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Title:

Genomic Surveillance and Multidrug Resistance Profiles of *Salmonella* Clinical Isolates in Fujian, China

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[Abstract]

Salmonella is a major foodborne pathogen imposes a substantial global disease burden. The rising prevalence of cephalosporin and quinolone resistance in *Salmonella* highlights the need for continued surveillance of resistance profiles and mechanisms. Here, we investigated the prevalence and antimicrobial resistance of *Salmonella* isolated from clinical patients in Fuzhou, China, between 2017 and 2020. Among 139 culture-positive cases, the male-to-female ratio was 1.53:1 and detections peaked from May to October. Twenty-nine serotypes were identified, with *S.* Enteritidis, *S.* Typhimurium, and *S.* Rissen being predominant. The overall resistance rate was 85.6%, with 64.0% of isolates were multidrug resistance (MDR). Isolates were highly resistance to ampicillin, tetracycline, and nalidixic acid, showed moderate resistance to ceftazidime, gentamicin, and ciprofloxacin, and were uniformly susceptibility to imipenem. All 58 nalidixic acid-resistant isolates carried QRDR mutations, most commonly *gyrA*:$_{\text{Asp87Tyr}}$, *gyrA*:$_{\text{Asp87Asn}}$, and *parC*:$_{\text{Thr57Ser}}$, whereas only two *S.* Typhimurium isolates harbored PMQR genes *aac(6')-Ib-cr* and *oqxAB*. Whole-genome sequencing of 61 *S.* Typhimurium isolates revealed ST34 as the dominant sequence type, with *bla*$_{\text{CTX-M}}$ ESBL genes and multiple mobile genetic elements facilitating resistance gene transfer. Phylogenomic analysis of 122 *S.* Typhimurium and monophasic variant isolates from Fujian Province revealed a bipartite

population structure comprising two major lineages, ST19 and ST34, with further sublineage differentiation driven by key resistance genes including *qnrS1*, *bla*$_{\text{CTX-M-55}}$, and *bla*$_{\text{OXA-1.}}$ Despite an overall sporadic epidemiological pattern, the detection of multiple highly related isolate pairs (⩽5 cgSNP differences)–including household-linked transmission and farm-level persistent contamination–strongly suggests that undiagnosed small-scale foodborne transmission events are substantially under-recognized. This study confirms high prevalence of MDR among clinical *Salmonella* in Fujian, with distinct serotype-specific patterns, and underscores the need for sustained local genomic surveillance.

[Key words] *Salmonella*, multidrug resistant, quinolone resistance, ESBL, plasmid, genetic environment, phylogenomics

Clinical trial number: not applicable.

1. Introduction

Salmonella is a zoonotic pathogen that colonizes the intestinal tracts of humans and animals and remains a leading cause of bacterial foodborne illness worldwide [1]. Infection produces a range of clinical presentations, including acute gastroenteritis, fever, diarrhea, and bacteremia [2]. The U.S. Centers for Disease Control and Prevention estimates approximately 1.2 million infections annually in the United States, resulting in ~450 deaths and hundreds of millions of dollars in economic losses [3].In China, *Salmonella* is estimated to cause 9.87 million cases of gastroenteritis annually, with recurrent outbreaks [4]. Between 2005 and 2019, China's National Infectious Disease Report Management System recorded 422,325 cases, making *Salmonella* the most commonly reported bacterial cause of diarrheal disease [5].*Salmonella* spp. are classified into three pathogenic groups: *Salmonella* Typhi, *Salmonella* Paratyphi (A, B or C), and non-typhoidal *Salmonella*(NTS)[6]. More than 2,600 serovars have been identified woldwide, of which 292 have been documented in China [7]. In Europe and North America, *S.* Enteritidis and *S.* Typhimurium account for more than 0% of human NTS infections [8,9], whereas other serovars show clear regional patterns [10]. Antimicrobial resistance also varies substantially among *Salmonella* serovars [11].

Although most NTS infections are self-limiting, antibiotic therapy remains essential for populations at high risk of invasive disease, such as

neonates and the elderly. Resistance levels differ markedly among serovars, and multidrug resistance (MDR) among clinical isolates now exceeds 60% in many regions [10, 11], up from approximately 40% in the late 20th century [12,13]. In *S.* Typhimurium, the ACSSuT (ampicillin, chloramphenicol, streptomycin, sulfonamides, and tetracycline) and ACSuT (ampicillin, chloramphenicol, sulfonamides, tetracycline) patterns remain common [14, 15]. At the same time, resistance to ceftriaxone and ciprofloxacin–last-line agents for invasive disease in children and the elderly–is rising and threatens current treatment options [16-18]. Much of this increase is driven by plasmid-mediated mechanisms, particularly extended-spectrum β-lactamases (ESBLs) such as *bla*$_{\text{CTX-M-15}}$ and plasmid-mediated quinolone resistance (PMQR) genes such as *aac(6')-Ib-cr* and *qnrS1* [19,20]. These genes are carried on mobile genetic elements, often within Tn3/IS26-flanked integrons or on IncI1/IncFIB plasmids, thereby enabling their rapid horizontal transfer among human, animal, and environmental reservoirs. Controlling their spread therefore requires a One Health approach.

Whole-genome sequencing (WGS) has become an important tool for precise pathogen identification, high-resolution genomic characterization, outbreak tracing, and real-time surveillance of antimicrobial resistance (AMR) evolution [11,21]. In addition to providing baseline data on microbial phenotypic and genetic traits and resolving phylogenetic

relationships, WGS yields epidemiologically contextualized evidence that can guide targeted public health interventions. Advances in high-throughput sequencing have made large-scale WGS feasible in routine epidemiological surveillance, improving the ability to track transmission dynamics of multidrug-resistant (MDR) pathogens. Fujian Province lies on the southeastern coast of China and has closely integrated poultry, livestock, and seafood aquaculture industries, a landscape that contributes to a relatively high regional burden of foodborne bacterial disease. Systematic WGS-based surveillance of foodborne pathogens and their AMR profiles in this region, however, remains limited. The present study characterized the serotypes and antimicrobial resistance phenotypes of 139 *Salmonella* isolates collected from four tertiary hospitals in Fuzhou between 2017 and 2020, to describe their local epidemiological profiles and resistance distribution patterns. From this collection, 58 isolates exhibiting resistance to nalidixic acid or ciprofloxacin were screened for chromosomal point mutations in the quinolone resistance-determining regions (QRDRs) of *gyrA* and *parC*, and for three major PMQR genes: *aac(6')-Ib-cr*, *oqxA*, and *oqxB*. A subset of 11 extended-spectrum β-lactamase (ESBL)-producing isolates and other 61 *S.* Typhimurium isolates were then subjected to WGS, to determine their multilocus sequence typing (MLST) profiles, plasmid replicon content, phylogenetic relationships,

AMR resistance genes, and the genetic contexts surrounding these resistance determinants. Together, these findings provide empirical evidence to support *Salmonella* infection control strategies and the rational use of antimicrobials in clinical and agricultural settings.

2. Materials and methods

2.1. Collection of clinical information and bacterial isolates

A total of 139 non-duplicate clinical *Salmonella* isolates were retrospectively recovered from patients admitted to four tertiary hospitals in Fuzhou City, Fujian Province, China, between January 2017 and December 2020. Demographic and clinical metadata, including patient age, sex, and documented site of infection, were extracted retrospectively from the standardized electronic medical record systems of the participating hospitals. Allpersonal identifiers were removed and replaced with anonymized unique study IDs before analysis, in order to ensure participant confidentiality and compliance with local ethical requirements. The 139 isolates were recovered from four clinical specimen types: stool (n = 112), blood (n = 18), urine (n = 6), and joint fluid (n = 3). All specimens were processed accordance to standard clinical microbiology procedures. Briefly, specimens were inoculated directly onto blood agar (BIOIVD, Zhengzhou, China) and Xylose Lysine Desoxycholate (XLD) selective agar (Oxoid, United Kingdom), and incubated aerobically at 36 °C ± 1 °C for 18–24 hours. Presumptive *Salmonella* colonies were

subcultured on fresh agar plates to obtain pure clonal isolates, which were then confirmed by biochemical identification and serotyping using previously described standard protocols [22, 23].

