Epidemic patterns of antimicrobial resistance of *Salmonella enterica* serovar Gallinarum biovar Pullorum isolates in China during the past half-century

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ABSTRACT Pullorum is a chicken-specific systemic disease caused by *Salmonella enterica* serovar Gallinarum biovar Pullorum (***S.* Pullorum**). This study was carried out to provide basic data for understanding the trends of *S.* Pullorum. A total of 652 *S.* Pullorum isolates collected in China during 1962–2019 were examined. Overall, 525 (80.5%) isolates were resistant to at least one antibiotic; 280 (42.9%) isolates resisted 3 or more classes of antibiotics and showed an increasing trend until 2015 and then decreased significantly. The most common multidrug-resistant pattern was ampicillin–tetracycline–nalidixic acid (13.6%). After 2008, 6 classes of antibiotic-resistant strains began to appear, and they have been prevalent ever since. In 2014, a strain resistant to 7 antibiotics (ampicillin–cefazolin–streptomycin–tetracycline–sulphonamides–nalidixic acid–nitrofurantoin) was isolated. The highest antimicrobial resistance was observed for nalidixic acid (71.9%), and the lowest was found for cefotaxime, meropenem, amikacin, gentamicin, fosfomycin, and polymyxin (0%). Our findings monitored the prevalence of the resistance of *S.* Pullorum during the past half-century in China. Continued surveillance of antimicrobial resistance and the rational use of antimicrobials is necessary and important to control the rapid increase in antimicrobial resistance in *S.* Pullorum.

Key words: *Salmonella enterica* serovar Gallinarum biovar Pullorum, antimicrobial susceptibility, resistance trend, chicken

2021 Poultry Science 100:100894
https://doi.org/10.1016/j.psj.2020.12.007

INTRODUCTION

Salmonella is an important pathogenic bacterium capable of infecting humans and animals. *Salmonella enterica* serovar Gallinarum biovar Pullorum (***S.* Pullorum**), a strictly chicken-adapted pullorum agent, is one of the more than 2,610 documented *Salmonella* lineages (Issenhuth–Jeanjean et al., 2014). Pullorum is a bacterial disease that results in high mortality in young chicks. Owing to its vertical and horizontal transmission, it is a threat to the modern poultry industry, causing great economic loss (Shivaprasad, 2000).

Although pullorum disease is well controlled in many developed countries, it remains common in many parts of the world. Antimicrobial therapy is being used as an important measure to control poultry disease in China, although the use of antimicrobials in controlling pullorum disease is not recommended. However, abuse of antimicrobial agents in industrial food animal production is regarded as one of the important reasons for the emergence of antimicrobial resistance in *Salmonella.* Moreover, the increasing appearance of multidrug-resistant (**MDR**) *S.* Pullorum has been increasingly observed in China (Nhung et al., 2017). This resistance can be transmitted to humans through animal foodstuffs, which poses a serious threat to public health. This study examined the tendency and the pattern of *S.* Pullorum to become resistant to antimicrobials with

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Received June 17, 2020.
Accepted December 1, 2020.

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time. It also explored whether resistance trends have changed under national policies to reduce and ban the use of antibiotics.

MATERIALS AND METHODS

Bacterial Isolates

A total of 652 *S.* Pullorum isolates collected over 58 consecutive years, from 1962 to 2019, were included in the study. The isolates were cultured from chickens with clinical signs of pullorum disease. All bacterial strains were isolated from the liver, except for 8 strains that were isolated from feces, of chickens in 10 different provinces in China: Jiangsu, Shandong, Xinjiang, Shanxi, Anhui, Shanghai, Beijing, Henan, Zhejiang, and Jilin (Supplementary Table 1). The study used the culture method of Gong et al. (2013) and Zhou et al. (2018). Once identified, the isolates were stored at −70°C in tryptic soy broth containing 30% glycerol.

Antimicrobial Susceptibility Testing

We tested 652 isolates for their sensitivity to 18 antimicrobial agents via the agar dilution method as per the Clinical and Laboratory Standards Institute recommendations VET01–S2 (CLSI, 2013) and M100–S25 (CLSI, 2015). The following antimicrobials were tested: ampicillin (**AMP**), cefazolin (**CFZ**), cefotaxime (**CTX**), meropenem (**MEM**), aztreonam (**ATM**), amikacin (**AMK**), gentamicin (**GEN**), streptomycin (**STR**), tetracycline (**TET**), sulphonamides (**SXT**), nalidixic acid (**NAL**), ciprofloxacin (**CIP**), chloramphenicol (**CHL**), florfenicol (**FFC**), nitrofurantoin (**NIT**), olaquindox (**OLA**), polymyxin (**CL**), and fosfomycin (**FOS**). Results were obtained after incubating samples at 37°C for 16 to 20 h. The *Escherichia coli* reference strain ATCC 25922 was used for quality control.

