Review Article

Prevalence of Fluoroquinolone-Resistant Campylobacter Species in Iran: A Systematic Review and Meta-Analysis

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Received 17 July 2020; Accepted 14 October 2020; Published 30 October 2020

1. Introduction

The genus Campylobacter includes small, motile, and curved Gram-negative bacteria [1–3]. These rod-shaped bacteria are thermophilic, 30°C to 46°C, and microaerophilic, 5% O₂, and belong to the family Campylobacteraceae [4]. Campylobacter is a zoonotic pathogen that is colonized in the intestinal tract of domestic and wild animals and birds and can infect human through consumption of contaminated water, different foods such as raw or uncooked meat, unpasteurized milk, and contact with infected animals or (rarely) human [4, 5]. Poultry, cattle, sheep, pigs, birds, dogs, and cats are common reservoir hosts for human infections [2]. This foodborne bacterial pathogen is the major cause of bacterial gastroenteritis and septicemia in humans in both developing and developed countries [1, 2]. In developed countries, Campylobacter bacteria are the most important causative agents for gastrointestinal infection [6]. It is estimated that between 400 and 500 million individuals become infected with Campylobacter species in the world annually [4, 5]. The most common species associated with bacterial gastroenteritis in human are Campylobacter jejuni and Campylobacter coli as well as Campylobacter fetus associated with systemic infections [2, 4]. Additionally, in some cases, these enteric pathogens are associated with two immune-related late complications, i.e., Guillain-Barré syndrome and reactive arthritis [1, 2]. The severity of Campylobacter infections...
2. Methods

2.1. Literature Search and Selection Criteria. We started at 1 August 2018 for a comprehensive literature search in international search engines including PubMed (https://www.ncbi.nlm.nih.gov), Scopus (https://www.scopus.com), ISI Web of Knowledge (https://www.isiw glofknowledge.com), Google Scholar (http://scholar.google.com), and Scientific Information Database (SID) (http://www.sid.ir), a national database, on each report about the prevalence of the antimicrobial susceptibility patterns of Campylobacter species in Iran. There was no date and language limitation for searching, and related keywords used were antibiotic resistance, Campylobacter species (C. jejuni, C. coli, and C. lari), and Iran. A number of missed studies were obtained by reviewing the list of references and searching for journals. The meta-analysis was performed step by step based on the PRISMA recommendations [10].

Inclusion or exclusion criteria for assessing eligibility in the study were all types of Persian- and English-language articles which had enough data on the prevalence of the resistance patterns of campylobacters, in species level, to different antibiotics in Iran. Review articles, case reports, abstracts of articles, and duplicates were excluded. Articles evaluating the resistance patterns of campylobacters only at the genus level or the resistance genes and those studies with unclear results were excluded.

2.2. Data Extraction of Articles. After completely reviewing all included studies by two authors, needed information was extracted and placed in Tables 1–3 based on organism species type. The quality of data was evaluated based on the Newcastle-Ottawa scale adapted for cross-sectional studies (data has not been shown). The checklist of items was based on three criteria including selection (representativeness of the sample, sample size, nonrespondents, and ascertainment of the exposure) (maximum 5 stars), comparability (comparability of outcome groups) (maximum 2 stars), and outcome (assessment of the outcome and statistical test) (maximum 3 stars).

Data obtained from eligible studies include publishing year, location of the study, number of strains, origin of samples, methods used for antimicrobial susceptibility testing, and antibiotic resistance profiles of C. jejuni, C. coli, and C. lari.

2.3. Meta-Analysis. The data for the quantitative data synthesis were transferred to the Comprehensive Meta-Analysis (CMA) software (Biostat, Englewood, NJ). Resistance rates of C. jejuni, C. coli, and C. lari were calculated for each antibiotic as a percentage and expressed as 95% confidence intervals (95% CIs). I² statistic was used to evaluate the existed heterogeneity, and considering the percent of inconsistency among studies, pooling of data was performed using fixed-or random-effects models. The assessment of publication bias was done using funnel plots.