To place the local *S.* Typhimurium isolates in a broader geographic context within Fujian Province, the analysis also included 44 additional *S.* Typhimurium genomes isolated in parallel from Ningde and Sanming during the same 2017-2020 surveillance period. In addition, high-quality whole-genome sequencing datasets of another 50 *S.* Typhimurium strains （Supplementary Table S1） collected from other administrative regions of Fujian Province over the same period were retrieved from the NCBI public genome database for comparative phylogenomic analysis.

2.2. Antimicrobial susceptibility testing

Antimicrobial susceptibility to 13 agents was determined by the Kirby-Bauer disk diffusion method according to Clinical and Laboratory Standards Institute (CLSI, 2024) guidelines [24]. The following disks (Oxoid, United Kingdom) were used: ampicillin (AMP, 10 μg); ampicillin/sulbactam 2:1 (SAM, 30 μg); aztreonam (ATM, 30 μg); cefotaxime (CTX, 30 μg); ceftazidime (CAZ, 30 μg); imipenem (MEM, 10 μg); nalidixic acid (NAL, 30 μg); ciprofloxacin (CIP, 5 μg); chloramphenicol (CHL, 30 μg); gentamicin (GEN, 10 μg); streptomycin (STR, 10 μg); sulfamethoxazole/trimethoprim (SXT, 25 μg); and tetracycline (TET, 30 μg). Minimum inhibitory concentrations (MICs)

were determined by broth microdilution for 11 the ESBL-producing isolates against 26 antibiotics (BIOFOSUN, China), comprising β-lactams (ampicillin, amoxicillin/clavulanate, cefazolin, cefotaxime, ceftazidime, cefoxitin, cefepime; carbapenemase (imipenem and meropenem); quinolones (nalidixic acid, ciprofloxacin, levofloxacin and gemifloxacin); aminoglycosides (streptomycin, kanamycin, amikacin and gentamicin); tetracyclines (minocycline, doxycycline and tetracycline); phenicols (chloramphenicol); sulfonamides (sulfisoxazole and trimethoprim/sulfamethoxazole); macrolides (azithromycin); and polymyxins (B and E). Results were interpreted as susceptible, intermediate, or resistant according to CLSI 2024 breakpoints. *Escherichia coli* ATCC 25922 was used as the quality control strain. ESBL production was screened by the Kirby–Bauer method and confirmed by comparing zone diameters (difference ≥5 mm) or MIC values (≥8-fold change, i.e. a decrease of ≥3 twofold dilutions) between disks/wells with and without clavulanic acid (cefotaxime/cefotaxime-clavulanate or ceftazidime/ ceftazidime-clavulanate).

2.3. Detection ofmutations in quinolone resistance genes

A total of 58 isolates resistant to nalidixic acidor ciprofloxacin were screened for mutations in the QRDRs of *gyrA* and *parC*, andfor the PMQR genes *aac(6')-Ib-cr, oqxAB*. Bacterial DNA was extracted withthe

QIAamp DNA Mini Kit (Qiagen GmbH, Hilden, Germany) and amplified by PCR using Taq PCR Master Mix (TaKaRa, Japan), according to the manufacturers' recommended protocols. Each 20 μl reaction contained 10 μl of 2× Taq High-Fidelity PCR Master Mix, 1 μl each of the forward and reverse primers (10 μmol/L), 4 μl of DNA template, and 4 μl of ddH_2O. Thermal cycling conditions were as follows: initial denaturation at 95 °C for 5 min; 33 cycles of denaturation at 95 °C for 30s, annealing at 52–58 °C for 30 s, and extension at 72 °C for 30–60 s; and a finally extension at 72 °C for 5 min. PCR products were verified by agarose gel electrophoresis, sequenced by Sangon Biotech (Shanghai, China), and analyzed by BLAST against the NCBI database. All primers used for PCR amplification and sequencing are listed in Supplementary Table S2 (Tab S1.).

Table S2. Primers used for PCR amplification of quinolone resistance determinants

2.4. Genomic DNA extraction, whole-genome sequencing, and bioinformatics analysis

Total DNA was extracted from LB broth cultures of 11 ESBL and 61 S. Typhimurium isolates (incubated for 16 h at 180 rpm and 36 °C) with the QIAamp DNA Mini Kit (Qiagen GmbH, Hilden, Germany) according to the manufacturer's instructions. After quality control, paired-end library with a 350-bp insert size were prepared with the Nextera XT v2 kit (Illumina, San Diego, USA) and sequenced on an Illumina HiSeq 2500

platform to generate 150-bp paired-end reads. Raw reads were quality-assessed with FastQC (v0.11.5), and de novo assembly was performed with SPAdes (v3.14) [25]. Serotyping followed the White-Kauffmann scheme, supported by SeqSero2 v1.1.1. Multilocus sequence typing (MLST) and plasmid screening were performed with the MLST 2.0 server and PlasmidFinder v2.0.1, at the Center for Genomic Epidemiology (CGE) (https://cge.food.dtu.dk/services).

2.5. Identification of resistance genes and the ESBL genetic environment

Antibiotic resistance genes and its mutations, together with mobile genetic elements (MGEs), including insertion sequences (ISs), were predicted using two freely accessible online platforms: CGE ResFinder v4.7.1, which uses BLAST with thresholds of 90% identity and 60% coverage, and the CARD Resistance Gene Identifier (RGI) (https://card.mcmaster.ca/analyze/rgi/). Contigs carrying ESBL genes were extracted and annotated by Prokka, NCBI BLAST, and MobileElementFinder v1.0.3 to characterize adjacent MGEs. Transposons or translocatable units associated with ESBL gene were determined, and genetic architectures were visualised with Chiplot [26] (https://www.chiplot.online/).

2.6. Phylogenetic analysis

To resolve the phylogenetic placement of local *S.* Typhimurium isolates from Fujian Province, two maximum likelihood (ML) phylogenetic trees

were constructed separately, using genomic data from 72 newly sequenced local clinical isolates and 50 publicly available *S.* Typhimurium isolates from across Fujian Province. Core genome single-nucleotide polymorphism (cgSNP) sites across all included *Salmonella* strains were identified by mapping sequencing reads to the complete reference genome of *S.* Typhimurium strain LT2 (RefSeq accession: GCF_000006945.2) with Snippy v4.4.4 using default alignment parameters. Putative homologous recombination regions, which can distort phylogenetic topology, were then detected and masked from the core SNP alignment using Gubbins v2.3.4. The recombination-filtered core SNP alignment was then used to construct a ML phylogenetic tree in IQ-TREE 2 (v2.0.7) under the generalized time-reversible model with gamma-distributed rate heterogeneity and ascertainment bias correction (GTR+G+ASC), with node support accessed via 1000 ultrafast bootstrap replicates. The annotated tree, together with the corresponding presence/absence profile of antimicrobial resistance genes across all isolates, was visualized using the tvBOT tool hosted on the ChiPlot online platform. To improve visual clarity, the tree scale legend was transformed using the negative logarithm of conventional branch length values. Pairwise core SNP distances between all isolate pairs were calculated using SNP-DISTs (v0.8.2). Clonal clustering was determined by integrating pairwise cgSNP distances,

isolate sampling dates, and the geographic distribution of the source administrative districts. Following the threshold widely accepted in genomic epidemiological investigations, isolate pairs with a pairwise cgSNP difference of $\leqslant$ 5 were defined as highly genetically related, indicating a plausible epidemiological linkage.

3. Results

3.1. Prevalence and Serotypes *Salmonella*

During the surveillance period, 139 unique *Salmonella* isolates were recovered from four tertiary hospitals in Fuzhou, Fujian Province, China. Isolates were detected throughout the year, with a marked seasonal increase during the warmer months (May–October), which accounting for 76.26% (106/139) of all cases (Fig. S1B). Among the 139 clinical cases, 84 (60.4%) were male and 55 (39.6%) were female, giving a male-to-female ratio of 1.53:1. Patients ranged from 11 days to 92 years, with a median age of 60 years. The highest infection rates occurred in three age groups: 0–5 years (25.18%, 35/139), 36–60 years (27.34%, 38/139), and 61–80 years (25.90%, 36/139)(Fig. S1A). In contrast, infections were significantly less frequent among adolescents and young adults (6–35 years).

