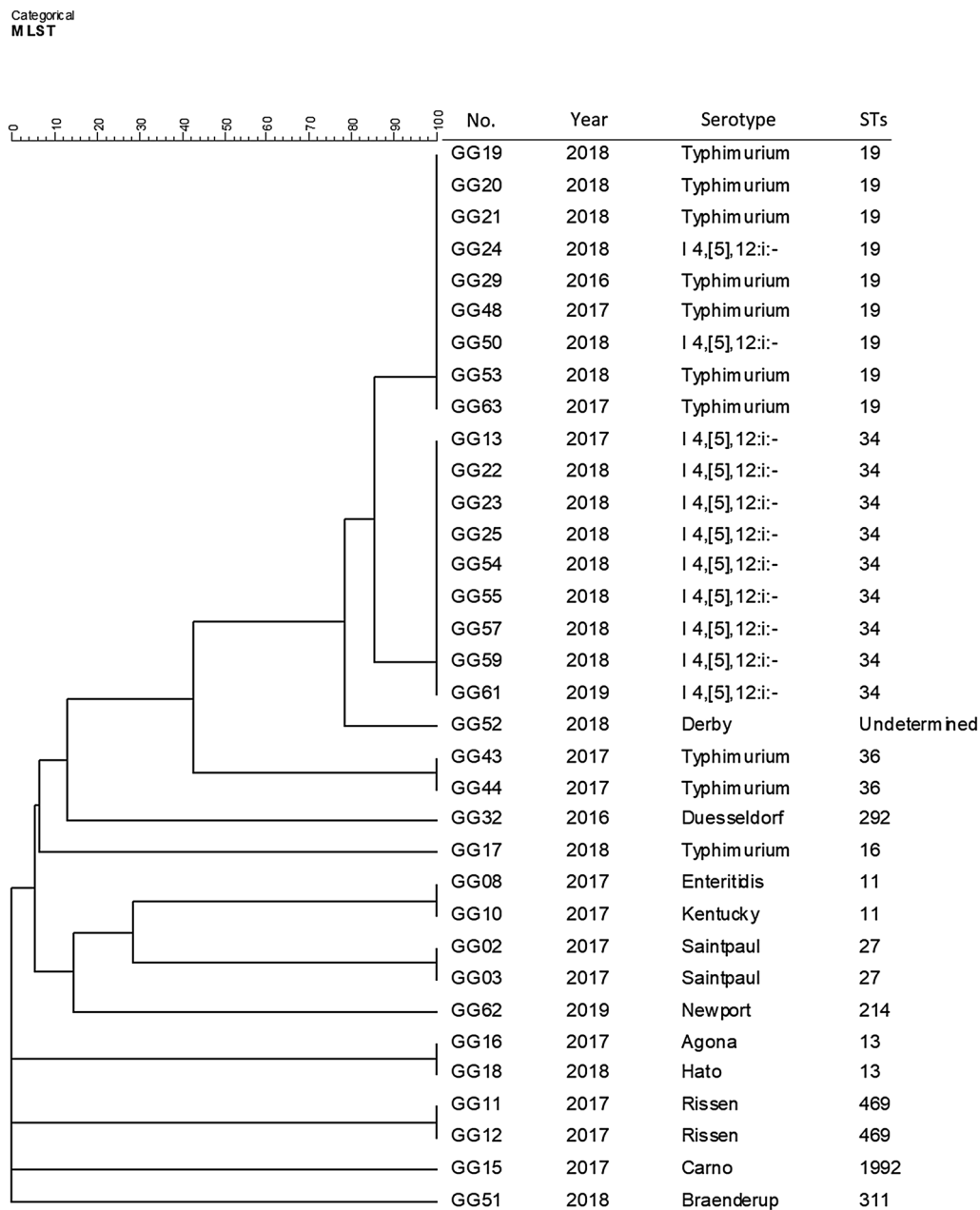


Fig. 1 Phylogenetic tree based on MLST sequence typing of PMQR-positive *Salmonella* isolates from South Korea. The cluster analysis was performed using the categorical coefficient and the UPGMA in BioNumerics

Conclusions

We isolated 34 *Salmonella* strains with reduced susceptibility to fluoroquinolones from human salmonellosis. Among them, *Salmonella* 4,[5],12:i:- and *Salmonella* Typhimurium were the most common serovars, and MLST revealed that ST19 and ST34 were the predominant lineages, with a high genetic similarity of over 80%. The spread of plasmid-mediated antibiotic resistance in

ST19 and ST34 strains requires careful attention in South Korea. Furthermore, all isolates carried one or two of the PMQR genes, suggesting that various genes associated with quinolone resistance can be transferred horizontally among *Enterobacteriaceae*, causing human infections in South Korea.

Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s13099-021-00431-7>.

Additional file 1: Table S1. *Salmonella* serovars isolated from clinical samples in Gyeonggi-do, South Korea. **Additional file 2: Table S2.** Primer sequences used for this experiment.

Acknowledgements

Not applicable.

Authors' contributions

SL, NP and SR participated in the conception and design of the study. SL and NP performed the laboratory work. NP and SR analyzed the data and wrote the manuscript. SL, SY, EH, JS, HL and YK contributed to the analysis and helped in writing the manuscript. All authors read and approved the final manuscript.

Funding

This research was supported by a Grant (19162MFD037) from the Ministry of Food and Drug Safety in 2020.

Availability of data and materials

Data sharing not applicable to this article.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

Author details

¹Gyeonggi-do Research Institute of Health & Environment, Suwon 16381, South Korea. ²Department of Food and Animal Biotechnology, Department of Agricultural Biotechnology, Research Institute for Agriculture and Life Sciences, Center for Food and Bioconvergence, Seoul National University, Seoul 08826, South Korea.

Received: 27 January 2021 Accepted: 21 May 2021

Published online: 01 June 2021

References

- World Health Organization (WHO). *Salmonella* (Non-Typhoidal). [http://www.who.int/news-room/fact-sheets/detail/salmonella-\(non-typhoidal\)](http://www.who.int/news-room/fact-sheets/detail/salmonella-(non-typhoidal)). Accessed 31 July 2020.
- Onwuezobe IA, Oshun PO, Odigwe CC. Antimicrobials for treating symptomatic non-typhoidal *Salmonella* infection. *Cochrane Database Syst Rev*. 2012;11(11):CD001167.
- World Health Organization (WHO). Critically important antimicrobials for human medicine, 5th revision 2016. <http://apps.who.int/iris/bitstream/handle/10665/255027/9789241512220-eng.pdf?sequence=1>. Accessed 31 July 2020.
- Ruiz J. Transferable mechanisms of quinolone resistance from 1998 onward. *Clin Microbiol Rev*. 2019;32(4):e00007-19.
- Seo KW, Lee YJ. Characterization of plasmid mediated quinolone resistance determinants in ciprofloxacin resistant-*Escherichia coli* from chicken meat produced by integrated broiler operations in Korea. *Int J Food Microbiol*. 2019;307:108274.
- Kim JH, Cho JK, Kim KS. Prevalence and characterization of plasmid-mediated quinolone resistance genes in *Salmonella* isolated from poultry in Korea. *Avian Pathol*. 2013;42(3):221–9.
- Tran JH, Jacoby GA, Hooper DC. Interaction of the plasmid-encoded quinolone resistance protein Qnr with *Escherichia coli* DNA gyrase. *Antimicrob Agents Chemother*. 2005;49:118–25.
- Tran JH, Jacoby GA, Hooper DC. Interaction of the plasmid-encoded quinolone resistance protein QnrA with *Escherichia coli* topoisomerase IV. *Antimicrob Agents Chemother*. 2005;49:3050–2.
- Robicsek A, Strahilevitz J, Jacoby GA, Macielag M, Abbanat D, Park CH, et al. Fluoroquinolone-modifying enzyme: a new adaptation of a common aminoglycoside acetyltransferase. *Nat Med*. 2006;12:83–8.
- Beth E, Karp D, Campbell JC, Chen, Jason P, Folster CR, Friedman. Plasmid-mediated quinolone resistance in human non-typhoidal *Salmonella* infections: an emerging public health problem in the United States. *Zoonoses Public Health*. 2018;65:838–49.
- Hooper DC, Jacoby GA. Mechanisms of drug resistance: quinolone resistance. *Ann N Y Acad Sci*. 2015;1354:12–31.