Data Analysis

The results were interpreted as per the European Committee on Antimicrobial Susceptibility Testing and Clinical and Laboratory Standards Institute breakpoints (EUCAST, 2016) (Supplementary Table 2). Multidrug resistance was defined as resistance to at least 3 different classes of antimicrobials (MDR $\geq$3). Magnitude of annual change was estimated by using a slope parameter, Q, and the Sen nonparametric method. Calculations were performed by using the Excel (Microsoft, Redmond, WA) . Trend and Sen slope estimates were tested by template Mann–Kendall. A t-test was used to test the difference between means using GraphPad Prism 8 software (GraphPad, La Jolla, CA). A *P*-value <0.05 was considered statistically significant.

RESULTS AND DISCUSSION

Overall, 80.5% (525) of the *Salmonella* isolates were resistant to at least one antimicrobial, and none were resistant to all 18 antimicrobials. The isolates exhibited the highest frequencies of resistance to NAL (71.9%), followed by TET (38.5%), AMP (27.9%), and SXT (32.1%). Relatively lower rates were observed for CFZ (8.4%), STR (4.3%), ATM (0.2%), CIP (0.3%), CHL (0.6%), OLA (0.6%), FFC (0.5%), and NIT (0.3%). None were resistant to CTX, MEM, AMK, GEN, FOS, and CL (Table 1). In China, AMP, TET, and SXT have been commonly used to control pullorum disease for a long time. Moreover, the irrational use of antibiotics may explain the high and increasing resistance rates in the period from 1962 to 2014 (Ministry of Agriculture and Rural Affairs of the People's Republic of China [MAPRC], 2013; Yang et al., 2013; Lai et al., 2014). By contrast, the Ministry of Agriculture and Rural Affairs of the People's Republic of China (2015a,b) policies for comprehensive administration of veterinary drugs from 2015 to 2019 might explain the decline in the resistance to AMP, CFZ, STR, TET, SXT, and NAL since 2015 (Figure 1). That was limited to use antimicrobials such as CFZ and so on. In addition, it is forbidden to change the dosage and the exaggeration of indications in the instructions, to use of antibiotics beyond the market circulation period, and to add antibiotic drugs illegally (Ministry of Agriculture and Rural Affairs of the People's Republic of China [MAPRC], 2002b).

Resistance to AMP was observed in 27.9% of the isolates. In addition, the resistance of *S.* Pullorum strains to AMP increased between the periods 1962–1999 and 2000–2019 ($P < 0.001$). Previously, a high level of AMP resistance by the *Salmonella* Gallinarum isolate was reported in Korea from 1995 to 2001 (Lee et al., 2003) and from 2002 to 2007 (Kang et al., 2010) and in China from 1962 to 2010 (Gong et al., 2013). Different to that found for AMP, a low level of resistance to CFZ was observed throughout the period studied (8.4%), which could be because of the limited use of these classes of antimicrobial agents in veterinary health sectors of China and concurs with previous studies conducted in other countries (Wang et al., 2017; Youn et al., 2017). All isolates were susceptible to CTX, similar to published studies (Taddele et al., 2012; Penha et al., 2016) but contrary to another report from Chinese researchers (Gong et al., 2013). This discrepancy could be explained by the high cost of the third-generation cephalosporins (e.g., CTX) or the successful efficacy of the first-generation cephalosporins (e.g., CFZ), which are rarely used in chickens.

The isolates displayed a low level of resistance to the aminoglycosides. All isolates were susceptible to AMK and GEN. Resistance to AMK was not frequent, which is consistent with that reported elsewhere (Lee et al., 2003; Parveen et al., 2007). The strains showed low resistance to STR (4.3%). Similar results have been reported in Korea (Kang et al., 2010) but differ from those previously reported in China (Pan et al., 2009). All of the isolates were susceptible to STR after 2015 ($P < 0.01$). Nhung et al. (2017) also found that the resistance to

Table 1. Characteristics of antimicrobial resistance of *S.* Pullorum isolates in terms of years.