Fig. S1. Distribution of *Salmonella* isolates by time, age group, and serovar; A. Isolation count by age group and serovar; B. Isolation count by month

All 139 isolates were classified as *Salmonella enterica* subsp. enterica using the White-Kauffmann-Le Minor serotyping scheme. They were

distributed across nine serogroups and 29 distinct serotypes, with four strains (2.88%) remaining untypeable due to atypical antigenic profiles (Table S3.). Serogroup D1 was predominant (nine serovars), followed by serogroups B and C2–C3 (five serovars each). The most prevalent serotypes were: *S.* Enterica (28.78%, 40/139), *S.* Typhimurium (23.02%, 32/139), *S.* Rissen (10.07%, 14/139).Notably, *S.* Typhi (1.44%, 2/139) and *S.* Paratyphi (3.60%, 5/139) were detected only sporadically (Table S3.).

Table S3. Prevalence of *Salmonella* serogroup/serovar among 139 clinical isolates

3.2. Phenotypic Antimicrobial Resistance

Of the 139 *Salmonella* isolates, 85.61% (119/139) were resistance to at least one antimicrobial agent. The highest resistance rates were observed for ampicillin (61.87%, 86/139) and tetracycline (50.36%, 70/139) (Table 1.). Substantial resistance was also observed for streptomycin (43.88%, 61/139) and nalidixic acid (41.73%, 58/139). By contrast, resistance to ciprofloxacin remained low (2.88%, 4/139), and all isolates were susceptible to imipenem. Serotype-specific analysis showered that *S.* Enterica isolates (n=40) exhibited an overall resistance rate of 95.00% (38/40), and *S.* Typhimurium isolates (n=32) showed a similarly high rate of 93.75% (30/32). Comparisonof resistance patterns indicated that *S.* Typhimurium was more frequently resistance to ampicillin (81.25%, 26/32) and tetracycline (84.38%, 27/32) than *S.* Enterica (ampicillin: 62.50%, 25/40; tetracycline: 57.50%, 23/40) (Table 1.). However, *S.*

Enterica showed greater resistance to nalidixic acid (50.00%, 20/40) than *S.* Typhimurium (34.38%, 11/32). Notably, the 14 *Salmonella* Rissen isolates were high resistance to tetracycline (100.00%, 14/14), trimethoprim-sulfamethoxazole (92.86%, 13/14), and ampicillin (85.71%, 12/14). The seven *S.* Typhi/Paratyphi isolates showed minimal resistance to the agents tested. In addition, extended-spectrum β-lactamase (ESBL) producers accounted for 11.51% (16/139) of the isolates. These exhibited resistance exceeding 50% to all evaluated antibiotics except imipenem (0% resistance), ciprofloxacin (18.75% resistance), and gentamicin (31.25% resistance), confirming their multidrug-resistant phenotype (Table 1.).

Table 1. Antimicrobial resistance patterns in different *Salmonella* serovars and ESBL-producing isolates

Antimicrobial	Resistance rate（%）/Number of isolates						
	Total（n=139）	*S.*Enteritidis（n=40）	*S.*Typhimurium（n=32）	*S.*Rissen（n=14）	*S.*Typhi/Paratyphi（n=7）	Others（n=46）	ESBLs (n=16)
Ampicillin	61.87(86)	60.00(24)	81.25(26)	85.71(12)	28.57(2)	47.83(22)	100.00(16)
Ampicillin/ sulbactam	10.79(15)	7.50(3)	9.38(3)	7.14(1)	14.29(1)	15.22(7)	50.00(8)
Aztreonam	8.63(12)	0.00(0)	12.5(4)	14.29(2)	0.00(0)	13.04(6)	68.75(11)
Cefotaxime	11.51(16)	0.00(0)	15.63(5)	7.14(1)	0.00(0)	21.74(10)	100.00(16)
Ceftazidime	5.76(8)	0.00(0)	6.25(2)	7.14(1)	0.00(0)	10.87(5)	50.00(8)
Meropenem	0.00(0)	0.00(0)	0.00(0)	0.00(0)	0.00(0)	0.00(0)	0.00(0)
Nalidixic acid	41.73(58)	95.00(38)	34.38(11)	0.00(0)	42.86(3)	15.22(7)	18.75(3)
Ciprofloxacin	2.88(4)	0.00(0)	6.25(2)	0.00(0)	0.00(0)	4.35(2)	18.75(3)
Chloramphenicol	26.62(37)	0.00(0)	37.50(12)	14.29(2)	14.29(1)	47.83(22)	62.50(10)
Gentamicin	7.19(10)	7.50(3)	6.25(2)	0.00(0)	0.00(0)	10.87(5)	18.75(3)
Streptomycin	43.88(61)	55.00(22)	62.50(20)	14.29(2)	14.29(1)	34.78(16)	68.75(11)
Cotrimoxazole	39.57(55)	12.50(5)	31.25(10)	92.86(13)	42.86(3)	52.17(24)	75.00(12)
Tetracycline	50.36(70)	15.00(6)	84.38(27)	100.00(14)	0.00(0)	50.00(23)	93.75(15)
Non-sensitive	85.61(119)	95.00(38)	93.75(30)	100.00(14)	28.57(2)	69.57(32)	100.00(16)

ESBLs: Extended-Spectrum β-Lactamase

The clustering heatmap of *S.* Typhimurium isolates reveals distinct antibiotic resistance profiles. A substantial cluster of isolates showed a MDR phenotype, characterized by concurrent non-susceptibility to β-lactams (ampicillin [AMP], ampicillin-sulbactam [AMS], cefotaxime [CTX], ceftazidime [CAZ]), quinolones (NAL, CIP), streptomycin (STR), and tetracycline (TET), whereas resistance to chloramphenicol (CHL), trimethoprim-sulfamethoxazole (SXT) and gentamicin (GEN) differed across clusters（Fig S2.）. All isolates tested remained susceptible to meropenem (MEM).These patterns clustered by drug class, suggesting co-selection of resistance determinants and implying that linked genetic elements (e.g., plasmids) may drive the dissemination of these MDR profiles.

Fig. S2. Antimicrobial resistance profile and clustering of *S.* Typhimurium isolates

The overall MDR rate among the 139 *Salmonella* isolates was 64.03% (89/139). Phenotypic analysis revealed that 17.99% (25/139) exhibited the ACSuT resistance profile (ampicillin, chloramphenicol, sulfonamides, tetracycline), while 9.35% (13/139) displayed the ACSSuT profile (ampicillin, chloramphenicol, streptomycin, sulfonamides, tetracycline). Serotype-specific resistance patterns varied considerably (Table 2.). *S.* Enteritidis showed the highest rates of resistance to one drug class (35.00%, 14/40) and 3 drug classes (40.00%, 16/40). Both *S.* Typhimurium and *S.* Rissen most frequently exhibited resistance to three

drug classes (31.25% [10/32] and 57.14% [8/14], respectively). *S.* Typhimurium had the broadest resistance spectrum (1-8 drug classes), with one isolate resistant to eight classes. Notably, one *S.* Thompson and one *S.* Corvallis isolate were resistance to 10 and 9 drug classes, respectively (Table 2.). All ESBL-producing isolates (16/16, 100%) were multidrug-resistant, among these, 56.25% (9/16) and 37.50% (6/16) exhibited ACSuT and ACSSuT phenotypes, respectively, with resistance ranging from 4 to 10 drug classes.