3. Results

3.1. Characteristics of Included Studies. As shown in Figure 1, a total of 1299 articles were obtained from five databases (PubMed, Scopus, ISI Web of Knowledge, Google Scholar, and SID). According to the presented inclusion or exclusion criteria in Figure 1, 1249 articles were removed and the eligibility of 50 remained articles was evaluated. Among them, 16 studies did not meet inclusion criteria because of reporting the resistance patterns of campylobacters only in the genus level or had inadequate information, while 34 articles (9 in Persian and 25 in English) had complete data and were included in our meta-analysis.

The characteristics of the 34 included studies are summarized in Tables 1–3. The main data was extracted from 3 studies from Ahvaz [11–13], 2 studies from Hamadan [14, 15], 4 studies from Isfahan [16–19], 1 study from Kerman [20], 1 study from Kurdistan [21], 2 studies from Mashhad [22, 23], 1 study from Mazandaran and Golestane [24], 1 study from Rafsanjan [25], 5 studies from Shahrkord [13, 18, 26–28], 2 studies from Semnan [29, 30], 4 studies from Shiraz [31–34], 8 studies from Tehran [35–42], 2 studies from Tonekabon [34, 43], 1 study from Yazd [19], and 1 study from Zahedan [44]. Disk diffusion, E-test, and agar dilution were the most common methods used to evaluate antibiotic-resistant Campylobacter species in Iran (Tables 1–3). Additionally, the most common Campylobacter species for which their antibiotic resistance has been evaluated were C. jejuni, C. coli, and C. lari. The origins of Campylobacter species were human and animal fecal samples as well as food samples with animal origin including milk, dairy products, and animal meats like poultry, cattle.
| Year        | City                      | Strains (n) | Origin | AST                | Antibiotic resistance (n) |
|-------------|---------------------------|-------------|--------|--------------------|----------------------------|
| 2007-2008   | Ahvaz                     | 177         | Animal | Disk diffusion     | AMP 14 AMX ND CST ND NFX ND SPT ND NEO ND STR 1 141 ND ND 3 119 ND ND 105 ND ND |
| 2007-2008   | Ahvaz                     | 9           | Human  | Disk diffusion     | 9 ND ND ND ND ND ND ND ND 6 ND 6 5 4 ND 0 ND 9 7 6 ND |
| 2009-2010   | Ahvaz-Shahrekord          | 24          | Animal | Disk diffusion     | 4 1 ND 6 ND ND 2 2 18 ND ND 0 7 ND 1 ND ND 9 ND ND |
| 2016        | Hamadan                   | 53          | Animal | Disk diffusion     | 23 22 43 ND ND ND ND 11 3 10 44 ND 3 15 ND 0 ND 40 0 ND ND |
| 2013-2014   | Hamadan                   | 6           | Human  | Disk diffusion     | ND ND ND ND ND ND ND ND 1 5 ND ND 4 6 ND 3 3 ND 2 ND ND |
| 2014-2015   | Isfahan                   | 22          | Animal | Disk diffusion     | 1 4 ND 5 ND ND 2 1 18 ND ND 1 16 ND 0 ND ND 12 ND ND |
| 2007-2008   | Isfahan                   | 13          | Animal | Disk diffusion     | 1 3 ND 3 ND ND 1 0 5 ND ND 0 9 ND 0 ND ND 7 ND ND |
| 2011-2012   | Isfahan-Shahrekord        | 10          | Animal | Disk diffusion     | 1 0 ND 0 ND ND 1 0 4 ND ND 0 3 ND 0 ND ND 5 ND ND |
| 2008-2009   | Isfahan-Yazd              | 42          | Animal | Disk diffusion     | 5 1 ND 10 ND ND 3 0 28 ND ND 0 21 ND 0 ND ND 18 ND ND |
| 2007-2009   | Kerman                    | 190         | Animal | Disk diffusion agar | 103 ND ND ND ND ND ND ND ND 103 173 ND ND ND ND ND ND ND ND ND ND ND |
| 2015-2016   | Kurdistan                 | 50          | Animal | Disk diffusion agar | 5 10 ND ND ND ND ND ND ND 34 ND ND 1 31 ND 0 0 ND ND ND ND ND |
| 2013        | Mashhad                   | 200         | Animal | Disk diffusion     | 13 26 ND 60 ND 42 ND 9 181 ND ND 76 168 ND 7 ND ND 132 ND ND |
| 2012        | Mashhad                   | 122         | Animal | Disk diffusion     | 20 4 25 11 1 8 6 6 88 ND ND 1 107 ND 0 ND ND 91 ND ND |
| 2014-2015   | Mazandaran-Golestan       | 79          | Animal | Disk diffusion     | 26 40 ND 28 ND ND 15 ND 59 ND ND 5 63 ND 1 ND ND 59 ND ND |
| 2010        | Rafsanjan                 | 19          | Animal | Disk diffusion     | ND ND ND ND ND ND ND ND ND ND ND ND ND ND ND ND ND ND ND ND ND ND ND ND |
| 2014        | Shahrekord                | 2           | Animal | Disk diffusion     | 1 1 ND 1 ND ND 1 0 0 ND ND 0 1 ND 0 ND ND 1 ND ND |
| 2009-2010   | Shahrekord                | 172         | Animal | Disk diffusion     | 29 3 ND 20 ND ND 3 4 125 ND ND 2 89 ND 0 ND ND 96 ND ND |
| ND          | Shahrekord                | 35          | Animal | Disk diffusion     | 2 6 ND 14 ND ND 3 1 28 ND ND 1 23 ND 0 ND ND 18 ND ND |
| 2007        | Semnan                    | 27          | Human  | Disk diffusion     | ND ND ND ND ND ND ND ND ND ND ND ND ND ND ND ND ND ND ND ND ND ND ND |