		No. of resistant isolates (%)					Total (%)	Sen's slope estimate			
Antimicrobial agent	Antimicrobial	1962–1979 (n = 63)	1980–1999 (n = 57)	2000–2009 (n = 200)	2010–2014 (n = 243)	2015–2019 (n = 89)	652	*P* value	Q (95% CI)	MIC_{50}	MIC_{90}
Penicillins	AMP	0	9 (15.8)	22 (11.0)	116 (47.7)	35 (39.3)	182 (27.9)	<0.001	10.93 (10.39 to 11.46)	128	512
Cephems	CFZ	0	1 (1.8)	8 (4.0)	35 (14.4)	11 (12.4)	55 (8.4)	<0.001	3.72 (3.58 to 3.86)	2	4
	CTX	0	0	0	0	0	0	-	-	0.25	1
Carbapenems	MEM	0	0	0	0	0	0	-	-	0.03	0.0625
Monobactams	ATM	0	0	0	0	1 (1.1)	1 (0.2)	<0.001	0.24 (0.22 to 0.26)	0.25	4
Aminoglycosides	AMK	0	0	0	0	0	0	-	-	0.5	1
	GEN	0	0	0	0	0	0	-	-	0.25	1
	STR	3 (4.8)	8 (14.0)	6 (3.0)	11 (4.5)	0	28 (4.3)	<0.001	−2.01 (−2.23 to −1.79)	8	16
Tetracyclines	TET	4 (6.3)	10 (17.5)	81 (40.5)	128 (52.7)	28 (31.5)	251 (38.5)	<0.001	7.76 (7.07 to 8.45)	4	256
Sulphonamides	SXT	0	3 (5.3)	77 (38.5)	111 (45.7)	18 (20.2)	209 (32.1)	<0.001	7.13 (6.28 to 7.98)	2/38	64/1216
Quinolones and fluoroquinolone	NAL	2 (3.2)	1 (1.8)	155 (77.5)	239 (98.3)	72 (80.9)	469 (71.9)	<0.001	24.11 (22.84 to 25.37)	256	>512
	CIP	0	0	1 (0.5)	1 (0.4)	0	2 (0.3)	<0.001	0.03 (0.01 to 0.04)	0.25	0.5
Amyl alcohols	CHL	1 (1.6)	2 (3.5)	1 (0.5)	0	0	4 (0.6)	<0.001	−0.67 (−0.72 to −0.62)	4	4
	FFC	1 (1.6)	2 (3.5)	0	0	0	3 (0.5)	<0.001	−0.66 (−0.72 to −0.60)	4	4
Nitrofurans	NIT	0	0	1 (0.5)	1 (0.41)	0	2 (0.3)	<0.001	0.03 (0.01 to 0.04)	32	64
Quinoxaline	OLA	0	5 (8.8)	25 (12.5)	4 (1.6)	0	4 (0.6)	<0.001	−1.00 (−1.30 to −0.71)	16	64
Lipopeptides	CL	0	0	0	0	0	0	-	-	4	128
Fosfomycin	FOS	0	0	0	0	0	0	-	-	0.5	1

Abbreviations: AMP, ampicillin; ATM, aztreonam; AMK, amikacin; CFZ, cefazolin; CHL, chloramphenicol; CIP, ciprofloxacin; CL, polymyxin; CTX, cefotaxime; FFC, florfenicol; FOS, fosfomycin; GEN, gentamicin; MEM, meropenem; NAL, nalidixic acid; NIT, nitrofurantoin; OLA, olaquindox; STR, streptomycin; SXT, sulphonamides; TET, tetracycline; Q, magnitude of annual percentage increase or decrease.

STR was high and then decreased from 2010 to 2012. One possible reason is that STR is rarely used in veterinary clinical settings. This idea supports the position that STR is not approved for use in feeds (McChesney et al., 1995).

High rates of resistance to SXT (32.1%) and TET (38.5%) were found among the isolates throughout the study period. The resistance to SXT and TET increased from 5.3 and 6.3%, respectively, in 1980–2014 to 45.7 and 52.7%, respectively, in 1962–2014 ($P < 0.01$). Since 2015, their trends have been downward. Similar effects have been reported by other researchers (Threlfall et al., 1997; Manie et al., 1998). *Salmonella* strains isolated from poultry with a high level of resistance to SXT and TET were also reported as widespread in previous studies (Thakur and Bajaj, 2006; Zhao et al., 2007). In poultry, TET is used in day-old chickens as a single injection or administered via the drinking water to control infection by *Salmonella* and *E. coli* (Levy et al., 1976). Sulphonamide compounds were commonly used to control pullorum disease. Perhaps, these antimicrobial drugs have not been frequently used for the treatment of pullorum disease in China since 2015 (Krishnasamy et al., 2015; Tang et al., 2016; Qiao et al., 2017).

There were few isolates resistant to amyl alcohols; 0.6% of the isolates were resistant to CHL. There were only 4 resistant strains from 1962 to 2009 and none after 2009. There were only 3 strains resistant to FFC between1962 and 1999, and no resistant strain has emerged since 2000. Chloramphenicol has been banned in food animals since 2002 in China (MAPRC, 2002), which explains why there have been no resistant strains since 2009. Similar effects have been reported by other researchers (Taddele et al., 2012; Dey et al., 2016). Florfenicol is a structural analog of CHL that was approved in China in 2002 for use in veterinary medicine (White et al., 2000). However, the resistance to FFC was low. Perhaps, this is because its resistance mechanism is not common. A group of researchers found similar results (Penha et al., 2016).