Table 2. Prevalence of multidrug-resistant *Salmonella* isolates by serovar and ESBL-producing status

Number of Resistance	Multidrug resistance rate（%）/Number of isolates						
	Total（n=139）	*S.*Enteritidis（n=40）	*S.*Typhimurium（n=32）	*S.*Rissen（n=14）	*S.*Typhi/Paratyphi（n=7）	Others（n=46）	ESBLs(n=16)
0	14.39(20)	5.00(2)	6.25(2)	0.00(0)	42.86(3)	28.26(13)	0.00(0)
1	17.27(24)	35.00(14)	3.13(1)	7.14(1)	14.29(1)	15.22(7)	0.00(0)
2	4.32(6)	0.00(0)	6.25(2)	7.14(1)	14.29(1)	4.35(2)	0.00(0)
3	27.34(38)	40.00(16)	31.25(10)	57.14(8)	14.29(1)	6.52(3)	0.00(0)
4	13.67(19)	10.00(4)	21.88(7)	14.29(2)	0.00(0)	13.04(6)	6.25(1)
5	9.35(13)	10.00(4)	18.75(6)	7.14(1)	14.29(1)	2.17(1)	6.25(1)
6	7.19(10)	0.00(0)	3.13(1)	7.14(1)	0.00(0)	17.39(8)	31.25(5)
7	2.88(4)	0.00(0)	3.13(1)	0.00(0)	0.00(0)	6.52(3)	25.00(4)
8	2.16(3)	0.00(0)	6.25(2)	0.00(0)	0.00(0)	2.17(1)	18.75(3)
9	0.72(1)	0.00(0)	0.00(0)	0.00(0)	0.00(0)	2.17(1)	6.25(1)
10	0.72(1)	0.00(0)	0.00(0)	0.00(0)	0.00(0)	2.17(1)	6.25(1)
MDR	64.03(89)	60.00(24)	84.38(27)	85.71(12)	28.57(2)	52.17(24)	100.00(16)
ACSxT	17.99(25)	0.00(0)	21.88(7)	14.29(2)	0.00(0)	34.78(16)	56.25(9)
ACSSxT	9.35(13)	0.00(0)	9.38(3)	7.14(1)	0.00(0)	19.56(6)	43.75(7)

MDR(Multidrug resistance): resistant to three or more different antibiotics；ACSxT: ampicillin-chloramphenicol-cotrimoxazole-tetracyclinemultidrug-resistant phenotype； ACSSxT: ampicillin-chloramphenicol-streptomycin-cotrimoxazole-tetracycline multidrug-resistant phenotype

3.3. Detection of Quinolone Resistance Determinants

Among 58 nalidixic acid-resistant *Salmonella* isolates, all carried quinolone resistance determinants, including chromosomal mutations in QRDRs and/or PMQR genes; QRDR mutations occurring in *gyrA* (n = 41), *gyrB* (n = 2), and *parC* (n = 9) (Table 3.). Serovar-specific mutation patterns were evident. *S.* Enteritidis predominantly harbored *gyrA* substitutions, namely Asp87Tyr in 36.2% (21/58) of isolates and Asp87Asn in 20.7% (12/58), whereas *S.* Typhimurium mainly exhibited the *gyrA* Ser83Tyr mutation in 13.8% (8/58). Other serovars, such as *S.* Braenderup (3 isolates), *S.* Paratyphi A (2), *S.* Derby (1), *S.* Kentucky (1), *S.* Thompson (1), and *S.* Albany (1), carried the *parC* Thr57Ser mutation in 15.5% (9/58)of isolates (Table 3). Among the four ciprofloxacin-resistant isolates, two *S.* Typhimurium strains contained *gyrA*: Asp87Asn and Asp87Tyr substitutions together with PMQR genes *aac(6')-Ib-cr, oqxA*, and *oqxB*; one *S.* Kentucky strain possessed dual *gyrA* mutations (Ser83Phe and Asp87Gly) as well as *parC* mutations (Thr57Ser and Ser80Ile); and one *S.* Thompson isolate had the *parC*Thr57Ser mutation combined with the *qepA1* (Table 3.).

Table 3. Distribution of PMQR genes and QRDRs mutations among the 58*Salmonella* isolates of different serovars.

Serovars Gene Type	*S.*Enteritidis 37(63.79%）	*S.*Typhimurium 11(18.97%）	Others 10(17.24%）	Total58(100 %）
gyrA:Asp87Tyr	21(60.80%)	1(1.73%)	3(5.17%)	25(43.10%)
Asp87Asn	12(20.69%)	1(1.73%)	1(1.73%)	14(24.14%)
Asp87Gly	3(5.17%)	0(0%)	0(0%)	3(5.17%)
Ser83Tyr	1(1.73%)	8(13.79%)	3(5.17%)	12(20.69%)
Ser83Phe	0(0%)	0(0%)	5(8.62%)	5(8.62%)
parC:Thr57Ser	0(0%)	0(0%)	9(20.69%)	9(15.52%)
Ser80Ile	0(0%)	0(0%)	1(1.73%)	1(1.73%)
gyrB:Ser464Pro	0(0%)	1(1.73%)	0(0%)	1(1.73%)
oqxA	0(0%)	2(3.45%)	0(0%)	2(3.45%)
oqxB	0(0%)	2(3.45%)	0(0%)	2(3.45%)
aac(6')-Ib-cr	0(0%)	2(3.45%)	0(0%)	2(3.45%)

3.4. Antimicrobial Resistance Profiles and Genetic Determinants of ESBL-Producing *Salmonella* Isolates

Whole-genome sequencing and de novo assembly of 11 ESBL-producing *Salmonell a*isolates yielded genome sequences of 4.7 to 5.1 mega bases (Mb), with contig N50 values spanning 148.4-358 kb and consistent GC content of 52.0%-52.2%. Serotype predictions from whole-genome sequencing were consistent with conventional serotyping results. Multilocus sequence typing (MLST) assigned four *S.* Typhimurium isolates to ST34, whereas the remaining isolates represented diverse sequence types: *S.*Agona (ST13), *S.* Bareilly (ST203), *S.* Bovismorbificans (ST142), *S.* Montevideo (ST 3667), *S.* Muenster (ST321), *S.* Thompson (ST26), *S.* Wandsworth (ST1498) (Table S4). Plasmid profiling showed that 10 isolates harbored 1-3 plasmids, predominantly of the IncHI (HI1, HI1A/B, HI2/A/C), IncX1, IncQ1, and IncR groups. In total, 29 antimicrobial resistance determinants across 11

drug classes were identified, including β-lactam resistance genes (*bla*$_{TEM}$, *bla*$_{CTX-M}$, *bla*$_{OXA}$, *bla*$_{DHA-1}$, *bla*$_{CMY-2}$); quinolones resistance determinants (*gyrA, gyrB, parC, qnrS/B, qepA1, oqxAB,* and *aac(6')-Ib-cr*); macrolides resistance genes (*mph(A), erm(B), msr(E)*); and genes conferring resistance to aminoglycosides (*aac*(*3/6'*), *aadA, aph*(*3''6*)), sulfamethoxazole and trimethoprim (*sul1/2/3*, *dfrA12/14*), phenicols (*floR, catB3, cmlA1*), tetracyclines (*tet(A/B/D)*), fosfomycin (*fosA4/7*), clindamycin (*lnuF*), rifamycins (*Arr-2/3*), and quaternary ammoniumdisinfectants (*qacE*) (Fig 1B.), demonstrating extensive multidrug resistance mechanisms in which plasmid-mediated genes complement chromosomal mutations.

Table S4. **Serovars, ST type, plasmids and mainly ESBL genes of 11 ESBL-producing *Salmonella***

Cluster analysis of 11 ESBL-producing *Salmonella* isolates from diverse serotypes, integrating antimicrobial susceptibility testing (AST) and antimicrobial resistance (AMR) gene profiles, revealed distinct multidrug-resistant (MDR) clusters through phenotypic and genotypic heatmap. Phenotypic clustering identified a major group with extensive resistance across multiple antibiotic classes, whereas genotypic analysis revealed a complex array of acquired resistance genes that correlated strongly with the observed resistance patterns (Fig 1A.). Hierarchical clustering of combined phenotypic and genotypic data showed high concordance, grouping isolates with similar MDR profiles. Isolates

carrying combinations of extended-spectrum β-lactamase genes (*bla*-CTX-M variants), plasmid-mediated quinolone resistance determinants (*qnrS, aac(6')-Ib-cr*), and diverse aminoglycoside (*aac, aadA, aph*) and sulfonamide (*sul, dfrA*) resistance genes formed tightly clustered subgroups corresponding to the most extensive phenotypic resistance spectra (Fig 1B.). This clustering indicates co-localization of multiple resistance determinants on mobile genetic element–predominantly IncHI and IncX plasmids–which facilitates the dissemination of complex MDR profiles across *Salmonella* serovars and has important implications for clinical management given restricted therapeutic options.