Table 1: The antibiotic resistance profiles of C. jejuni.
| Year     | City                  | Strains (n) | Origin        | AST               | AMP | AMX | CST | NFX | SPT | NEO | STR | CHL | TET | TMP-SMX | CTX | ERY | CIP | IPM | GEN | MEM | CEF | NAS | CAZ | LEX |
|----------|-----------------------|-------------|---------------|-------------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| 2007     | Semnan                | 38          | Human         | Disk diffusion    | ND  | ND  | ND  | ND  | ND  | ND  | ND  | 11  | 20  | 2    | 5    | ND  | 1    | ND  | ND  | ND  | ND  | ND  |
| 2014-2015| Shiraz                | 7           | Human         | Disk diffusion    | 5   | ND  | ND  | ND  | ND  | ND  | ND  | 7    | ND  | ND  | ND  | 7    | ND  | 0    | ND  | 7   | ND  | ND  |
| 2011-2013| Shiraz                | 48          | Animal        | Disk diffusion    | 22  | ND  | 0   | 8   | ND  | 0   | ND  | 4    | 13  | ND  | 13   | 3    | 30   | ND  | 4    | ND  | 44  | 7   | ND  |
| ND       | Shiraz                | 15          | Animal        | Disk diffusion    | 2   | ND  | ND  | ND  | ND  | ND  | ND  | 4    | 1   | 2   | 4    | 1    | 0    | ND  | 2    | ND  | ND  | ND  | 8   |
| ND       | Shiraz                | 15          | Animal        | Disk diffusion    | 2   | ND  | ND  | ND  | ND  | ND  | ND  | 4    | 1   | 1   | 0    | ND  | 2    | ND  | ND  | ND  | ND  |
| 2011-2012| Tehran                | 93          | Animal        | Disk diffusion    | 12  | 26  | 32  | ND  | 4   | 3   | 5    | 33  | ND  | ND  | 4    | 48   | ND  | 3    | ND  | ND  | 66  | ND  |
| 2011     | Tehran                | 9           | Human         | Disk diffusion    | ND  | ND  | ND  | ND  | ND  | ND  | ND  | 3    | 5   | 2   | 1    | ND  | 0    | ND  | ND  | ND  | ND  |
| 2010     | Tehran                | 19          | Animal        | Disk diffusion    | 19  | ND  | ND  | ND  | ND  | ND  | ND  | 11   | ND  | 5   | ND  | ND  | 16   | ND  | ND  | ND  | 18  | ND  |
| 2008–2010| Tehran                | 138         | Animal        | Disk diffusion    | 15  | 44  | 32  | ND  | 3   | 3   | 6    | 109 | ND  | ND  | 5    | 118  | ND  | 0    | ND  | 103 | ND  |
| 2008-2009| Tehran                | 34          | Human         | Disk diffusion    | 6   | ND  | 5   | ND  | ND  | 4   | 3    | 12  | ND  | 19   | 4    | 29   | 0    | 2    | ND  | 27  | 21  |
| 2006-2007| Tehran                | 70          | Animal        | Disk diffusion    | 5   | 18  | 22  | ND  | 1   | 2   | 2    | 1    | 22  | ND  | ND  | 1    | 34   | ND  | 0    | ND  | ND  | 47  | ND  |
| 2004-2005| Tehran                | 29          | Human         | Disk diffusion    | 3   | ND  | 0   | ND  | ND  | 1   | 0    | 1    | 7   | ND  | 3    | 1    | 17   | 0    | 0    | ND  | 28  | 22  | 12  |
| ND       | Tonekabon             | 12          | Animal        | Disk diffusion    | 12  | ND  | ND  | ND  | ND  | ND  | 2    | 2    | ND  | 9    | 3    | 0    | ND  | 4    | ND  | ND  | ND  | 10  |
| ND       | Tonekabon             | 16          | Animal        | Disk diffusion    | 16  | 16  | ND  | ND  | ND  | ND  | 1    | 1    | 1    | ND  | 2    | 0    | ND  | 1    | ND  | ND  | ND  | 14  |
| 2011–2013| Zahedan               | 19          | Human         | Disk diffusion    | ND  | ND  | ND  | ND  | ND  | ND  | ND  | 0    | ND  | ND  | ND  | ND  | ND  | ND  | ND  | ND  |