From 1962 to 2019, the strains were highly resistant to NAL, with MIC_{50} and MIC_{90} values of 256 and >512 μg/mL, respectively (Table 1). However, the isolates showed low levels of resistance to CIP (0.3%), and the resistance existed only during 2000–2014. It may be that these drugs were forbidden used. Similar effects have been reported by other researchers (Taddele et al., 2012; Dey et al., 2016). In line with other studies (Padungtod and Kaneene, 2006; Cheong et al., 2007), we found that *Salmonella*, found predominantly in chickens, emerged as particularly resistant to the quinolone NAL after 2000 ($P < 0.05$).

Long-term use of antimicrobial agents causes the accumulation of drug residues and many other public health problems (Barrow et al., 2012). Multidrug-resistant strains were observed in 42.9% of the isolates recovered in this study. The isolates showed an increasing trend of MDR strains between 1962 and 2014 ($P < 0.001$), and then, the trend declined after

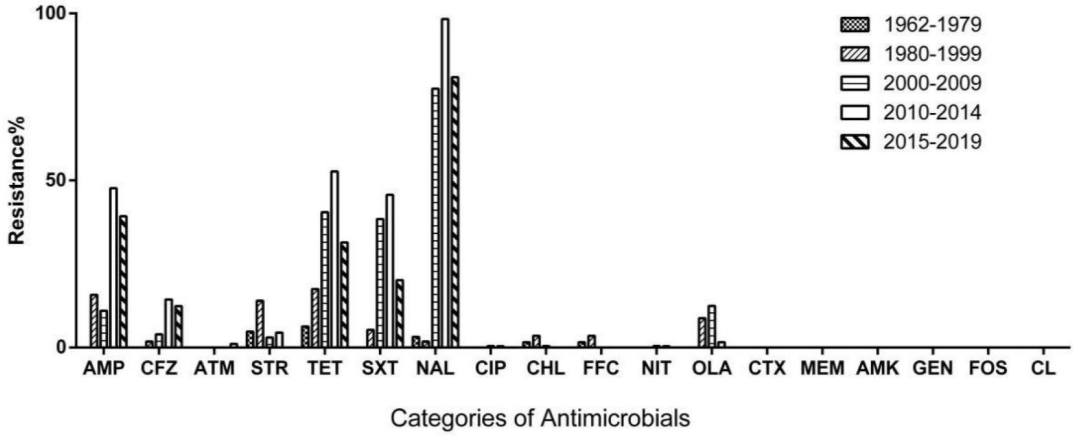

Figure 1. Antimicrobial resistance rate among *S.* Pullorum isolates collected from chickens in China during 1962–2019. Abbreviations: AMP, ampicillin; AMK, amikacin; ATM, aztreonam; CFZ, cefazolin; CHL, chloramphenicol; CIP, ciprofloxacin; CL, polymyxin; CTX, cefotaxime; FFC, florfenicol; FOS, fosfomycin; GEN, gentamicin; MEM, meropenem; NAL, nalidixic acid; NIT, nitrofurantoin; OLA, olaquindox; STR, streptomycin; SXT, sulphonamides; TET, tetracycline.

2015 ($P < 0.01$). This decrease might be because of the country's policies on antibiotics introduced in 2015 (Krishnasamy et al., 2015; Tang et al., 2016; Qiao et al., 2017). Since 2000, meat production has plateaued in high-income countries but grown by 68, 64, and 40% in Africa, Asia, and South America, respectively (Van Boeckel et al., 2019), which is concurrent with a dramatic increase in strains with resistance to one or more classes of antimicrobials. In the period of 1962–1979, resistance to 5 or more drugs was not observed. However, during 1980–1999, 1.8% of the isolates were resistant to 5 classes of antimicrobials. In the span of 2000–2009, 1.5% of the isolates were resistant to 5 or more antimicrobials. The number of isolates exhibiting resistance to 4 or more antimicrobials increased from 7.0% during 2000–2009 to 37.8% in 2010–2014. It is noteworthy that from 2000 to 2019, 4.1% of the isolates were resistant to 6 antimicrobials. In 2014, there was a strain resistant to 7 classes of antimicrobials (Figure 2). Although the trend of drug resistance presents an obvious downward trend, it is projected that antimicrobial consumption will rise by 67% by 2030 and nearly double in Brazil, Russia, India, China, and South Africa. This rise is likely to be driven by the growth in consumer demand for livestock products in middle-income countries. We should call for initiatives to preserve antibiotic effectiveness (Thomas et al., 2015; Founou et al., 2016).