- Centers for Disease Control and Prevention (CDC). National Antimicrobial Resistance Monitoring System for Enteric Bacteria: human isolates final report 2013. <https://www.cdc.gov/narms/pdf/2013-annual-report-narms-508c.pdf>.
- Kim J, Han X, Bae J, Chui L, Louie M, Finley R, Mulvey MR, Ferrato CJ, Jeon B. Prevalence of plasmid-mediated quinolone resistance (PMQR) genes in non-typhoidal *Salmonella* strains with resistance and reduced susceptibility to fluoroquinolones from human clinical cases in Alberta, Canada, 2009–13. *J Antimicrob Chemother*. 2016;71(10):2988–90.
- He J, Sun F, Sun D, Wang Z, Jin S, Pan Z, Xu Z, Chen X, Jiao X. Multidrug resistance and prevalence of quinolone resistance genes of *Salmonella enterica* serotypes 4,[5],12:i:- in China. *Int J Food Microbiol*. 2020;330:108692.
- CLSI. Performance standards for antimicrobial susceptibility testing. CLSI Supplement M100. 29th ed. Wayne: Clinical and Laboratory Standards Institute; 2019.
- Robicsek A, Strahilevitz J, Sahn D, Jacoby GA, Hooper DC. *qnr* prevalence in ceftazidime-resistant *Enterobacteriaceae* isolates from the United States. *Antimicrob Agents Chemother*. 2006;50:2872–2874.
- Park CH, Robicsek A, Jacoby GA, Sahn D, Hooper DC. Prevalence of *aac*(6')-Ib-cr encoding a ciprofloxacin-modifying enzyme in the United States. *Antimicrob Agents Chemother*. 2006;50:3953–5.
- Young Kang H, Dorji TM, Seol SY, Kim J. Dissemination of plasmid-mediated *qnr*, *aac*(6')-Ib-cr, and *qepA* genes among 16S rRNA methylase producing *Enterobacteriaceae* in Korea. *J Bacteriol Virol*. 2009;39:173–82.
- Casin I, Breuil J, Darchis JP, Guelpa C, Collatz E. Fluoroquinolone resistance linked to *GyrA*, *GyrB*, and *ParC* mutations in *Salmonella enterica* typhimurium isolates in humans. *Emerg Infect Dis*. 2003;9(11):1455–7.
- Lee DY, Lee E, Min JE, Kim SH, Oh HB, Park MS. Epidemic by *Salmonella* I 4,[5], 12: i:- and characteristics of isolates in Korea. *Infect Chemother*. 2011;43:186–90.
- Kim AR, Lim SK, Lee KC, Jung SC, Cho YS, Yun SJ, et al. Characterization of *Salmonella enterica* serovar 4,[5],12: i:- isolates from Korean food animals. *Foodb Pathog Dis*. 2015;12:766–9.
- Elnekave E, Hong S, Mather AE, Boxrud D, Taylor AJ, Lappi V, Johnson TJ, Vannucci F, Davies P, Hedberg C, Perez A, Alvarez J. *Salmonella enterica* serotype 4,[5],12:i:- in Swine in the United States Midwest: an emerging multidrug-resistant clade. *Clin Infect Dis*. 2018;66(6):877–85.
- Gunell M, Aulu L, Jalava J, Lukinmaa-Aberg S, Osterblad M, Ollgren J, et al. Cefotaxime-resistant *Salmonella enterica* in travelers returning from Thailand to Finland. *Emerg Infect Dis*. 2014;20:1214–7.
- Acheampong G, Owusu M, Owusu-Ofori A, Osei I, Sarpong N, Sylverken A, Kung HJ, Cho ST, Kuo CH, Park SE, Marks F, Adu-Sarkodie Y, Owusu-Dabo E. Chromosomal and plasmid-mediated fluoroquinolone resistance in human *Salmonella enterica* infection in Ghana. *BMC Infect Dis*. 2019;19(1):898.
- Kim HB, Park CH, Kim CJ, Kim EC, Jacoby GA, Hooper DC. Prevalence of plasmid-mediated quinolone resistance determinants over a 9-year period. *Antimicrob Agents Chemother*. 2009;53:639–45.
- Cavaco LM, Korsgaard H, Sørensen G, Aarestrup FM. Plasmid-mediated quinolone resistance due to *qnrB5* and *qnrS1* genes in *Salmonella enterica* serovars Newport, Hadar and Saintpaul isolated from turkey meat in Denmark. *J Antimicrob Chemother*. 2008;62(3):632–4.