**Table 1: Continued.**

Abbreviations: AMP: ampicillin; AMX: amoxicillin; CST: colistin; NFX: enrofloxacin; SPT: spectinomycin; NEO: neomycin; STR: streptomycin; CHL: chloramphenicol; TET: tetracycline; TMP-SMX: trimethoprim/sulfamethoxazole; CTX: cefotaxime; ERY: erythromycin; CIP: ciprofloxacin; IPM: imipenem; GEN: gentamicin; MEM: meropenem; CEF: cephalothin; NAS: nalidixic acid; CAZ: ceftazidime; LEX: cephalexin; AST: antimicrobial susceptibility testing; ND: not determined.
| Year       | City                | Strains (n) | Origin | AST                | AMP | AMX | CST | NFX | SPT | NEO | STR | CHL | TET | TMP-SMX | CTX | ERY | CIP | IPM | GEN | MEM | CEF | NAL | CAZ | LEX |
|------------|---------------------|-------------|--------|--------------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| 2007-2008  | Ahvaz               | 21          | Animal | Disk diffusion     | 4   | 0   | ND  | 3   | ND  | ND  | 1   | 0   | 14  | ND  | ND  | 0   | 4   | ND  | ND  | 11  | ND  | ND  | ND  | ND  | ND  |
| 2007-2008  | Ahvaz               | 5           | Human  | Disk diffusion     | 5   | ND  | ND  | ND  | ND  | ND  | ND  | ND  | 3   | 3   | 4   | 1   | ND  | ND  | 1   | ND  | 5   | 2   | 4   | ND  |
| 2009-2010  | Ahvaz-Shahrekord    | 7           | Animal | Disk diffusion     | 0   | 1   | ND  | 0   | ND  | ND  | 1   | 0   | 3   | ND  | ND  | 1   | 3   | ND  | ND  | ND  | 1   | ND  | ND  | ND  | ND  |
| 2016       | Hamadan             | 19          | Animal | Disk diffusion     | 10  | 8   | 12  | ND  | ND  | ND  | 4   | 1   | 5   | 13  | ND  | 2   | 7   | ND  | 0   | ND  | 12  | 1   | ND  | ND  | ND  |
| 2013-2014  | Hamadan             | 3           | Human  | Disk diffusion     | ND  | ND  | ND  | ND  | ND  | ND  | 0   | 2   | ND  | 3   | 2   | ND  | 1   | 2   | ND  | 1   | ND  | ND  | ND  |
| 2014-2015  | Isfahan             | 6           | Animal | Disk diffusion     | 0   | 0   | ND  | 0   | ND  | ND  | 0   | 0   | 3   | ND  | ND  | 0   | 0   | ND  | 0   | ND  | 2   | ND  | ND  | ND  |