The resistance patterns of *S.* Pullorum isolates were further analyzed. There were 62 unique resistance patterns among the strains resistant to 3 or more antimicrobials of the total 652 *S.* Pullorum isolates. The most common MDR patterns were AMP–TET–NAL

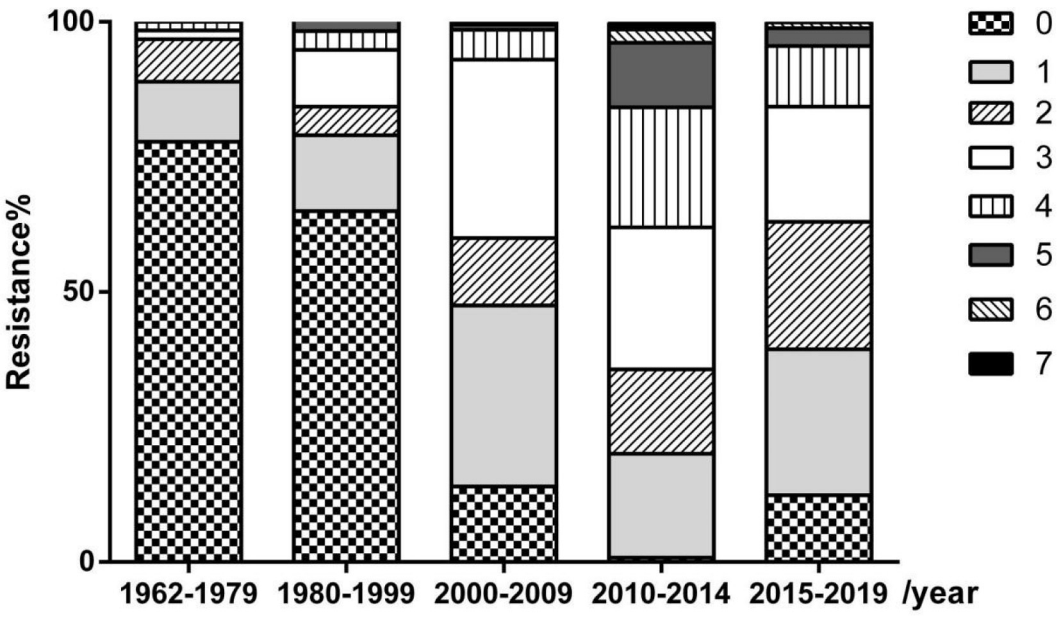

Figure 2. Multidrug resistance of *S.* Pullorum isolates collected from chickens in China between 1962 and 2019. Numbers "0" to "7" and the corresponding shadings indicate that isolates are resistant to 1, 2, 3, 4, 5, 6, and 7 antimicrobial agents, respectively.

Table 2. Multidrug-resistant patterns of 652 *S.*Pullorum isolates collected from chickens in China from 1962 to 2019.

Year	No. of resistant drugs	Multidrug-resistant pattern	No. of isolates	Resistant rates (%)
1960–1979 (n = 63)	3	STR–TET–NAL	1	1.6
	4	STR–TET–NAL–OLA	1	1.6
1980–1999 (n = 57)	3	AMP–STR–TET	4	7.0
		AMP–TET–OLA	1	1.8
		TET–CHL–FFC	1	1.8
	4	AMP–STR–TET–NIT	2	3.5
	5	AMP–STR–NAL–CHL–FFC	1	1.8
2000–2009 (n = 200)	3	TET–SXT–NAL	1	0.5
		SXT–NAL–OLA	1	0.5
		TET–SXT–OLA	1	0.5
		AMP–CFZ–SXT	2	1.0
		AMP–TET–SXT	4	2.0
	4	TET–SXT–NAL–OLA	1	0.5
	5	AMP–TET–SXT–NAL–OLA	2	1.0
	6	AMP–STR–TET–SXT–CHL–NIT	1	0.5
2010–2014 (n = 243)	3	TET–SXT–NAL	29	11.9
		AMP–CFZ–NAL	1	0.4
		AMP–CFZ–TET	1	0.4
		AMP–TET–NAL	18	7.4
		AMP–SXT–NAL	16	6.6
		AMP–NAL–OLA	1	0.4
		TET–NAL–OLA	2	0.8
		STR–SXT–NAL	4	1.6
		SXT–NAL–OLA	1	0.4
		STR–TET–NAL	2	0.8
		AMP–CFZ–NAL	1	0.4
		AMP–NAL–OLA	1	0.4
	4	AMP–CFZ–TET–NAL	18	7.4
		AMP–TET–SXT–NAL	8	3.3
		AMP–TET–NAL–OLA	2	0.8
		AMP–SXT–NAL–OLA	5	2.1
		AMP–TET–SXT–NAL	9	3.7
		AMP–CFZ–SXT–OLA	1	0.4
		AMP–CFZ–SXT–NAL	2	0.8
		STR–TET–SXT–NAL	5	2.1
		TET–SXT–NAL–OLA	3	1.6
		ATM–TET–SXT–NAL	1	0.4
	5	AMP–CFZ–TET–SXT–NAL	3	1.2
		AMP–CFZ–TET–NAL–OLA	1	0.4
		AMP–TET-–SXT–NAL–NIT	1	0.4
		STR–TET–SXT–NAL–OLA	2	0.8
		AMP–STR–TET–SXT–NAL	1	0.4
		AMP–CFZ–SXT–NAL–OLA	1	0.4
		AMP–CFZ–TET–SXT–NAL	1	0.4
	6	AMP–CFZ–TET–SXT–NAL–OLA	2	0.8
		AMP–STR–TET–SXT–NAL–NIT	1	0.4
		AMP–STR–SXT–NAL–NIT–OLA	1	0.4
	7	AMP–CFZ–STR–TET–SXT–NAL–NIT	1	0.4
2015–2019 (n = 89)	3	TET–SXT–NAL	6	9.1
		AMP–CFZ–NAL	1	1.1
		AMP–TET–NAL	9	13.6
		AMP–CFZ–NAL	2	2.2
		SXT–NAL–OLA	1	1.5
	4	AMP–CFZ–SXT–NAL	1	1.5
		AMP–ATM–NAL–OLA	1	1.5
		AMP–SXT–NAL–OLA	1	1.5
		AMP–CFZ–TET–NAL	2	2.2
		CFZ–TET–SXT–OLA	1	1.5
		TET–SXT–NAL–OLA	3	3.4
	5	AMP–CFZ–SXT–NAL–OLA	1	1.5
		AMP–CFZ–TET–SXT–NAL	2	2.2
	6	AMP–CFZ–TET–SXT–NAL–OLA	1	1.5
Total		62		