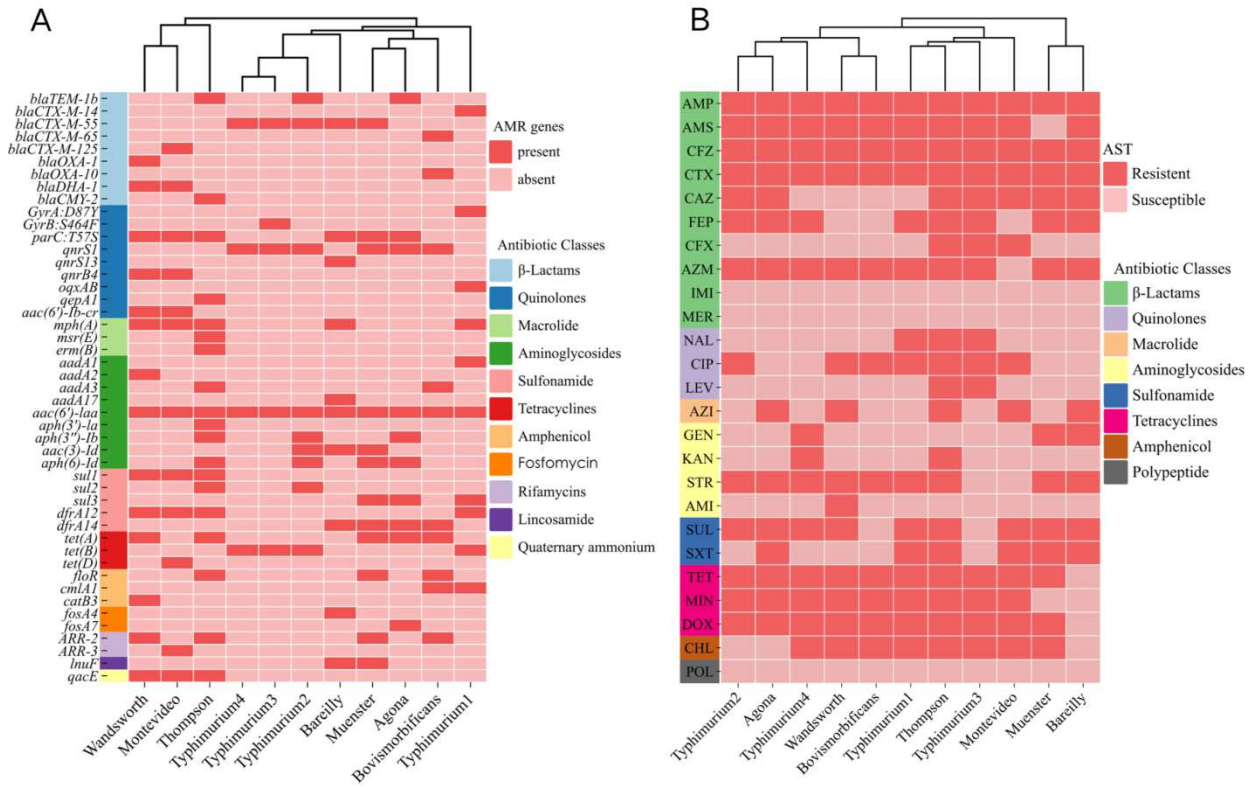


Fig.1. Genotypic and phenotypic clustering of antimicrobial resistance among 11 ESBL-producing *Salmonella* isolates; A. Clustering of antimicrobial resistance genes in different *Salmonella* Serovars; B. antimicrobial resistance phenotype

profile and clustering heatmap of different *Salmonella* Serovars.

3.5. MGEs associated with AMR and genetic environment of *bla*$_{\text{CTX-M}}$, *bla*$_{\text{TEM}}$ and *bla*$_{\text{OXA}}$

The 11 ESBL-producing *Salmonella* isolates collectively harbored 70 insertion sequence (IS) elements representing 30 distinct classes, with *S.* Agona, *S.* Thompson, and *S.* Wandsworth each carrying eight IS elements. The transposon Tn6196was identified exclusively in one *S.* Wandsworth isolate. ISMITEEc1 was present in 10 isolates (90.9%), being absent only from one *S.* Muenster strain. The predominant IS elements were MITEEc1 (n=10), IS903 (n=5), ISKpn8 (n=4), ISKpn19 (n=4), and ISSty2 (n=4).

The genetic environment flanking the *bla*$_{\text{CTX-M}}$ genes showed three configurations: type I (*ISEcp1-bla*$_{CTX}$*-IS903B*; (n=3), type II (*ISEcp1-bla*$_{\text{CTX}}$*-WbuC-ΔTn3*; (*n*=1), and type III(*IS26-Δtran-bla*$_{CTX}$*-WbuC-ΔTn3;* (*n*=4), with ISEcp1 consistently located upstream and IS903B/WbuC-ΔTn3 primarily downstream of resistance genes (Fig 2A.). All three *bla*$_{\text{TEM}}$ positive isolates carried IS26 upstream, although downstream elements varied (Fig 2B.). Both *bla*$_{\text{OXA}}$ carrying isolates contained the gene within a multidrug resistance island bounded by intI1 integrase, yet they displayed distinct architectures (Fig 2C.): strain F18101 had IS26 flanking both ends of the resistance cassette, while F2021 featured transposon TnAs1 upstream of intI1 and the

resistance genes, indicating divergent mobilization pathways for β-lactamase genes.

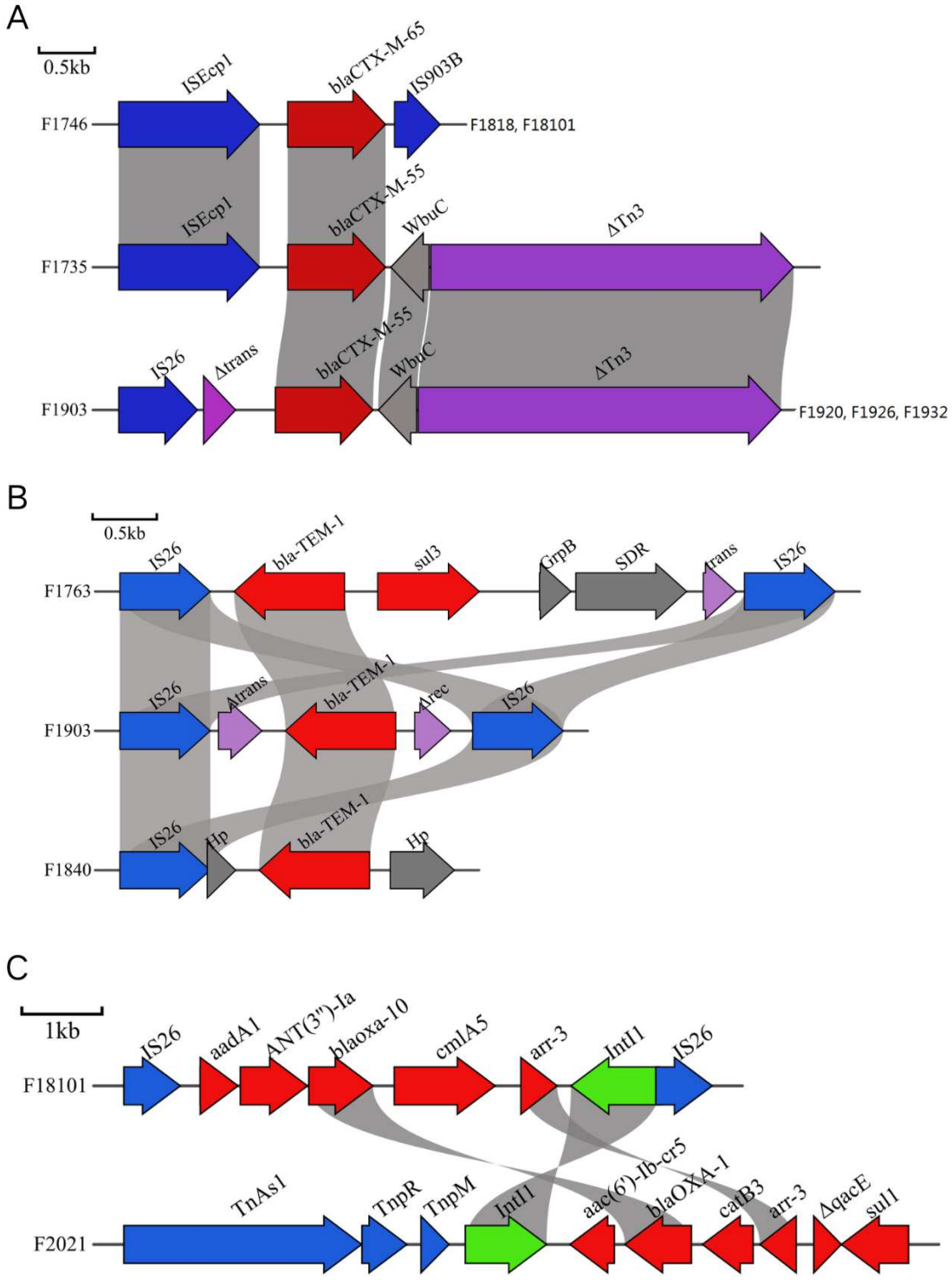


Fig.2. Genetic environments flanking β-lactamase genes in the 11 ESBL-producing *Salmonella* isolates; A. Gene structure and mobile genetic elements surrounding *bla*$_{CTX-M}$; B. Gene structure and mobile genetic elements