| 2006-2008  | Isfahan             | 4           | Animal | Disk diffusion     | 0   | 1   | ND  | 2   | ND  | ND  | 0   | 0   | 2   | ND  | ND  | 0   | 1   | ND  | 0   | ND  | 1   | ND  | ND  | ND  |
| 2011-2012  | Isfahan-Shahrekord  | 3           | Animal | Disk diffusion     | 0   | 0   | ND  | 1   | ND  | ND  | 0   | 0   | 1   | ND  | ND  | 1   | 1   | ND  | 0   | ND  | 1   | ND  | ND  | ND  |
| 2008-2009  | Isfahan-Yazd       | 8           | Animal | Disk diffusion     | 0   | 0   | ND  | 1   | ND  | ND  | 0   | 0   | 6   | ND  | ND  | 0   | 2   | ND  | 0   | ND  | 2   | ND  | ND  | ND  |
| 2015-2016  | Kurdistan           | 8           | Animal | Disk diffusion      | 5   | 6   | ND  | ND  | ND  | ND  | ND  | ND  | 7   | ND  | ND  | 0   | 6   | ND  | 0   | ND  | ND  | ND  | ND  |
| 2013       | Mashhad             | 27          | Animal | Disk diffusion      | 3   | 6   | ND  | 4   | ND  | 5   | ND  | 3   | 17  | ND  | 9   | 12  | ND  | 1   | ND  | ND  | 13  | ND  | ND  |
| 2012       | Mashhad             | 27          | Animal | Disk diffusion      | 2   | 1   | 9   | 7   | 1   | 0   | 2   | 1   | 13  | ND  | 0   | 15  | ND  | 0   | ND  | 18  | ND  | ND  |
| 2014-2015  | Mazandaran-Golestan | 41          | Animal | Disk diffusion      | 17  | 15  | ND  | 16  | ND  | ND  | 15  | ND  | 36  | ND  | 2   | 36  | ND  | 2   | ND  | 32  | ND  | ND  |
| 2010       | Rafsanjan           | 12          | Animal | Disk diffusion      | ND  | ND  | ND  | ND  | ND  | ND  | ND  | ND  | 12  | ND  | 0   | 0   | ND  | 12  | ND  | 0   | ND  | ND  | ND  |
| 2014       | Shahrekord          | 13          | Animal | Disk diffusion      | 0   | 3   | ND  | 4   | ND  | ND  | 0   | 0   | 7   | ND  | ND  | 0   | 5   | ND  | 0   | ND  | 4   | ND  | ND  |
| 2009-2010  | Shahrekord          | 15          | Animal | Disk diffusion      | 2   | 0   | ND  | 2   | ND  | ND  | 1   | 0   | 7   | ND  | ND  | 0   | 4   | ND  | 0   | ND  | 5   | ND  | ND  |
| 2011-2013  | Shiraz              | 17          | Animal | Disk diffusion      | 5   | ND  | 0   | 3   | ND  | 0   | ND  | 1   | 2   | ND  | 4   | 5   | 14  | ND  | 1   | ND  | 10  | 8   | ND  | ND  |