Abbreviations: AMP, ampicillin; ATM, aztreonam; CFZ, cefazolin; CHL, chloramphenicol; FFC, florfenicol; NAL, nalidixic acid; NIT, nitrofurantoin; OLA, olaquindox; STR, streptomycin; SXT, sulphonamides; TET, tetracycline.

(13.6%) and TET–SXT–NAL (11.9%). Moreover, one isolate exhibited resistance to 7 antimicrobials in 2014 (0.4%), displaying the pattern AMP–CFZ–STR–TET–SXT–NAL–NIT (Table 2). This report is the first to show so many MDR patterns for this veterinary pathogen. However, quite different MDR patterns have been previously reported for 227 *S.* Gallinarum strains isolated in Korea in 1997 and 2001 (Lee et al., 2003).

This article is also the first to study the changes in resistance of *S.* Pullorum through time under national policy conditions. The *Salmonella* isolates showed an overall increasing trend of antimicrobial resistance and

MDR patterns between 1962 and 2014, which declined after 2015. Most of the *S.* Pullorum strains were resistant to NAL, mainly after 2000. High levels of resistance were found for AMP, TET, and SXT. As per these results, we suggest strengthening the monitoring programs for pathogenic bacteria and their drug resistance in veterinary clinical practice and the food production chain. The results also suggest that the promotion of national policies is another important measure to reduce the emergence of drug-resistant strains. Moreover, interventions, such as vaccines and probiotics, can be considered to reduce salmonellosis.

ACKNOWLEDGMENTS

This work was supported by the National Key Research and Development Program of China (grant number: 2017YFD0500102), the Six Talent Peaks Project (SWYY-083), and the Priority Academic Program Development of Jiangsu Higher Education Institutions (PAPD).

DISCLOSURES

The authors declare no conflicts of interest.

SUPPLEMENTARY DATA

Supplementary data associated with this article can be found in the online version at https://doi.org/10.1016/j.psj.2020.12.007.

REFERENCES

Barrow, P. A., M. A. Jones, A. L. Smith, and P. Wigley. 2012. The long view: *Salmonella*–the last forty years. Avian Pathol. 41:413–420.

Cheong, H. J., Y. J. Lee, I. S. Hwang, S. Y. Kee, H. W. Cheong, J. Y. Song, J. M. Kim, Y. H. Park, J. H. Jung, and W. J. Kim. 2007. Characteristics of non–typhoidal *Salmonella* isolates from human and broiler–chickens in Southwestern Seoul, Korea. J. Korean Med. Sci. 22:773–778.

Clinical and Laboratory Standards Institute. 2013. Performance Standards for Antimicrobial Disk and Dilution Susceptibility Tests for Bacteria Isolated from Animals. Second Informational Supplement VET01–S2. CLSI, Wayne. PA.

Clinical and Laboratory Standards Institute. 2015. Performance Standards for Antimicrobial Susceptibility Testing: Twenty–Fifth Informational Supplement M100–S25. CLSI, Wayne. PA.

