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Prevalence, antibiotic resistance, resistance and virulence determinants of *Campylobacter jejuni* in China: A systematic review and meta-analysis

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ABSTRACT

Campylobacter jejuni (C. jejuni) is recognized as a serious food contaminant that extensively results in foodborne diseases. Numerous studies have been conducted on the prevalence and antibiotic resistance of C. jejuni, but there is a lack of comprehensive analysis of published data. This study provides a comprehensive overview of the epidemiology, antibiotic resistance, and virulence determinants of C. jejuni in China through a systematic review and meta-analysis. The prevalence levels of C. jejuni from low to high were the humans (5.2 %, 95 % CI: 4.2-6.4 %), foods (12.5 %, 95 % CI: 9.7-15.6 %), animals (15.4 %, 95 % CI: 13.2-17.6 %), and environment (17.8 %, 95 % CI: 9.7-27.7 %), respectively. Furthermore, C. jejuni exhibits high resistance rates to antibiotics such as cefoperazone, nalidixic acid, ciprofloxacin, cefradine, and tetracycline. The overall multi-drug resistance rate (MDR) of C. jejuni was 72.8 % (95 % CI: 62.4-82.2 %), indicating a serious problem with MDR. The resistance of C. jejuni to most antibiotics has increased in the last 20 years. Among the main resistance determinants of C. jejuni, gyrA T86I and tet(O) had a higher pooled prevalence of 94.8 % (95 % CI: 88.7-99.0 %) and 79.0 % (95 % CI: 66.9-89.2 %), respectively. Furthermore, the high prevalence of virulence-related genes was shown in C. jejuni, such as adhesion (cadF, racR), invasion (ciaB, iamA, ceuE), and toxin (cdtB, cdtC). In summary, C. jejuni has a high prevalence with regional characteristics, and antibiotic resistance of this bacterium especially animal sources remains a serious problem in China. Comprehensive monitoring and control measures for this pathogen are urgently needed to ensure food safety and public health.

1. Introduction

Campylobacter jejuni (*C. jejuni*) represents one of the leading causative agents of foodborne diarrheal diseases in humans [1]. Infections with foodborne *C. jejuni* can lead to symptoms such as fever, acute gastroenteritis, and reactive arthritis [2]. One of the most severe complications of *C. jejuni* infection is *Guillain-Barré* syndrome (GBS), an acute demyelinating disease of the peripheral nervous system, for which *C. jejuni* is the most common antecedent infectious trigger, potentially causing respiratory muscle paralysis and death in severe cases [3,4]. According to recent estimates from the World Health Organization (WHO), *C. jejuni* is responsible for approximately 96 million intestinal infections annually globally [5]. The risk assessment results suggest that the average incidence of campylobacteriosis from poultry consumption in China in 2010 was estimated to be 0.00118 % (118 cases per 100,000 people) [6]. In 2007, an outbreak of GBS occurred in a rural town in Jilin, China, resulting in 36 cases associated with *C. jejuni* infection [7]. During April 2021–November 2022, *C. jejuni* caused five foodborne outbreaks in five local schools in Wenzhou, southeastern China, infecting about 83 inhabitants [8]. The elevated prevalence and incidence rates of *C. jejuni* from different sources have established it as a major public health threat [9,10].

Antimicrobial resistance (AMR) has emerged as one of the major public health threats. The misuse and overuse of antimicrobial agents in humans, animals, and plants are primary drivers for the emergence of resistant pathogens [11]. According to related studies, AMR directly contributed to 1.27 million deaths globally in 2019 and was associated with an additional 4.95 million deaths [12]. From 2017 to 2018, the isolation rate of *Campylobacter* from patients with diarrhea was 7.81 % in the Beijing area of China, with *C. jejuni* showing resistance rates to ciprofloxacin, tetracycline, and nalidixic acid all greater than 90 % [13]. In Sichuan and Jiangsu regions, *C. jejuni* isolated from broiler chickens

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exhibited extremely high resistance rates to ciprofloxacin and erythromycin [14,15].

In terms of drug resistance mechanisms, various bacteria, including C. jejuni, have evolved multiple strategies to counteract the selective pressures imposed by antibiotics in a stringent antibiotic environment. The principal mechanisms that have been clearly defined are: (1) reducing cell membrane permeability and enhancing the expression of efflux pumps to prevent antibiotics from binding to their target sites; (2) modifying or protecting the sites of antibiotic action; and (3) producing inactivating or deactivating enzymes that render antibiotics ineffective or alter their structure [16,17]. In terms of pathogenicity, the primary pathogenic mechanisms of C. jejuni can be categorized into five major systems: the flagellar system, chemotaxis system, adhesion proteins, exotoxins, and endotoxins. The synergistic action of these five systems constitutes the complex pathogenic framework of C. jejuni. During this process, the expression of various virulence genes plays a key role. Genes such as flaA, flaB, plb1A, cadF, and ciaB are among those that are expressed and contribute to pathogenicity [18,19].

Despite the extensive research on *C. jejuni*, the overall contamination and resistance profile of this bacterium in China remains unclear. Therefore, this study aims to comprehensively quantify the prevalence, antibiotic resistance, resistance determinants, and virulence genes of *C. jejuni* isolated from different sources in China using a meta-analysis, providing a reference for relevant departments to implement appropriate risk management strategies.

2. Materials and methods

2.1. Search strategy and screening criteria

This systematic review was performed according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA), which includes a total of 27 checklist items (Supplementary Table S1) [20]. Two databases were systematically searched for relevant scientific reports published between January 2000 and December 2023, including the Web of Science (WOS, https://www.webofscience.com/wos /alldb/basic-search) database and the China National Knowledge Infrastructure (CNKI, https://chn.oversea.cnki.net/index/) database. In the initial stages of our research, we included PubMed and Scopus in our search protocol. After conducting an exhaustive comparison and crossreferencing process, we found that all relevant literature from these databases was comprehensively covered in the WOS database.

The following search strategy was utilized to gather relevant publications from the WOS database: [("prevalence" OR "incidence" OR "occurrence" OR "drug" OR "antibiotic" OR "antimicrobial" OR "quality" OR "contamination" OR "survey" OR "sampling" OR "character*" OR "quanti*" OR "epidemiol*" OR "isolate*" OR "enumerat*"]] AND [("*Campylobacter jejuni*" OR "*Campylobacter*")] AND [("China" OR "Chinese")] AND (2000:2023). The asterisk (*) serves as a truncation symbol to represent any number of characters in the search terms for the WOS database. For the CNKI database, the search strategy was formulated as: [(*Campylobacter OR Campylobacter jejuni*]] AND [(contamination rate OR prevalence OR incidence OR drug OR antibiotic OR antimicrobial OR contamination OR epidemiology OR isolation OR resistance)] AND (2000,2023), with terms in Chinese.