Table 2: Antibiotic resistance profiles of *C. coli*. 
| Year      | City       | Strains (n) | Origin | AST        | Antibiotic resistance (n) |
|-----------|------------|-------------|--------|------------|---------------------------|
|           |            |             |        |            | AMP | AMX | CST | NFX | SPT | NEO | STR | CHL | TET | TMP-SMX | CTX | ERY | CIP | IPM | GEN | MEM | CEF | NAL | CAZ | LEX |
| ND        | Shiraz     | 10          | Animal | Disk diffusion E-test | 1 | ND | ND | ND | ND | ND | 2 | 1 | 1 | 6 | 1 | 0 | ND | 1 | ND | ND | ND | ND | 4 |
| ND        | Shiraz     | 10          | Animal | Disk diffusion E-test | 1 | ND | ND | ND | ND | ND | 2 | 1 | 1 | 6 | 1 | 0 | ND | 1 | ND | ND | ND | ND | 4 |
| 2011-2012 | Tehran     | 28          | Animal | Disk diffusion        | 1 | 5 | 4 | ND | 2 | 2 | 1 | 1 | 6 | ND | ND | 1 | 13 | ND | 1 | ND | ND | 24 | ND | ND |
| 2012      | Tehran     | 39          | Animal | Disk diffusion        | 32 | 30 | ND | ND | ND | ND | 35 | 27 | 38 | 31 | ND | 33 | 34 | ND | 0 | ND | ND | 36 | ND | ND |
| 2010      | Tehran     | 33          | Animal | Disk diffusion        | 25 | ND | ND | ND | ND | 0 | ND | ND | 31 | ND | ND | 10 | ND | ND | 0 | ND | ND | 0 | ND | ND |
| 2008–2010 | Tehran     | 23          | Animal | Disk diffusion        | 1 | 3 | 8 | ND | ND | ND | 1 | 1 | 0 | 15 | ND | ND | 1 | 15 | ND | 0 | ND | ND | 18 | ND | ND |
| 2008–2009 | Tehran     | 12          | Human  | Disk diffusion        | 2 | ND | ND | ND | ND | 1 | 1 | 1 | 3 | ND | 6 | 1 | 6 | 0 | 0 | ND | ND | 6 | 5 | ND |
| 2006-2007 | Tehran     | 22          | Animal | Disk diffusion        | 0 | 3 | 2 | ND | 1 | 1 | 0 | 0 | 4 | ND | ND | 0 | 9 | ND | 0 | ND | ND | 18 | ND | ND |
| 2004–2005 | Tehran     | 5           | Human  | Disk diffusion        | 1 | ND | 0 | ND | ND | ND | 0 | 0 | 0 | 0 | ND | 2 | 0 | 4 | 0 | 0 | ND | 5 | 5 | 4 | 5 |
| ND        | Tonekabon  | 8           | Animal | Disk diffusion E-test | 8 | ND | ND | ND | ND | ND | 2 | 1 | ND | 7 | 2 | 0 | ND | 1 | ND | ND | ND | ND | 8 |
| ND        | Tonekabon  | 9           | Animal | Disk diffusion E-test | 9 | ND | ND | ND | ND | ND | 1 | 2 | 1 | ND | 1 | 0 | ND | 0 | ND | ND | ND | ND | 9 |