Dey, S., A. Mahanti, K. Batabyal, S. N. Joardar, I. Samanta, D. P. Isore, and M. C. Pakhira. 2016. Identification and antimicrobial susceptibility of *Salmonella* Gallinarum isolated from fowl typhoid outbreak in backyard *Vanaraja* fowl. Explor. Anim. Med. Res. 6:63–67.

European Committee on Antimicrobial Susceptibility Testing (EUCAST). 2016. Breakpoint tables for interpretation of MICs and zone diameters. Version 6.0. https://www.eucast.org/ast_of_bacteria/previous_versions_of_documents/. Accessed Jul. 2019.

Founou, L. L., R. C. Founou, and S. Y. Essack. 2016. Antibiotic resistance in the food chain: a developing country–perspective. Front. Microbiol. 7:1881.

Gong, J., M. Xu, C. Zhu, J. Miao, X. Liu, B. Xu, J. Zhang, Y. Yu, and X. Jia. 2013. Antimicrobial resistance, presence of integrons and biofilm formation of *Salmonella* Pullorum isolates from eastern China (1962–2010). Avian Pathol. 42:290–294.

Issenhuth–Jeanjean, S., P. Roggentin, M. Mikoleit, M. Guibourdenche, E. de Pinna, S. Nair, P. I. Fields, and F.-X. Weill. 2014. Supplement 2008–2010 (no. 48) to the White–Kauffmann–Le Minor scheme. Res. Microbiol. 165:526–530.

Kang, M. S., A. Kim, B. Y. Jung, M. Her, W. Jeong, Y. M. Cho, J. Y. Oh, Y. J. Lee, J. H. Kwon, and Y. K. Kwon. 2010. Characterization of antimicrobial resistance of recent *Salmonella enterica* serovar Gallinarum isolates from chickens in South Korea. Avian Pathol. 39:201–205.

Krishnasamy, V., J. Otte, and E. Silbergeld. 2015. Antimicrobial use in Chinese swine and broiler poultry production. Antimicrob. Resist. Infect. Control 17:4.

Lai, J., C. Wu, C. Wu, J. Qi, Y. Wang, H. Wang, Y. Liu, and J. Shen. 2014. Serotype distribution and antibiotic resistance of *Salmonella* in food-producing animals in Shandong province of China, 2009 and 2012. Int. J. Food Microbiol. 180:30–38.

Lee, Y. J., K. S. Kim, Y. K. Kwon, and R. B. Tak. 2003. Biochemical characteristics and antimicrobials susceptibility of *Salmonella* Gallinarum isolated in Korea. J. Vet. Sci. 4:161–166.

Levy, S. B., G. B. Fitzgerald, and A. B. Macone. 1976. Spread of antibiotic-resistant plasmids from chicken to chicken and from chicken to man. Nature 260:40–42.

Manie, T., S. Khan, V. S. Brözel, W. J. Veith, and P. A. Gouws. 1998. Antimicrobial resistance of bacteria isolated from slaughtered and retail chickens in South Africa. Lett. Appl. Microbiol. 26:253–258.

McChesney, D. G., G. Kaplan, and P. Gardner. 1995. FDA survey determines *Salmonella* contamination. Feedstuffs 67:20–23.

Ministry of Agriculture and Rural Affairs of the People's Republic of China (MAPRC). 2002. Maximum Residual Limitations for Veterinary Drugs in Animal Food (in Chinese). Notice no. 235, Beijing, China. Accessed Jan. 2021. https://www.docin.com/p-1666487561.html.

Ministry of Agriculture and Rural Affairs of the People's Republic of China (MAPRC). 2013. Catalogue of Veterinary Prescription Drugs–Batch 1 (in Chinese), 1997, Beijing, China. Accessed Jan. 2021. http://www.cnki.com.cn/Article/CJFDTotal-ZGDB201311041.htm.

Ministry of Agriculture and Rural Affairs of the People's Republic of China. 2015a. Notice no. 6. Beijing, China. Accessed Jan. 2021. https://www.docin.com/p1603561358.html.

Ministry of Agriculture and Rural Affairs of the People's Republic of China. 2015b. Notice no. 235. Beijing, China. Accessed Jan. 2021. http://www.doc88.com/p-9572098381364.html.

Nhung, N. T., N. Chansiripornchai, and J. J. Carrique–Mas. 2017. Antimicrobial resistance in bacterial poultry pathogens: a review. Front. Vet. Sci. 4:126.

Padungtod, P., and J. B. Kaneene. 2006. *Salmonella* in food animals and humans in northern Thailand. Int. J. Food Microbiol. 108:346–354.

Pan, Z., X. Wang, X. Zhang, S. Geng, X. Chen, W. Pan, Q. Cong, X. Liu, X. Jiao, and X. Liu. 2009. Changes in antimicrobial resistance among *Salmonella enterica* subspecies enterica serovar Pullorum isolates in China from 1962 to 2007. Vet. Microbiol. 136:387–392.