surrounding *bla*$_{TEM}$; C. Gene structure and mobile genetic elements surrounding *bla*$_{OXA}$.

3.6 Phylogenetic characteristics of the *S.* Typhimurium in Fujian

A phylogenetic tree of 28 strains of *S.* typhimurium and its variants from the Fuzhou region shows no obvious clustering of strains based by time, location, or source (Fig 3.). The strains were clearly divided into distinct clusters according to serotype and the corresponding ST types (indicated by the colors of the branches and leaves). Some clustering was also observed according to antibiotic resistance profile; for example, multidrug-resistant and non-multidrug-resistant *S.* typhimurium ST19 strains were clearly divided into two distinct clades, ST19.1 and ST19.2. One ST99 *S.* typhimurium strain (201858) isolated from blood was genetically the most distant from the other strains and occupied the outermost part of the tree (Fig 3.). *S.* typhimurium ST34 monophasic variants generally carried more resistance genes than *S.* typhimurium ST19 strains.

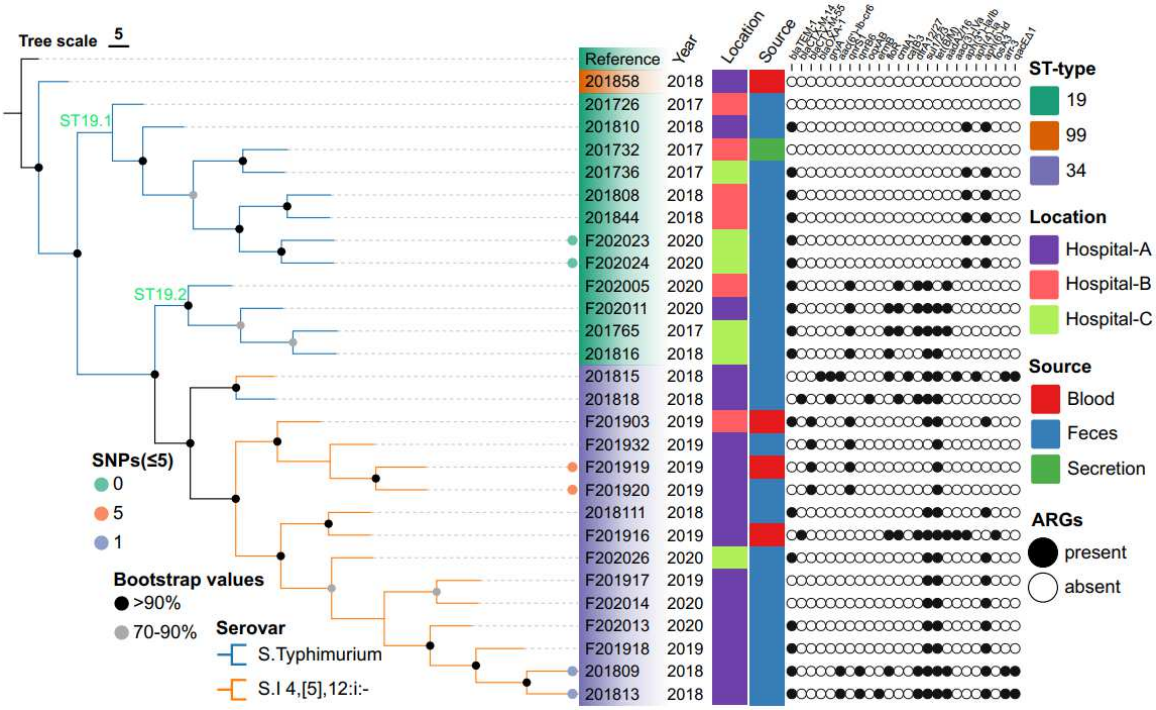


Fig.3. Phylogenetic and antimicrobial resistance characteristics of *S.* typhimurium and its variants in Fuzhou. The genome of *S.* Typhimurium strain LT2 (RefSeq accession: GCF_000006945.2) was used as a reference and outgroup to root the tree.

Consistent with the epidemiological pattern observed in Fuzhou City, *S.* Typhimurium and its monophasic variants across Fujian Province remained predominantly sporadically distributed across temporal, geographical, and source dimensions. The entire strain collection was phylogenetically delineated into two major clusters corresponding to sequence types ST19 and ST34, while multidrug-resistant isolates showed a marked tendency to form aggregated subclades (Fig 4.). Within the large ST19 lineage, strains were further divided into two subclusters stratified by the presence or absence of the *qnrS1* resistance gene. Within the ST34 cluster, isolates also segregated into discrete sublineages,

defined by their multidrug resistance profiles and by carriage of specific resistance determinants, including *bla*$_{\text{CTX-M-55}}$ and *bla*$_{\text{OXA-1}}$ (Fig 4.). A small subset of strains also showed limited but detectable signals of geographical and source-associated clustering at the subcluster level.