27. García-Fernández A, Fortini D, Veldman K, Mevius D, Carattoli A. Characterization of plasmids harbouring *qnrS1*, *qnrB2* and *qnrB19* genes in *Salmonella*. *J Antimicrob Chemother*. 2009;63(2):274–81.
28. Antunes P, Mourão J, Pestana N, Peixe L. Leakage of emerging clinically relevant multidrug-resistant *Salmonella* clones from pig farms. *J Antimicrob Chemother*. 2011;66(9):2028–32.
29. Antunes P, Coque TM, Peixe L. Emergence of an IncIy plasmid encoding CMY-2 β -lactamase associated with the international ST19 OXA-30-producing β -lactamase *Salmonella* Typhimurium multidrug-resistant clone. *J Antimicrob Chemother*. 2010;65(10):2097–100.
30. Mulvey MR, Finley R, Allen V, Ang L, Bekal S, El Bailey S, et al. Emergence of multidrug-resistant *Salmonella enterica* serotype 4,[5], 12:i- involving human cases in Canada: results from the Canadian Integrated Program on Antimicrobial Resistance Surveillance (CIPARS), 2003–10. *J Antimicrob Chemother*. 2013;68:1982–6.
31. Dong N, Li Y, Zhao J, Ma H, Wang J, Liang B, Du X, Wu F, Xia S, Yang X, Liu H, Yang C, Qiu S, Song H, Jia L, Li Y, Sun Y. The phenotypic and molecular characteristics of antimicrobial resistance of *Salmonella enterica* subsp. *enterica* serovar Typhimurium in Henan Province, China. *BMC Infect Dis*. 2020;20(1):511.
32. Al-Gallas N, Khadraoui N, Hotzel H, Tomaso H, El-Adawy H, Neubauer H, Belghouthi K, Ghedira K, Gautam HK, Kumar B, Laouini D, Zarrouk S, Abbassi MS, Aissa RB. Quinolone resistance among *Salmonella* Kentucky and Typhimurium isolates in Tunisia: first report of *Salmonella* Typhimurium ST34 in Africa and *qnrB19* in Tunisia. *J Appl Microbiol*. 2021;130(3):807–18.
33. Tay MYF, Pathirage S, Chandrasekaran L, Wickramasuriya U, Sadeepanie N, Waidyarathna KDK, Liyanage LDC, Seow KLG, Hendriksen RS, Takeuchi MT, Schlundt J. Whole-genome sequencing analysis of nontyphoidal *Salmonella enterica* of chicken meat and human origin under surveillance in Sri Lanka. *Foodb Pathog Dis*. 2019;16(7):531–7.
34. Zhang CZ, Zhang Y, Ding XM, Lin XL, Lian XL, Trampari E, Thomson NM, Ding HZ, Webber MA, Jiang HX. Emergence of ciprofloxacin heteroresistance in foodborne *Salmonella enterica* serovar Agona. *J Antimicrob Chemother*. 2020;75(10):2773–9.
35. Lozano-Leon A, Garcia-Omil C, Dalama J, Rodriguez-Souto R, Martinez-Urtaza J, Gonzalez-Escalona N. Detection of colistin resistance *mcr-1* gene in *Salmonella enterica* serovar Rissen isolated from mussels, Spain, 2012–to 2016. *Euro Surveill*. 2019;24(16):1900200.
36. Campos J, Cristino L, Peixe L, Antunes P. MCR-1 in multidrug-resistant and copper-tolerant clinically relevant *Salmonella* 1,4,[5],12:i- and S. Rissen clones in Portugal, 2011 to 2015. *Euro Surveill*. 2016;21:26.
37. Zhu Z, Huang Q, Hong X, Chen X, Lu Y, Chen Z, Wang C, Meng X, Xu Q, Li S. Isolation and characterization of *Salmonella* in pork samples collected from retail and wholesale markets in each season from 2016 to 2018 in Wuhan, China. *J Appl Microbiol*. 2020;128(3):875–83.

Publisher's Note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Ready to submit your research? Choose BMC and benefit from:

- fast, convenient online submission
- thorough peer review by experienced researchers in your field
- rapid publication on acceptance
- support for research data, including large and complex data types
- gold Open Access which fosters wider collaboration and increased citations
- maximum visibility for your research: over 100M website views per year

At BMC, research is always in progress.

Learn more biomedcentral.com/submissions