After removing duplicate records, all the publications were checked against a set of exclusion criteria. A study was excluded if (1) it was published as a conference abstract or was not a research paper; (2) it was not relevant, such as studies focusing on the detection method, predictive modeling, or hurdle technology; (3) it was a duplicate report; (4) non-available data; (5) inadequate sample: sample number of <30; (6) not *C. jejuni*; and (7) the study was not conducted in mainland China.

2.2. Data extraction and synthesis

Two authors (Z. Li and X-J. Qin) independently extracted the

following data from the final selected studies: authors, year of publication, sampling time, sampling location (the minimum resolution is restricted in the province), total sample size and positive rates of *C. jejuni* contamination prevalence, sample size, and antibiotic usage rate, total number of resistant strains, antibiotics detected, antibiotic resistance level and MDR rates, source of the strains, drug susceptibility testing methods, antibiotic resistance gene information and virulence gene information. Recorded data were compiled in Microsoft Excel for further statistical analysis.

2.3. Meta-analysis and statistical analyses

This meta-analysis was performed using R-software (meta-package, version 4.9.2). Antibiotic resistance rates were estimated by dividing the number of antibiotic-resistant isolates by the total number of isolates, expressed as a percentage. A random-effects model was applied to analyze the pooled prevalence. In all instances, rates were calculated using a 95 % confidence interval (CI). Heterogeneity among studies was assessed using I^2 statistics (Deeks, Higgins, Altman, & Group, 2019). I^2 values with percentages of 25 %, 50 %, and 75 % were considered low, moderate, and high heterogeneity levels, respectively (Paudyal et al., 2018). Subgroup analyses were conducted to explore the potential causes of heterogeneity based on the source of isolates (i.e., human, animal, food, environment), time, and region. All statistical tests with a p < 0.05 were considered significant.

3. Results

3.1. Characteristics of eligible studies and datasets

The comprehensive flowchart detailing the literature search process is presented in.

Initially, a total of 1224 publications (323 in English databases, 901 in Chinese databases) were identified from the two selected electronic databases. From these, 10 duplicate articles were removed. The remaining 1214 articles were subjected to screening for relevant information, which resulted in the exclusion of 616 articles. Then, the remaining 598 articles were checked against predefined eligibility criteria. Additional 408 articles were excluded because they were not journal articles, reported duplicate data, or lacked relevant data in the literature. Finally, a meta-analysis included 190 studies, 49 in English and 141 in Chinese (Fig. 1).

Of the 190 final articles included, 146 were eligible for pooling the prevalence. Of these, 22 provinces and municipalities were included, representing most provinces in China. In the context of AMR, 92 studies were utilized for single-resistance analysis, while 48 studies were employed for multiple-resistance analysis. Furthermore, the meta-analysis of resistance gene carriage rates included 14 studies, whereas the meta-analysis of virulence gene carriage rates included 29 studies.

3.2. Pooled prevalence of C. jejuni in different sources

The pooled prevalence of *C. jejuni* from animals, environment, foods, and humans using the random effects model is provided in Fig. 2. Results showed that the prevalence of *C. jejuni* was the highest in the environment (17.8 %, 95 % CI: 9.7–27.7 %). The pooled prevalence rates for animals, food, and humans were 15.4 % (95 % CI: 13.2–17.6 %), 12.5 % (95 % CI: 9.7–15.6 %) and 5.2 % (95 % CI: 4.2–6.4 %), respectively.

To understand the prevalence of *C. jejuni* in major types of food and animals in China, a subgroup analysis of *C. jejuni* from food and animal sources was subsequently conducted. The prevalence of *C. jejuni* in specific food types and animal species is presented in Table 1. In different animal categories, swine exhibited the highest prevalence (62.3 %, 95 % CI: 9.1–100.0 %), followed by chicken (24.0 %, 95 % CI: 20.6–27.5 %), goose (14.3 %, 95 % CI: 5.7–25.6 %), cattle (9.4 %, 95 % CI: 5.1–14.8 %), and duck (6.5 %, 95 % CI: 1.5–14.1 %). In different food



Fig. 1. Flowchart of the literature search and collection.





categories, chicken meat displayed the highest prevalence (19.3 %, 95 % CI: 11.7–28.3 %), followed by duck (15.9 %, 95 % CI: 3.9–33.4 %), and swine (8.5 %, 95 % CI: 0–29.6 %). Even though most of the environmental data came from places where animals were raised and food was processed, there were not enough data to do subgroup analyses to show how the prevalence of *C. jejuni* from environmental sources varied. Additionally, due to limited information in the literature regarding whether the food samples were chilled or frozen, the relationship between the prevalence of *C. jejuni* and food storage methods could not be determined.

The overall prevalence of *C. jejuni* found before and after 2010 in different sources is shown in Fig. 3. Before the year 2010, the prevalence of *C. jejuni* from animal, food, and human sources was 10.6 % (95 % CI: 6.3-15.9 %), 7.4 % (95 % CI: 1.9-15.7 %), and 5.2 % (95 % CI: 2.9-8.0 %), respectively. After 2010, the respective prevalence from these different sources increased to 12.5 % (95 % CI: 9.8-15.4 %), 13.6 % (95 % CI: 10.3-17.2 %), and 5.4 % (95 % CI: 4.2-6.8 %). Overall, there was an apparent increase in the detection rates of *C. jejuni* in different sources both before and after 2010. Due to the unavailability of environmental source data for *C. jejuni* before 2010, such comparisons were not included in this analysis.

Table 1

The prevalence of C. jejuni in specific food types and animal species

Category		No. of studies	Total	Positive	Pooled Prevalence (%)	95 % CI (%)	τ^2	I ² (%)
Animal	Chicken	40	29,776	5586	24.0	20.6-27.5	0.0154	97.7
	Cattle	10	6606	424	9.4	5.1-14.8	0.0116	96.5
	Swine	3	555	123	62.3	9.1-100	0.1801	98.0
	Duck	3	786	63	6.5	1.5-14.1	0.0096	86.8
	Goose	4	1834	139	14.3	5.7-25.6	0.0150	79.6
Food	Chicken	19	4730	947	19.3	11.7-28.3	0.0523	98.0
	Duck	2	313	38	15.9	3.9-33.4	0.0186	85.9
	Swine	4	1126	43	8.5	0–29.6	0.0570	97.1

95 % CI: 95 % confidence interval; τ^2 : between-study variance; I^2 : inverse variance index;



Fig. 3. Overall prevalence of *C. jejuni* in different sources before 2010 and after 2010 in China.