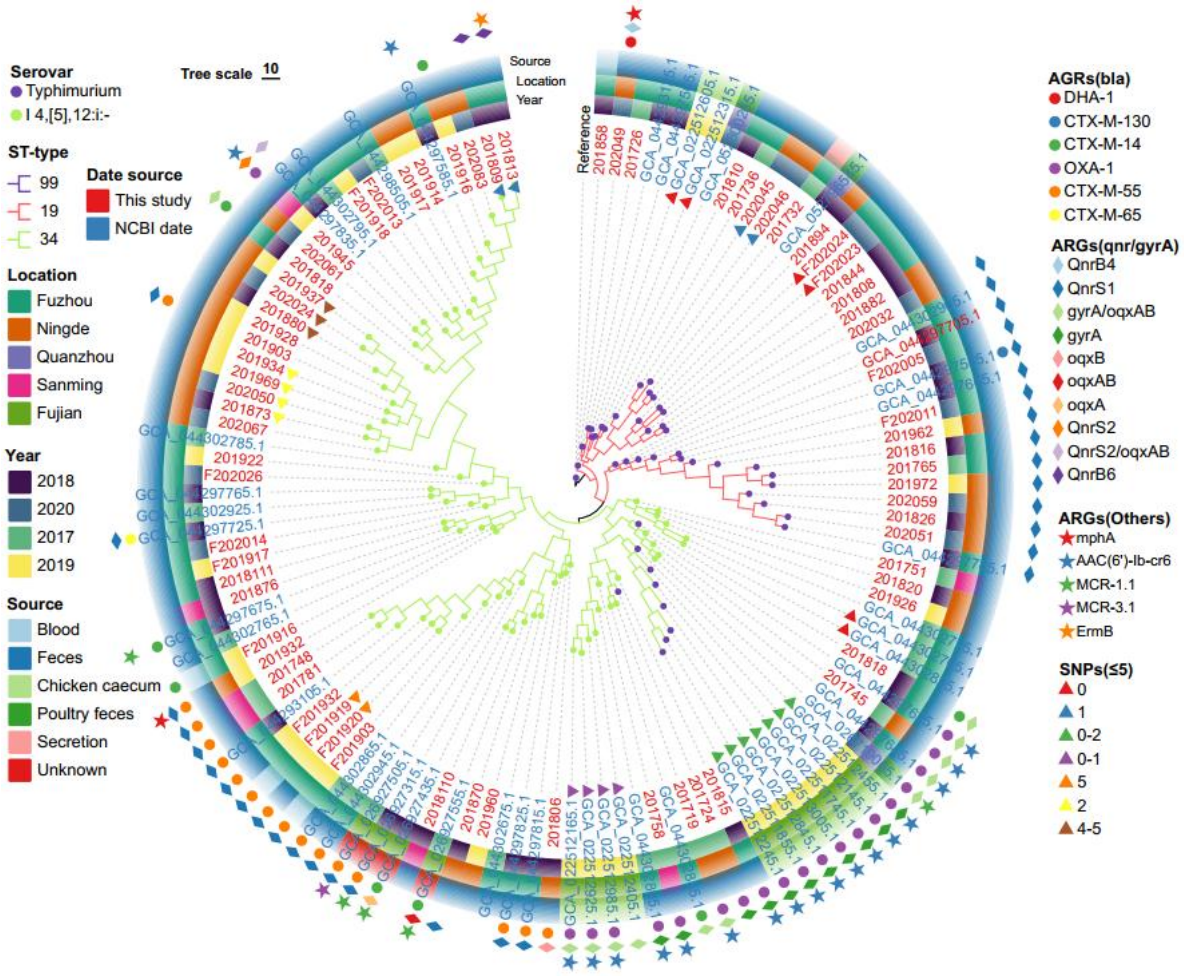


Fig.4. Phylogenetic tree for core-genome SNPs of *S.* typhimurium and its variants in Fujian Province. The genome of *S.* Typhimurium strain LT2 (RefSeq accession: GCF_000006945.2) was used as a reference and outgroup to root the tree.

Pairwise core-genome single-nucleotide polymorphism (cgSNP) distance analysis demonstrated that genetic divergence between the ST34 and ST19 lineages spanned 370 to 980 SNPs (median 829 SNPs). Within-lineage pairwise distances ranged from 0 to 137 SNPs (median:

84 SNPs) for the ST34 cluster, whereas the ST19 cluster, comprising 34 isolates, exhibited a notably wider intra-group distribution of 0 to 1031 SNPs (median: 882 SNPs). Across the full phylogenetic strain collection (n=122), a total of 11 isolate pairs (involving 30 strains) differed by ⩽5 cgSNPs, of which three pairs were genetically identical (0 SNP differences) (Fig 4.).

Of these highly related pairs, nine were recovered from the same administrative region within the same calendar year, and the remaining two were isolated from geographically distinct locations during the same year (refer to Figure 3 for full visualization). Among the three genetically indistinguishable pairs, one pair (designated F202023 and F202024) recovered in this study came from clinical cases residing in the same household, providing strong epidemiological evidence of a localized foodborne transmission event. No associated epidemiological metadata could be retrieved for the other two identical pairs obtained from the NCBI public dataset. Notably, three clonal groups contained more than two closely related isolates: one group generated in this study comprised three strains recovered from the same geographic site across different sampling years, indicating the potential long-term persistence and ongoing transmission of a single clonal lineage in this region. The remaining two clonal groups, sourced from the NCBI database, were all isolated from chicken caecal samples collected at a single commercial

poultry farm, confirming persistent clonal contamination within the livestock production environment.

4. Discussion

Epidemiological analysis of *Salmonella* isolates from four tertiary hospitals in Fuzhou (2017-2020) revealed a distinct summer-autumn seasonality, consistent with the subtropical climate of the region, where elevated temperatures from May-October favor proliferation of enteric pathogen. This temporal pattern aligns with reported *Salmonella* isolation trends in Guangdong and Fujian [7, 27]. Age-stratified distribution indicated increased susceptibility among children under 5 years and adults aged 36-60 and 60-80 years, reflecting the greater vulnerability of immunocompromised populations. Notably, although the infection rates in the under-5 groups were comparable to those in the older age, it did not represent the absolute peak–a deviation from patterns reported elsewhere in China [8]. This discrepancy may reflect the non-pediatric specialization of the participating hospitals. Although *Salmonella* infections usually manifest as self-limiting gastroenteritis, appropriate antimicrobial treatment is essential for invasive or systemic cases, and the rising prevalence of MDR strains further complicates therapeutic management [9,11]. Among the 139 isolates analyzed, 85.61% were resistance to at least one antibiotic and 64.03% were MDR, exceeding previous regional surveillance data and suggesting an ascending

resistance trajectory [28], suggesting an upward trend in *Salmonella* resistance. These MDR rates were higher than those historically reported in Guangzhou and Chongqing [29, 30], yet lower than recent findings from Guizhou and Zhejiang Province [12, 13]. Such spatiotemporal variations probably reflect regional differences in circulating serotypes and antimicrobial prescribing practices.

The emergence of resistance to first-line antimicrobial agents for severe infections, particularly third-generation cephalosporins and fluoroquinolones, poses substantial clinical challenges [31]. Quinolone resistanceis mediated by multiple mechanisms [32], and this study examined the primary mechanisms of quinolone resistance mediated by QRDRs and PMQR genes. Among the 58 nalidixic acid-resistant isolates, predominant mutations were*gyrA*:$_{\text{Asp87Tyr}}$, *gyrA*:$_{\text{Asp87Asn}}$, and *parC*:$_{\text{Thr57Ser}}$, consistent with findings reported by Kuang et al [33].Notably, *S.* Enteritidis mainly showed mutations at amino acid position 87 of *gyrA*, whereas *S.* Typhimurium predominantly carried mutations at position 83,and other serotypes mainly carried mutations at position 57 of *parC*. These differences in mutation patterns across serovars warrant validation in larger strain collections. In addition, PCR amplification and whole-genome sequencing confirmed the presence of PMQR genes, including *qnrS, oqxAB, qepA* and *aac(6')-Ib-cr*, in certain strains, highlighting the complexity of quinolone resistance mechanisms. Of note,

ceftriaxone resistance in the present collection exceeding the rates reported in Taiwan (5.9%) [34], the United States (3%) [35], and Europe (1.9%) [9]. Critically, all ESBL-producing isolates were MDR, with nearly all displaying ACSuT or ACSSuT phenotypes. Moreover, co-resistance to ciprofloxacin and azithromycin in some ESBL-producing isolates points to the emergence of strains that pose formidable therapeutic challenges.

Whole genome sequencing of 11 ESBL-producing *Salmonella* strains identified 29 antimicrobial resistance determinants–including mutations in *gyrA, gyrB*, and *parC*–conferring resistance to 11 distinct antibiotic classes, which underscores the extensive diversity of resistance mechanisms circulating in Fuzhou. β-lactam resistance arose mainly through β-lactamase production encoded by *bla* genes and AmpC-mediated hydrolysis [36]. We detected 16 resistance genes spanning five classes in these isolates, including three β-lactamase genes ($bla_{\text{CTX-M}}$, bla_{TEM} and bla_{OXA}) and two AmpC genes (bla_{DHA} and bla_{CMY2}), consistent with global patterns [37-39]. Notably, 5 of 11 isolates co-harbored two β-lactamase genes, indicating complex ESBL resistance mechanisms, as previously observed in a *S.* Wandsworth isolate [22]. Collectively, these ESBL-producing strains represent a substantial public health threat, exhibiting extensive MDR phenotypes driven by diverse horizontally acquired resistance determinants. The strong

genotype-phenotype correlation shown by heatmap analysis confirms the genetic basis of the observed resistance, and the lustering patterns further reveal the successful dissemination of specific, complex resistance gene arrays across multiple serovars. Mobile genetic elements are a primary driver of the widespread dissemination of antimicrobial resistance, facilitating the interbacterial transfer of resistance determinants. Among these, plasmids are critically important vectors and serve as the principal mechanism for global spread of antibiotic resistance genes (ARGs) and virulence factors in *Salmonella* [40]. In this study, 10 of 11 ESBL-producing isolates harbor 1–3 plasmid replicons, suggesting possible plasmid localization of *bla* and other resistance genes–a hypothesis requires further validation. Previous studies have extensively documented the genetic environments flanking *bla* resistance genes in *Salmonella* [41,42]. Our findings corroborate substantial variation in these genetic contexts: the upstream regions of bla_{CTX} was predominantly associated with ISEcp1 and IS26, bla_{TEM} gene transmitted mainly by IS26 insertions, and bla_{OXA} was disseminated by intI1 integrons, transposons and additional insertion sequences. Together, these observations highlight the key role of mobile genetic elements into accelerating the horizontal transfer of resistance genes among bacterial populations. Sustained research into the dynamics of resistance gene spread via mobile genetic elements is essential for developing effective containment strategies

against MDR pathogens.