Parveen, S., M. Taabodi, J. G. Schwarz, T. P. Oscar, J. Harter–Dennis, and D. G. White. 2007. Prevalence and antimicrobial resistance of *Salmonella* recovered from processed poultry. J. Food Prot. 70:2466–2472.

Penha, R. A., J. C. Ferreira, A. M. Kanashiro, A. L. Costa, and A. J. Berchieri. 2016. Antimicrobial susceptibility of *Salmonella* gallinarum and *Salmonella* pullorum isolated from ill poultry in Brazil. Cienc Rural 46:513–518.

Qiao, M., G. G. Ying, A. C. Singer, and Y. G. Zhu. 2017. Review of antibiotic resistance in China and its environment. Environ. Int. 110:160–172.

Shivaprasad, H. L. 2000. Fowl typhoid and pullorum disease. Rev. Sci. Tech. Off. Int. Epiz. 19:405–424.

Taddele, M. H., R. Rathore, and K. Dhama. 2012. Antibiogram assay of *Salmonella* Gallinarum and other *Salmonella enterica* serovars of poultry origin in India. Asian J. Anim. Vet. Adv. 7:309–317.

Tang, Q., P. Song, J. J. Li, F. L. Kong, L. Sun, and L. Z. Xu. 2016. Control of antibiotic resistance in China must not be delayed: the current state of resistance and policy suggestions for the government, medical facilities, and patients. Biosci. Trends 10:1–6.

Thakur, Y. R., and B. K. Bajaj. 2006. Antibiotic resistance and molecular characterization of poultry isolates of *Salmonella* by RAPD-PCR. World J. Microbiol. Biotechnol. 22:1177–1183.

Thomas, P. V. B., C. Brower, M. Gilbert, T. B. Grenfell, S. A. Levin, T. P. Robinson, A. Teillant, and R. Laxminarayan. 2015. Global trends in antimicrobial use in food animals. PNAS 112:5649–5654.

Threlfall, E. J., L. R. Ward, and B. Rowe. 1997. Increasing incidence of resistance to trimethoprim and ciprofloxacin in epidemic *Salmonella typhimurium* DT104 in England and Wales. Euro. Surveill. 2:81–84.

Van Boeckel, T. P., J. Pires, R. Silvester, C. Zhao, J. Song, N. G. Criscuolo, M. Gilbert, S. Bonhoeffer, and R. Laxminarayan. 2019. Global trends in antimicrobial resistance in animals in low–and middle–income countries. Science 365:eaaw1944.

Wang, Y., C. Cao, W. Q. Alali, S. Cui, F. Li, J. Zhu, X. Wang, J. Meng, and B. Yang. 2017. Distribution and antimicrobial susceptibility of foodborne *Salmonella* serovars in eight provinces in China from 2007 to 2012 (except 2009). Foodborne. Pathog. Dis. 14:393–399.

White, D. G., C. Hudson, J. J. Maurer, S. Ayers, S. Zhao, M. D. Lee, L. Bolton, T. Foley, and J. Sherwood. 2000. Characterization of chloramphenicol and florfenicol resistance in *Escherichia coli* associated with bovine diarrhea. J. Clin. Microbiol. 38:4593–4598.

Yang, B., L. Qiao, X. Zhang, Y. Cui, X. Xia, S. Cui, X. Wang, X. Meng, W. Ge, X. Shi, D. Wang, and J. Meng. 2013. Serotyping, antimicrobial susceptibility, pulse field gel electrophoresis analysis of *Salmonella* isolates from retail foods in Henan Province, China. Food Control 32:228–235.

Youn, S. Y., O. M. Jeong, B. K. Choi, S. C. Jung, and M. S. Kang. 2017. Comparison of the antimicrobial and sanitizer resistance of *Salmonella* isolates from chicken slaughter processes in Korea. J. Food Sci. 82:711–717.

Zhao, S., P. F. McDermott, D. G. White, S. Qaiyumi, S. L. Friedman, J. W. Abbott, A. Glenn, S. L. Ayers, K. W. Post, W. H. Fales, R. B. Wilson, C. Reggiardo, and R. D. Walker. 2007. Characterization of multidrug resistant *Salmonella* recovered from diseased animals. Vet. Microbiol. 123:122–132.

Zhou, Z., X. Jin, H. Zheng, J. Li, C. Meng, K. Yin, X. Xie, C. Huang, T. Lei, X. Sun, Z. Xia, Y. Zeng, Z. Pan, and X. Jiao. 2018. The prevalence and load of *Salmonella*, and key risk points of *Salmonella* contamination in a swine slaughterhouse in Jiangsu province, China. Food Control 87:153–160.