3.3. Pooled prevalence of C. jejuni in different geographical regions

Due to the inherent limitations of literature searches in metaanalyses, the prevalence data of *C. jejuni* covered 17 provinces, major municipalities, and autonomous regions in China. In these regions, the prevalence levels of *C. jejuni* are illustrated in Fig. 4 and Supplementary Table S2 (indicated as low (< 10 %), medium (\geq 10 % and < 20 %) and high level (\geq 20 %)), without considering the time and sample sources tested. The highest prevalence level of *C. jejuni* was reported in Heilongjiang (33.6 %, 95 % CI: 30.0–40.5 %). In comparison, the overall prevalence of *C. jejuni* was relatively lower in Liaoning, Hubei, Shanghai, Xinjiang, Yunnan, Henan, and Guangxi, ranging from 0.75 % to 9.8 %.

3.4. Antibiotic resistance of C. jejuni

In all eligible studies, the antibiotic resistance of C. jejuni was interpreted according to Clinical and Laboratory Standards Institute (CLSI) guidelines. Data on eight major types of antibiotics, including 32 individual antibiotic agents, were covered in the studies resulting from the meta-analysis, allowing us to calculate antibiotic resistance rates for β-lactams (i.e., ampicillin, cefotaxime, cefoperazone, amoxicillin, ceftriaxone, imipenem, meropenem, penicillin, cefradine, and cefaclor), aminoglycosides (i.e., gentamicin, streptomycin, amikacin, kanamycin, and tobramycin), macrolides (i.e., erythromycin and azithromycin), quinolones (i.e., nalidixic acid, ciprofloxacin, norfloxacin, levofloxacin, ofloxacin, and enrofloxacin), sulfonamide (i.e., sulfamethoxazole), lincosamides (i.e., clindamycin and lincomycin), tetracyclines (i.e., tetradoxycycline. and oxvtetracvcline). cycline. ketolides (i.e., telithromycin) and phenicols (i.e., chloramphenicol and florfenicol).

The results of the meta-analysis of AMR in *C. jejuni* are shown in Table 2. According to the pooled prevalence of AMR, the highest resistance rate was observed for cefoperazone (98.1 %, 95 % CI: 95.2–99.8 %), while the lowest resistance rate was to amikacin (8.8 %, 95 % CI: 3.1–19.0 %). The most commonly used antibiotics, including tetracycline, ciprofloxacin, erythromycin, gentamicin, azithromycin, lincomycin, florfenicol, nalidixic acid, and chloramphenicol, exhibited resistance rates ranging from 13.3 % to 89.0 %. Rather high levels of heterogeneity and wide CI ranges for resistance rates derived from the literature were observed for the other antibiotic agents.



Fig. 4. Pooled prevalence of C. jejuni in different geographical regions.

Table 2

Meta-analysis results of the antibiotic resistance of C. jejuni.

Antibiotic Class	Antibiotic Agents	No. of studies	Total	Positive	Resistance Rate (%)	95 % CI (%)	τ^2	I ² (%)
β-Lactams	Ampicillin	31	2714	1361	57.3	46.6–67.7	0.0843	96.6
	Cefotaxime	23	1978	531	27.2	15.8-40.3	0.1101	97.3
	Cefoperazone	18	1825	1775	98.1	95.2-99.8	0.0231	89.7
	Amoxicillin	15	1117	441	43.0	22.2-65.2	0.1845	98.2
	Ceftriaxone	8	1072	692	72.8	49.4-91.0	0.1284	98.3
	Imipenem	11	1419	259	11.6	1.2-29.3	0.1333	98.5
	Meropenem	8	912	218	10.7	0-40.2	0.2492	99.1
	Penicillin	10	663	483	67.8	50.5-83.0	0.0727	94.9
	Cefradine	10	889	625	83.2	60.4-97.7	0.1630	98.2
	Cefaclor	7	549	375	78.9	54.8-95.6	0.1143	97.2
Aminoglycosides	Gentamicin	99	8069	1946	19.8	15.4-24.5	0.0711	95.8
	Streptomycin	43	2772	636	21.4	15.2-28.3	0.0590	93.8
	Amikacin	23	3325	695	8.8	2.1-19.0	0.1176	98.4
	Kanamycin	20	1356	529	33.0	21.3-45.8	0.0797	95.5
	Tobramycin	10	1075	378	34.8	16.7-55.5	0.1058	97.8
Macrolides	Erythromycin	98	8443	1167	13.0	9.7-16.8	0.0586	95.2
	Azithromycin	66	6221	1241	13.3	9.0-18.2	0.0653	96.0
Quinolones	Nalidixic acid	70	4931	4136	89.0	84.7-92.8	0.0626	94.6
	Ciprofloxacin	98	8985	6759	83.5	77.5-88.8	0.1320	97.9
	Norfloxacin	20	1814	1249	79.3	65.5-90.4	0.1152	97.6
	Levofloxacin	17	1430	955	79.8	64.4-91.8	0.1243	97.6
	Ofloxacin	11	1307	738	62.9	48.6-76.2	0.0547	96.1
	Enrofloxacin	15	2398	1346	75.1	58.5-88.6	0.1152	98.4
Sulfonamide	Sulfamethoxazole	27	3380	2482	79.6	67.0-89.9	0.1338	98.4
Lincosamides	Clindamycin	76	6204	1763	25.3	19.1 - 32.1	0.0974	96.9
	Lincomycin	6	696	214	34.8	16.4-55.9	0.0661	96.7
Tetracyclines	Tetracycline	99	9167	6908	83.2	78.3-87.6	0.0861	96.9
	Doxycycline	23	2258	1225	70.1	54.9-83.5	0.1355	97.8
	Oxytetracycline	5	373	301	79.9	72.5-86.4	0.0055	60.8
Ketolides	Telithromycin	32	2056	278	11.9	7.7-16.9	0.0301	88.4
Phenicols	Chloramphenicol	56	4037	680	14.6	9.4-20.6	0.0752	95.6
	Florfenicol	62	5669	2245	34.7	27.2-42.7	0.0958	97.1

95 % CI: 95 % confidence interval; τ^2 : between-study variance; I^2 : inverse variance index;

3.5. Antibiotic resistance of C. jejuni from different isolated sources and times

The results showed that there was considerable heterogeneity among the included studies for each antibiotic. Subgroup analyses were conducted to analyze the heterogeneity by sources.