The phylogenetic analysis of *S.* Typhimurium and its monophasic variants in Fujian Province reveals a clear population structure dominated by two major lineages, ST19 and ST34, which aligns closely with the global epidemiological shift of this pathogen over recent decades [43]. Previous national surveillance in China has already identified ST34 monophasic *S.* Typhimurium as one of the most rapidly expanding *Salmonella* subtypes linked to human salmonellosis, particularly in southeastern coastal regions [10, 44]. This study further showed that the ST34 lineage in Fujian carries a richer repertoire of resistance determinants, including $bla_{\text{CTX-M-55}}$ and $bla_{\text{OXA-1}}$, than the local ST19 population, consistent with the finding that ST34 has a stronger capacity to acquire and accumulate mobile genetic elements carrying antimicrobial resistance genes in food production chains. The distinct bipartite division within the ST19 cluster, strictly stratified by the presence or absence of the plasmid-mediated quinolone resistance gene *qnrS1*, provides direct genomic evidence that antimicrobial selection pressure has profoundly reshaped the local clonal evolution of *S.* Typhimurium. This observation echoes a longitudinal study conducted in the United Kingdom, which showed that acquisition of antimicrobial resistance plasmids acted as a key driver of clonal expansion and population structure in *S.* Typhimurium under long-term antimicrobial selection pressure [45]. The cgSNP distance data in this

study supports this divergence pattern: the median intra-cluster distance of the ST19 population reaches 882 SNPs, far exceeding the median of 84 SNPs within the ST34 cluster, indicating that the local ST19 group has a longer evolutionary history and a more complex genetic background, whereas ST34 represents a relatively newly emerged and rapidly expanding clonal group.

Notably, the identification of multiple isolate pairs with ≤5 cgSNP differences, including a 0-SNP-difference pair recovered from cases in the same household, strongly suggests that undiagnosed small-scale foodborne transmission events caused by MDR*S.* Typhimurium are likely uneported in Fujian. This finding is in line with a previous provincial investigation, which pointed out that a large proportion of sporadic salmonellosis cases in China are actually unrecognized clustered outbreaks linked to contaminated retail food, owing to limited routine whole-genome sequencing capacity in local clinical surveillance systems [46-47]. The detection of persistent clonal strains spanning multiple years at the same site, together with the highly related isolates from a single poultry farm, further indicates that the continuous transmission of resistant clones between livestock production environments and human populations forms a critical hidden transmission chain that requires targeted intervention in future prevention and control efforts.

While this study provides valuable genomic and epidemiological insights

into the antimicrobial resistance patterns and phylogenetic characteristics of *S.* Typhimurium and its monophasic variants in Fujian, several limitations should be acknowledged. First, the strain collection used for whole-genome sequencing was recovered predominantly from four tertiary sentinel hospitals in Fuzhou with very limited sampling coverage across livestock farms, slaughterhouses, retail food chains and remote mountainous regions; it is there for not a fully representative random sample of the local circulating population, which may underestimate the true genetic diversity of the ST19 lineage in animal reservoirs and miss geographically restricted clonal clusters, limiting the generalizability of the conclusions to the full provincial or national scale. Second, the retrospective laboratory-based design only captures cross-sectional epidemiological snapshots rather than continuous long-term trends, and the public ST34 and ST19 sequences retrieved from NCBI lack complete standardized epidemiological metadata, preventing robust quantitative source-attribution analysis to clarify the relative contribution of different transmission routes to local human salmonellosis. Third, the study remains at a descriptive genomic epidemiology stage, and complete genome assembly of all resistant strains and follow-up functional experiments are still required to verify the actual in vivo fitness differences between ST34 and the distinct ST19 subclades with varying resistance gene profiles. Despite these constraints, the findings provide

critical baseline data for monitoring emerging antimicrobial resistance threats in local enteric pathogens, and future multicenter prospective studies incorporating year-round longitudinal surveillance across the "farm-to-table" continuum and expanded high-resolution genomic analyses will effectively address these gaps.

Conclusions

This study characterized the antimicrobial resistance (AMR) profile and underlying genetic mechanisms of *Salmonella* isolates collected from clinical settings in Fuzhou, China. The *Salmonella* strains circulating in this region are characterized by marked serotype diversity and high rates of both overall and MDR. Among 139 isolates, 85.61% were resistant to at least one agent and 64.03% were MDR, with ESBL producers accounting for 11.51%. These resistance patterns were consistent with the diversity of resistance genes identified by whole-genome sequencing. The presence of multiple plasmid types, insertion sequences, and transposons provides preliminary insights into the mechanisms underlying the transmission of resistance genes. The study highlights the serious and growing public health posed by MDR and ESBL-producing *Salmonella* in the region. The convergence of resistance to third-generation cephalosporins and fluoroquinolones, together with the mobilisation of resistance genes via plasmids and other genetic elements, substantially restricts treatment options. Phylogenomic analysis of *S.* Typhimurium and

its monophasic variants in Fujian Province revealed a clearly structured population comprising two major lineages, ST19 and ST34, with further subclustering defined by key resistance genes including *qnrS1*, $bla_{\text{CTX-M-55}}$, and $bla_{\text{OXA-1}}$. Despite an overall sporadic epidemiological pattern across time, geography, and source, the detection of multiple closely related isolate pairs (⩽5 cgSNPs differences) and of persistent clonal groups indicates that small-scale foodborne transmission events and localized clonal dissemination are substantially under-recognized by current surveillance systems. These results emphasize the urgent need for enhanced AMR surveillance using molecular methods, such as whole-genome sequencing, and stringent antibiotic stewardship in both human and veterinary medicine within a One Health framework.

Declarations:

Data availability

The genome sequences of 11 ESBL-producing and 118 *S.* Typhimurium strains were deposited in the NCBI GenBank database under BioProject number PRJNA872212 and BioSample Accession numbers (SAMN61094965-SAMN61094974, and SAMN48744360).

Authors contribution

Yufeng Qiu: Conceptualization, Data curation, Formal analysis, Investigation, Software, Visualization, Writing-original draft. Yulan

Lin: Data curation, Resources, Investigation. Chaochen Luo: Formal analysis, Methodology. Xinlan Hu: Data curation, Resources. Yuyan Li: Data curation, Investigation. Jianhui Chen: Data curation, Supervision, Project administration. Mengyin Huang: Formal analysis, Methodology. Shenggen Wu: Funding acquisition, Resources, Project administration, Writing-review & editing. JinsongYang: Project administration, Conceptualization, Validation, Writing-review & editing.

Ethical approval

This study was a retrospective analysis of de-identified clinical Salmonella isolates and anonymized demographic and clinical data that were generated during routine patient care. No additional samples were collected, and no intervention on or contact with human participants was involved. The study protocol was submitted to and reviewed by the Medical Ethics Committee of Fujian Provincial Center for Disease Control & Prevention, Fuzhou, Fujian Province, China. The Committee determined that this study used anonymized information data and pre-existing leftover clinical bacterial isolates, caused no harm to the human body, and involved neither sensitive personal information nor commercial interests; it therefore met the criteria for exemption from ethics review specified in Article 32 of the Measures for the Ethical Review of Life Science and Medical Research Involving Human Subjects (National Health Commission, Ministry of Education, Ministry of

Science and Technology and National Administration of Traditional Chinese Medicine of the People's Republic of China; Guo Wei Ke Jiao Fa [2023] No. 4). The Committee formally approved the request for exemption from ethics review. Because all patient identifiers had been removed prior to data analysis and the study involved no identifiable personal information, the requirement for informed consent was also waived by the Committee. All procedures were performed in accordance with relevant guidelines and regulations, including the Declaration of Helsinki.

Declaration of competing interest

The authors declared that they have no competing interests or personal relationships that could have appeared to influence the work reported in this paper.

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Clinical trial number: not applicable.

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