The antibiotic resistance of C. jejuni from different isolated sources (human, animal, food and environment) is presented in Supplementary Tables S3-S6. The majority of C. jejuni isolates from human sources were resistant to cefoperazone, sulfamethoxazole, cefradine, cefaclor and nalidixic acid, with resistance rates of 99.9 % (95 % CI: 98.8-100 %), 97.7 % (95 % CI: 92.9-100 %), 96.0 % (95 % CI: 84.9-100 %), 91.5 % (95 % CI: 83.9-97.0 %), and 91.1 % (95 % CI: 87.6-94.1 %), respectively, while the lowest resistance rates were observed to amikacin (0.2 %, 95 % CI: 0-1.6 %) and imipenem (0.2 %, 95 % CI: 0-2.6 %) (Supplementary Table S3). C. jejuni isolated from animals showed the highest AMR prevalence to cefoperazone (95.1 %, 95 % CI: 79.7–100 %) and the lowest resistance rate to meropenem (4.9 %, 95 % CI: 1.3-10.1 %) (Supplementary Table S4). C. jejuni isolates from food sources had the highest resistance to norfloxacin (95.1 %, 95 % CI: 72.8-100 %) and the lowest resistance to meropenem (2.0 %, 95 % CI: 0-6.7 %) (Supplementary Table S5). Due to limited data availability for environmental sources, comprehensive AMR data were not able to be presented comprehensively; however, the available data indicated that the highest level of resistance was observed to tetracycline (92.4 %, 95 % CI: 82.3–98.9 %) and the lowest to telithromycin (4.1 %, 95 % CI: 0–23.4 %) (Supplementary Table S6).

Changes in resistance of domestic *C. jejuni* to 16 major antibiotics around 2010 are shown in Fig. 5. Regardless of the source of *C. jejuni* isolation, the resistance rates of *C. jejuni* to ampicillin, cefotaxime, gentamicin, kanamycin, erythromycin, azithromycin, ciprofloxacin, norfloxacin, clindamycin, and chloramphenicol showed an increasing trend over time. The prevalence of resistance to chloramphenicol increased 4.63 times from the period before 2010 (4.0 %, 95 % CI: 0–12.23 %) to after 2010 (18.4 %, 95 % CI: 11.9–25.9 %). However, around the year 2010, the resistance rate to ciprofloxacin only increased by a factor of 1.03. Around 2010, an increase in resistance was observed in *C. jejuni* isolated from human sources to 13 antibiotics, namely ampicillin, cefotaxime, gentamicin, kanamycin, erythromycin, azi-thromycin, nalidixic acid, ciprofloxacin, norfloxacin, sulfamethoxazole, clindamycin, chloramphenicol, and enrofloxacin. The fastest rate of resistance increase was for kanamycin (4.60-fold), while the slowest was for nalidixic acid (1.05-fold). In animal sources, increased resistance was observed for ampicillin, cefotaxime, gentamicin, streptomycin, kanamycin, azithromycin, levofloxacin, clindamycin, tetracycline, and chloramphenicol, with cefotaxime resistance increasing 8.38-fold.

3.6. Pooled prevalence of MDR in C. jejuni

MDR was defined as resistance to three or more antimicrobials classes in this study. The results of the meta-analysis on the prevalence of *C. jejuni* MDR are presented in Table 3. Overall, the MDR rate of *C. jejuni* in China was 72.8 % (95 % CI: 62.4–82.2 %). Isolates from environmental sources had the highest MDR rates (80.0 %, 95 % CI: 50.0–98.6 %), followed by food sources, animal sources, and human sources, at 79.8 % (95 % CI: 53.8–97.2 %), 77.8 % (95 % CI: 64.0–89.2 %), and 58.7 % (95 % CI: 41.5–75.0 %), respectively. Due to the data limitations, it was not possible to compile the MDR spectra for *C. jejuni* from each isolation source.

3.7. The prevalence of antibiotic resistance determinants in C. jejuni

A meta-analysis was performed to collate the prevalence of eight antibiotic and resistance determinants (quinolones: $gyrA_T86I$; tetracyclines: tet(O), tet(L); macrolides: 23S rRNA_A2075G, erm(B); β -Lactams: $bla_{OXA-184}$, $bla_{OXA-193}$, $bla_{OXA-460}$, $bla_{OXA-465}$; aminoglycosides: aph(3')-



Fig. 5. Subgroup analysis for prevalence of antibiotic resistance *C. jejuni* in different sources (A: Total; B: Human; C: Animal).

IIIa, ant(6)-Ia, aph(2")-If, aac(6')-Ie, aph(2")-Ia, aadE, aad9; phenicols: catA13; lincosamides: inu(C); multidrug efflux pump: cmeB, RE-cmeABC) in C. jejuni isolates (Table 4). T86I mutations in gyrA were identified in 94.8 % (95 % CI: 88.7–99.0 %) of C. jejuni isolates. A2075G substitution in 23S rRNA was identified in 15.6 % (95 % CI: 0–51.3 %) of C. jejuni

isolates. The detection rates of horizontally transferable resistance genes ranged from 4.9 % to 79.0 %, including genes such as *tet*(O), *tet*(L), and *erm*(B). (Table 4). The prevalence for the muti-drug efflux pump key determinants *cmeB* and RE-*cmeABC* was 74.7 % (95 % CI: 42.8–97.0 %) and 71.3 % (95 % CI: 0–100 %), respectively. Low heterogeneity was observed for *gyrA*_T86I (53.2 %) and *bla*_{OXA-460} (17.9 %) among the eligible studies, which may be due to the small number of relevant studies.

3.8. Virulence genes of C. jejuni

When collecting the data of antibiotic resistance profiles, it was found that many studies performed virulence genes of C. jejuni. Accordingly, in this study, the prevalence of pooled genes was analyzed in parallel (Table 5). The findings of the results demonstrated that the prevalence of virulence genes involved in adhesion and colonization, specifically cadF and racR, were as follows: 99.2 % (95 % CI: 98.0–99.9 %) and 82.1 % (95 % CI: 63.0-95.6 %) respectively. For invasionassociated genes such as ciaB, iamA, pldA, ceuE and virB11, the pooled prevalence was 89.3 % (95 % CI: 78.8-96.8 %), 89.9 % (95 % CI: 76.3-98.6 %), 59.0 % (95 % CI: 23.5-90.0), 90.4 % (95 % CI: 75.3-99.1 %), and 1.5 % (95 % CI: 0.2-3.7 %), respectively. The gene associated with flagellar movement, flaA, was present at 87.4 % (95 % CI: 73.5-97.0 %). For toxin regulation-related genes, cdtB, cdtA, cdtC, and wlaN, the pooled prevalence amounted to 97.1 % (95 % CI: 93.0-99.7 %), 83.2 % (95 % CI: 74.3-90.6 %), 97.0 % (95 % CI: 94.3-99.0 %), and 23.1 % (95 % CI: 9.1-40.6 %), respectively. The chemotaxis-related genes, cheW and cheY, exhibited a pooled prevalence of 100.0 % (95 % CI: 99.7-100.0 %) and 99.6 % (95 % CI: 98.7-100.0 %), respectively. Moreover, C. jejuni exhibited a low level of heterogeneity with respect to specific virulence genes (cheW and cheY), possibly due to the limited number of studies investigating these genes.

4. Discussion

Food safety and bacterial resistance are among the key issues of concern to both the Chinese government and the public [21]. In this study, we tried to determine the prevalence and antibiotic resistance of *C. jejuni* from animals, foods, humans, and environment samples in China based on a systematic review of published studies.

In this meta-analysis, environmental samples were primarily derived from the food animal breeding environments (feces, water, etc.) and the processing environments (rinsing water, cutting boards, etc.), with a minority from large central kitchens. Fig. 1 illustrates the widespread prevalence of C. jejuni in both breeding and processing settings. Consequently, C. jejuni identified in the breeding environment can colonize food animals, once introduced into the processing line, can spread to poultry meat through cross-contamination, particularly during defeathering and evisceration steps [22]. A recent meta-analysis conducted in South Korea reported that the pooled prevalence of Campylobacter in environmental samples varied from 4.99 % to 36.33 %, with the highest prevalence in fecal samples, followed by wash water and equipment. This highlights the significance of environmental factors in breeding and processing, which may pose a serious threat to public health indirectly through food consumption [23]. The prevalence of C. jejuni was lower in animals and food sources than that in environment sources. Subgroup analysis indicated that among animals, swine had the highest pooled prevalence (62.3 %), followed by chickens (24.0 %), whereas among foods, chicken meat exhibited the highest pooled prevalence (19.3 %) (Table 1). The 95 % confidence interval (9.1-100 %) for the prevalence of C. jejuni from swine sources was relatively wide, suggesting a lower reliability of the results, which may be due to the limited sample size. Studies have shown that globally, pigs and poultry have the highest rates of Campylobacter contamination, with some variation in the prevalence of each Campylobacter species [24]. In terms of meat products from food animals, Zbrun M V et al. [25] reported that

Table 3

The MDR rates of C. jejuni isolates from various sources in China.

Origin	Total	No. of studies	Positive	Resistance Rate (%)	95 % CI (%)	τ^2	I ² (%)
Total	5398	48	2922	72.8	62.4-82.2	0.7281	98.4
Human	1655	11	603	58.7	41.5-75.0	0.5872	97.4
Animal	2371	19	1582	77.8	64.0-89.2	0.7782	97.8
Environment	156	3	114	80.0	50.0-98.6	0.7999	91.0
Food	360	10	242	79.8	53.8–97.2	0.7981	96.3

95 % CI: 95 % confidence interval; τ^2 : between-study variance; I^2 : inverse variance index;

Table 4

The 1	prevalence	of	antibiotic	resistance	determinants	in	С.	jejuni.
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Antibiotic and Resistance Determinants		No. of studies	Total	Positive	Prevalence Rate (%)	95 % CI (%)	τ^2	I^{2} (%)
Quinolones	gyrA_T86I	7	316	299	94.8	88.7–99.0	0.0085	53.2
Tetracyclines	tet(O)	10	374	296	79.0	66.9-89.2	0.0318	79.5
	tet(L)	4	95	34	45.9	3.9-91.9	0.2484	95.6
Macrolides	23S rRNA_A2075G	3	246	15	15.6	0-51.3	0.1051	95.5
	erm(B)	7	280	17	6.4	0-20.0	0.0567	88.6
β-Lactams	bla _{OXA-184}	4	266	33	21.8	4.0-47.2	0.0628	91.6
	bla _{OXA-193}	5	245	96	40.3	12.2-72.0	0.1107	92.1
	bla _{OXA-460}	3	211	12	4.9	0.9-11.0	0.0022	17.9
	bla _{OXA-465}	4	257	20	14.3	0-42.8	0.0889	93.3
Aminoglycosides	aph(3')-IIIa	7	304	61	30.4	7.0-60.5	0.1409	94.6
	ant(6)-Ia	4	234	23	12.8	3.8-25.1	0.0134	61.1
	aph(2")-If	9	411	117	39.2	13.9-67.8	0.1725	96.4
	aac(6')-Ie	7	342	26	6.9	0.7 - 17.2	0.0289	81.6
	aph(2")-Ia	5	306	25	9.1	0.7-23.4	0.0358	86.7
	aadE	5	289	17	7.0	0.9-16.9	0.0177	74.2
	aad9	4	257	13	5.9	0-23.8	0.0515	89.0
Phenicols	catA13	4	257	13	5.9	0-21.3	0.0381	85.7
Lincosamides	inu(C)	3	246	16	10.3	1.0-25.9	0.0238	82.6
Multidrug Efflux Pump	cmeB	3	214	136	74.7	42.8-97.0	0.0674	88.2
	RE-cmeABC	2	165	131	71.3	0–100	0.0452	96.7

95 % CI: 95 % confidence interval; τ^2 : between-study variance; I^2 : inverse variance index;

Table 5

The prevalence of virulence genes in C. jejuni.

Virulence Factors Class	Virulence Genes	No. of studies	Total	Positive	Prevalence Rate (%)	95 % CI (%)	τ^2	$I^2(\%)$
Adhesion	cadF	33	2200	2148	99.2	98.0–99.9	0.0081	67.9
	racR	10	990	837	82.1	63.0–95.6	0.1095	97.5
Invasion	ciaB	20	1056	846	89.3	78.8–96.8	0.0857	94.0
	iamA	8	309	271	89.9	76.3–98.6	0.0543	88.7
	pldA	10	990	757	59.0	23.5-90.0	0.3313	99.2
	ceuE	7	867	795	90.4	75.3–99.1	0.0675	96.8
	virB11	18	1241	23	1.5	0.2-3.7	0.0090	69.6
Motility	flaA	24	1632	1360	87.4	73.5–97.0	0.1663	97.7
Toxin	cdtB	29	1800	1680	97.1	93.0–99.7	0.0457	91.6
	cdtA	24	1658	1241	83.2	74.3–90.6	0.0599	94.1
	cdtC	24	1658	1600	97.0	94.3–99.0	0.0142	78.9
	wlaN	9	331	66	23.1	9.1-40.6	0.0663	90.1
Chemotaxis	cheW	7	918	913	100.0	99.7-100.0	0.0000	0.0
	cheY	13	1171	1155	99.6	98.7–100.0	0.0008	21.2

95 % CI: 95 % confidence interval; τ^2 : between-study variance; I^2 : inverse variance index;

the prevalence of *Campylobacter* was highest in products derived from laying hens and broilers, with an overall average prevalence of 29.6 % in animal-derived foods. Similar findings have been reported in other regions of the world, including the United States [26], Ethiopia [27], Iran [22], Turkiye [28], and South Korea [23].

The results of this study showed that poultry remained the primary host for *C. jejuni*, with chickens and chicken meat being the most severely contaminated. However, other poultry sources (ducks, goose) should not be overlooked [29]. The prevalence of *C. jejuni* among domestic populations was 5.2 %, which is lower than a previous study result from Ethiopia (9.0 %, 95 % CI: 1.3–16.7 %) [27]. This may be because the latter studies targeted *C. jejuni* and *C. coli*, while this study focused solely on *C. jejuni*. In the study by Kang et al. [30], it was found that the isolation rate of *C. jejuni* from fecal samples in the Korean

population was 2.5 %, which is lower than this study. Similarly, a 2023 report from Turkey indicated that the isolation rate of *C. jejuni* from 860 human fecal samples in a hospital was 3.88 % [31]. This may be because many studies in the meta-analysis focused on hospital patient populations (diarrhea, fever, etc.), hence the results of this study may not fully represent the entire Chinese population. Additionally, the difference may be due to the sanitary conditions [32]. Due to the sample size, it was not possible to comprehensively reflect the contamination levels of *C. jejuni* in different subgroups of the population (age, gender, presence of illness). However, these findings still have an important reference value for policy makers and the relevant population.

From a temporal perspective, around 2010, there was a varying degree of increase in *C. jejuni* pooled prevalence from animal sources, food sources, and human sources (Fig. 3). Over the past decade, the incidence and prevalence of *Campylobacter* infections have increased in both developed and developing countries in North America, Europe, Africa, and Asia, particularly among children. This suggests that campylobacteriosis is likely to remain a significant global health challenge in the coming years [33]. The potential reasons for this could be attributed to advancements in microbial detection technologies and current climate changes. Techniques such as molecular biology counting, immunological detection methods, and biosensor technology have significantly enhanced pathogen detection sensitivity and accuracy [34]. The impact of climate change (temperature variations, precipitation changes, extreme weather events, etc.) on the growth, persistence, and virulence of pathogens (such as *Campylobacter*) is often complex [35]. According to a recent study, there is a positive correlation between temperature and *Campylobacter* contamination, which increases exposure risk across all transmission routes [36].

In terms of the geographical prevalence levels, the occurrence of C. jejuni is more prevalent in the Northeast, Southwest East, and Coastal areas of East China, whereas its occurrence is relatively less prevalence in the Central China, southern South China, southern Southwest China, and northern Northwest China. (Fig. 4) There is no known scientific rationale for the observed geographical differences in C. jejuni prevalence levels. Geographically, the distribution of avian species, mainly including chickens, ducks, and geese, exhibits their density being significantly higher in the eastern and southern regions of China compared to the western and northern regions [37]. This geographical distribution shows some similarity to the prevalence rates of C. jejuni in different regions observed in this study. Given that poultry is one of the primary hosts of C. jejuni, the variations in their distribution density may directly or indirectly influence the prevalence levels of C. jejuni across different areas [38]. Additionally, factors such as dietary habits [39], sanitation conditions [40], retail environments [41], economic development levels [42], and market regulatory intensity [43] in various regions may also impact the prevalence levels and transmission of C. jejuni to some extent.

In terms of antibiotic resistance, this study identified the highest AMR rates of C. jejuni isolates from various sources to cefoperazone (98.1 %), nalidixic acid (89.0 %), ciprofloxacin (83.5 %), cefradine (83.2 %), and tetracycline (83.2 %), which is consistent with previous result [15,44-47]. Overall, the resistance to aminoglycosides and macrolides antibiotics was relatively low. C. jejuni resistance rates to other antibiotics were 11.6 % to 79.9 % (Table 2). Notably, high levels of heterogeneity were observed in the resistance rates calculated for most antibiotics. Subgroup analysis elucidated the heterogeneity origins of C. jejuni. Supplementary Table S3 demonstrates that the resistance rates of C. jejuni from human sources to cefoperazone, cefradine, cefaclor, nalidixic acid, and sulfamethoxazole have exceeded 90 %. In comparison to human-sourced C. jejuni, animal-sourced strains demonstrate a resistance rate greater than 90 % only to cefoperazone (Supplementary Table S4). However, they exhibit higher resistance rates to most other antibiotics than human-sourced strains. This elevated resistance is particularly evident in animal-specific antibiotics (such as florfenicol and enrofloxacin) and those shared between humans and animals (such as ceftriaxone, penicillin, ciprofloxacin, and tetracyclines), underscoring the severe drug resistance in animal-sourced C. jejuni. This situation may arise from the use and misuse of antibiotics in farm animal environments as growth promoters or for the prevention and treatment of non-specific infections, significantly increasing antibiotic consumption and resistance in bacteria within animal habitats [48]. In food and environment sources, resistance rates range from 2 % to 95.1 % (Supplementary Table S5 and Supplementary Table S6). This study demonstrates that the resistance rates of C. jejuni isolated from humans to ciprofloxacin, nalidixic acid, tetracycline, and sulfamethoxazole are similar to those in the Middle East, yet lower for antibiotics such as amoxicillin, ampicillin, azithromycin, and chloramphenicol compared to the region. In contrast, C. jejuni isolated from domestic animals in our country exhibit higher resistance rates to ampicillin, ciprofloxacin, nalidixic acid,

streptomycin, and tetracycline than those reported in the Middle East, while showing relatively lower resistance to amoxicillin, azithromycin, chloramphenicol, and erythromycin [49]. The European Union's summary report on antimicrobial resistance in 2018/2019 noted that Campylobacter isolates from humans, food-producing animals, and their meats exhibited high resistance to ciprofloxacin and relatively low resistance to erythromycin, which is consistent with the findings of this study [50]. In 2017, the WHO established the AWaRe classification of antibiotics, which categorizes antibiotics into three groups: Access, Watch, and Reserve. This classification is designed to guide the appropriate use of antibiotics at local and national levels, with the ultimate aim of curbing the global spread of antibiotic resistance [51]. Briefly, antibiotics such as cefoperazone, ciprofloxacin, and norfloxacin, which fall under the Watch category, generally possess a higher potential for selecting antibiotic-resistant bacteria [52]. In this study, C.jejuni exhibited a high level of resistance to these antibiotics. In contrast, although antibiotics like imipenem, meropenem, erythromycin, and azithromycin also belong to the Watch category, they demonstrated relatively low resistance levels. Antibiotics in the Access category, including cephradine, penicillin, sulfamethoxazole, tetracycline, and doxycycline, are commonly used as first or second choice empiric treatment options for infectious syndromes. Previous research has indicated that these antibiotics tend to have lower resistance rates compared to those in other categories [53]. However, in this study, a high level of resistance of C.jejuni to these Access category antibiotics was detected. This implies that the clinical application of these antibiotics in the treatment of campylobacteriosis caused by C.jejuni might lead to treatment failure. Therefore, further monitoring and standardized use of these antibiotics are urgently required to ensure their future effectiveness.

In addition, the results obtained in this study revealed that in China, the resistance of C. jejuni to antibiotics such as ampicillin, cefotaxime, gentamicin, kanamycin, azithromycin, clindamycin, and chloramphenicol has exhibited an upward trend over time, regardless of whether the sources are human or animal (Fig. 5). This trend could potentially be linked to the misuse of antibiotics in both clinical settings and agriculture. In contrast, there has been a decline in the resistance of humansourced C. jejuni to streptomycin, levofloxacin, and tetracycline, whereas animal-sourced strains displayed reduced resistance to erythromycin, nalidixic acid, ciprofloxacin, sulfamethoxazole, and florfenicol. Between 2015 and 2019, the resistance of C. jejuni isolates from humans to ciprofloxacin increased in nine EU member states, while the resistance to erythromycin decreased in five member states. Differences in occurrence or trends of resistance from animals were observed between countries [50]. Between 2000 and 2010, institutions such as the National Medical Products Administration, the Ministry of Health, and the Ministry of Agriculture successively introduced policies and actions to address antibiotic resistance [54]. However, these measures were limited to the rational use of antibiotics and clinical drug resistance monitoring. Since 2011, China has comprehensively initiated the monitoring and control of antibiotic resistance. In 2012, the National Health Commission issued the clinical application management methods for antimicrobial drugs [55]. In the agricultural sector, antibiotics such as lumefantrine and colistin sulphate were successively banned for use in food-producing animals from 2015 to 2017 [56,57]. The Ministry of Agriculture and Rural Affairs implemented a comprehensive ban on the addition of antibiotics in feed in 2020, and the following year, the national action plan for the reduction of veterinary antimicrobial use (2021-2025) was released and implemented [58,59]. From 2017 to 2022, the Ministry of Agriculture released a plan for monitoring bacterial drug resistance in animal sources. The implementation of the abovementioned antibiotic resistance management strategies has effectively strengthened the supervision of antibiotic use and further inhibited the growth of bacterial drug resistance [60]. The decrease in resistance of C. jejuni to certain antibiotics observed in this study correlates with the implementation and application of the above-mentioned management plans. However, China's status as a major global producer and user of antibiotics, combined with widespread abuse and residue of antibiotics, makes the domestic problem of antibiotic resistance still very severe [61].

In the prevention and treatment of diseases in animals and humans, the cross-use of antibiotics has facilitated the emergence of multidrugresistant bacteria (MDRB), posing a grave challenge to clinical therapy and hospital infection control [62]. In this study, the overall multidrug resistance rate of C. jejuni reached 72.8 %. Compared to other sources, the MDR rate of human-sourced C. jejuni was the lowest (Table 3). This trend may be associated with the relatively cautious use of antibiotics in clinical settings [63]. Noreen Z et al. [64] found that over 90 % of C. jejuni strains isolated from children with diarrhea in Pakistan exhibited MDR, a proportion higher than this study. Moreover, cluster analysis indicates that these strains can persist in the food chain and spread from animals to humans. Similar scenarios of C. jejuni MDR have been reported in other countries and regions [65-67]. Further elucidation of the MDR pattern of C. jejuni from different regions and sources within China is needed to better coordinate surveillance programs and strategies for antibiotic use control in both the medical and agricultural fields.

The T86I point mutation in the C. *jejuni* DNA gyrase A (gyrA) gene can lead to the emergence of resistance to quinolone antibiotics, which is currently the most frequently detected mechanism [68]. In this study, the pooled prevalence of gyrA_T86I reached as high as 94.8 %, and similar results have been reported in other studies [69-72]. Additionally, these findings indicate a correlation between the phenotypic and genotypic resistance of C. jejuni to quinolones, which can partly explain the high resistance of C. jejuni isolated in China to quinolone antibiotics (Table 4). Similarly, a strong correlation was observed between the genotypic and phenotypic resistance to tetracyclines, with a high pooled prevalence of the tet(O) gene (79.0 %), which has also been reflected in other studies, such as in C. jejuni isolated from an abattoir in Argentina, where the tet(O) gene was detected in over 70 % of the isolates [73]. In contrast, the pooled prevalence of resistance determinants for macrolides, β-lactams, aminoglycosides, phenicols, and lincosamides were lower (such as 23S rRNA_A2075G, erm(B), blaoXA-184, aph(3')-IIIa, catA13, inu(C), etc.), and similar results have been reported in other studies [72,74–78]. Notably, the pooled prevalence of the functional multidrug efflux pump RE-cmeABC was as high as 71.3 %, which will further contribute to the increased resistance of C. jejuni to quinolones, macrolides, tetracyclines, β -lactams, and phenicols [79].

The pathogenicity of Campylobacter is closely associated with flagellar motility, adhesion, invasion, and the production of cytolethal distending toxin (CDT). These characteristics are regulated by specific genes, leading to infections and colonization in humans and animals [80]. Adhesion, a prerequisite for invasion, is regulated by several genes including cadF and racR [81]. In this study, both cadF and racR genes were detected at higher pooled prevalence (Table 5), consistent with findings from Sierra-Arguello et al. [82] and Jribi et al. [83], who discovered that C. jejuni isolated from poultry and its by-products all carried the *cadF* gene. Although the carriage rate of the *racR* gene varies depending on the source of the isolates, the higher carriage rate remains similar to the results of this study, a phenomenon also observed in other countries or regions [84-87]. Regarding invasion-related genes, this study found high pooled prevalence of *ciaB*, *iamA*, *pldA*, and *ceuE* genes, highlighting their potential importance in the pathogenesis and survival of C. jejuni. These genes are widely present in isolates from various sources [88,89]. The pooled prevalence of the virB11 gene in this study was only 1.5 %, similar to the results from Jribi et al. [83] and Datta et al. [84]. However, Wysok et al. [90] found a higher prevalence of virB11 in C. jejuni isolates from poultry and humans, which may be related to genetic variations among isolates from different geographical regions and the plasmid nature of *virB11* [91]. The motility mediated by the flagellar protein gene flaA plays a crucial role in the survival and pathogenicity of C. jejuni. In this study, the pooled prevalence of this

gene was 87.4 %. El-Hamid et al. [92], in their study of the genetic diversity of C. jejuni from poultry and human sources in Egypt, found that all isolates possessed the flaA gene. The significant overlap of genes among C. jejuni isolates from different sources suggests that poultry may play a role in Campylobacter transmission to humans. Similar findings have been reported globally [31,93-95]. In contrast, a computational characterization of C. jejuni virulence genes worldwide by Panzenhagen et al. [96] revealed an average prevalence of *flaA* below 35 %, with Asia having a prevalence of 35.9 %, significantly lower than the results of this study. This discrepancy might be related to the distribution of the gene in overlapping groups or the integrity/quality of the genomes. The CDT consists of three subunits (CdtA, CdtB, and CdtC), encoded by cdtA, cdtB, and cdtC genes, respectively [75]. In this study, the pooled prevalences of the toxin genes *cdtA*, *cdtB*, and *cdtC* were 83.2 %, 97.1 %, and 97.0 %, respectively. According to reports, the prevalence of *cdtA*, *cdtB*, and *cdtC* in C. jejuni isolated from food, animals, and humans in northern Italy was 100 % [97]. A high prevalence has also been reported in countries and regions like Bangladesh [98], Lithuania [99], Turkiye [95] and Egypt [100]. Current research suggests that the wlaN gene is closely related to GBS following Campylobacter infection [101]. The distribution of this gene varies among C. jejuni isolates from different sources and regions. In the study by Guirado et al. [102], the *wlaN* gene was detected at a rate of ≤ 20 % in *C. jejuni* isolated from human and animal sources. Ramires et al. [103] found that 25 % of isolates (2/8) from the broiler chicken production chain tested positive for the wlaN gene, similar to the 23.1 % rate in this study (Table 5), but the small sample size may limit comparability. More pronounced differences in wlaN distribution were observed in studies by Gharbi et al. [86] and Andrzejewska et al. [104], necessitating further research to clarify these distribution discrepancies. The chemotaxis system of Campylobacter exhibits unique precision and sensitivity in responding to external stimuli, critical for its colonization and pathogenicity. In this process, cheW and cheY genes involved in chemotaxis have been proven to play key roles [105]. In this study, the pooled prevalence of cheW and cheY genes in C. jejuni in China were 100.0 % and 99.6 %, respectively, obviously higher than other virulence genes included in this study. Woyda et al. [106] found that cheW and cheY genes were present in all C. jejuni isolates from broiler chicken feces, which may allow them to adhere to surfaces and persist through cleaning and flagellin glycosylation that increases their ability to adhere and invade human epithelial cells.

5. Conclusion

Analysis of literature published between 2000 and 2023 confirmed that the pooled prevalences of C. jejuni varies by source. The overall prevalence of C. jejuni showed an increasing trend over time. Coastal areas of China had a higher pooled prevalence of C. jejuni than other regions, despite the significant heterogeneity. This study also revealed the prevalence of resistant C. jejuni. Regardless of the source of isolation, C. *jejuni* overall showed high resistance to β -lactams, quinolones, and tetracyclines. Compared to other sources of isolation, the issue of AMR in C. jejuni originating from animals is particularly severe. From a temporal perspective, although there has been a decline in resistance to certain antibiotics, an increase in resistance to more antibiotics is prevalent. Furthermore, the problem of MDR in C. jejuni is particularly severe, which could potentially have a significant impact on the effectiveness of antibiotic use in clinical and agricultural settings domestically. The results on antibiotic resistance determinants and virulence genes reveal that domestic C. jejuni exhibits a high prevalence of major resistance and virulence genes, with a significant correlation between resistance and the carriage rate of these genes. Although China has currently implemented effective measures to address the prevalence and resistance issues of C. jejuni, many long-term strategies focus more on monitoring, especially in the environmental and agricultural sectors. In the future, a systematic surveillance framework for the epidemiology and drug resistance of C. jejuni under the multi-angle perspective of

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"environment-animal-food-human" should be established based on the "One Health" theory. Corresponding control strategies should be formulated to ensure public health and hygiene safety.

Declaration of generative AI in scientific writing

During the preparation of this work, the authors used Moonshot AI and iFLYTEK Spark to enhance the readability and clarity of this manuscript. The AI assistance was limited to language polishing and did not contribute to the research design, data analysis, interpretation, or authorship of the content. After using this tool, the authors reviewed and edited the content as needed and took full responsibility for the content of the publication.

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CRediT authorship contribution statement

Zhao Li: Writing – review & editing, Writing – original draft, Validation, Investigation, Formal analysis, Conceptualization. **Hua Cai:** Visualization, Data curation. **Biyao Xu:** Visualization, Data curation. **Qingli Dong:** Writing – review & editing, Supervision, Funding acquisition. **Kai Jia:** Methodology, Investigation, Formal analysis. **Zijie Lin:** Writing – review & editing, Formal analysis. **Xiang Wang:** Methodology, Investigation, Formal analysis. **Yangtai Liu:** Methodology, Investigation, Formal analysis. **Xiaojie Qin:** Writing – review & editing, Validation, Supervision, Resources, Funding acquisition, Formal analysis, Conceptualization.

Declaration of competing interest

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

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.onehlt.2025.100990.

Data availability

Data will be made available on request.

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