Abbreviations: AMP: ampicillin; AMX: amoxicillin; CST: colistin; NFX: enrofloxacin; SPT: spectinomycin; NEO: neomycin; STR: streptomycin; CHL: chloramphenicol; TET: tetracycline; TMP-SMX: trimethoprim/sulfamethoxazole; CTX: cefotaxime; ERY: erythromycin; CIP: ciprofloxacin; IPM: imipenem; GEN: gentamicin; MEM: meropenem; CEF: cephalothin; NAL: nalidixic acid; CAZ: ceftazidime; LEX: cephalaxin; AST: antimicrobial susceptibility testing; ND: not determined.
Table 3: Antibiotic resistance profiles of *C. lari*.

| Year | City     | Strains (n) | Origin  | AST               | Antibiotic resistance (n) |
|------|----------|-------------|---------|-------------------|----------------------------|
| ND   | Shiraz   | 12          | Animal  | Disk diffusion E-test | AMP 3 AMX ND CST ND NFX ND NEO ND STR 2 CHL 1 TET 2 TMP-SMX CTX ND ERY ND CIP ND IPM ND GEN ND MEM ND CEF ND NAL ND CAZ ND LEX 5 |
| ND   | Shiraz   | 12          | ND      | Disk diffusion E-test | AMP 3 AMX ND CST ND NFX ND NEO ND STR 2 CHL 1 TET 2 TMP-SMX CTX ND ERY ND CIP ND IPM ND GEN ND MEM ND CEF ND NAL ND CAZ ND LEX 5 |
| ND   | Tonekabon| 8           | ND      | Disk diffusion E-test | AMP 8 AMX ND CST ND NFX ND NEO ND STR 2 CHL 1 TET ND TMP-SMX CTX ND ERY ND CIP ND IPM ND GEN ND MEM ND CEF ND NAL ND CAZ ND LEX 7 |
| ND   | Tonekabon| 7           | Animal  | Disk diffusion     | AMP 7 AMX ND CST ND NFX ND NEO ND STR 1 CHL 2 TET ND TMP-SMX CTX ND ERY ND CIP ND IPM ND GEN ND MEM ND CEF ND NAL ND CAZ ND LEX 7 |
sheep, camels, beef, water buffalo, ducks, and geese. A random-effects model was used for pooling data on the prevalence of antibiotic resistance of *Campylobacter* species due to the presence of high heterogeneity ($I^2 > 25\%$). There was some evidence of publication bias (Figures 2 and 3).

3.2. Characteristics of *C. jejuni* Antibiotic Resistance. In our presented meta-analysis, a total of 34 studies determined the prevalence of *C. jejuni* antibiotic resistance (Table 1). Antimicrobial resistance patterns of *C. jejuni* in Iran were as follows: 22.8% (95% CI: 15.9–31.6) to ampicillin, 17.7% (95% CI: 11.4–26.5) to amoxicillin, 25.8% (95% CI: 14.5–41.7) to colistin, 24.3% (95% CI: 16.8–33.7) to enrofloxacin, 23.3% (95% CI: 0.8–6.4) to spectinomycin, 8.6% (95% CI: 3.9–17.7) to neomycin, 7.1% (95% CI: 4.7–10.7) to streptomycin, 6% (95% CI: 4.1–8.6) to chloramphenicol, 50.7% (95% CI: 41.1–60.4) to tetracycline, 66.9% (95% CI: 40.5–85.8) to trimethoprim/sulfamethoxazole, 41.2% (95% CI: 25.1–59.5) to cefotaxime, 6.4% (95% CI: 3.6–11.1) to erythromycin, 53.6% (95% CI: 43.9–62.9) to ciprofloxacin (Figure 4), 0% to imipenem, 4.5% (95% CI: 2.5–7.7) to gentamicin, 9.5% (95% CI: 0.6–65.5) to meropenem, 89.4% (95% CI: 73.8–96.2) to cephalexin, 59.6% (95% CI: 52.1–66.7) to nalidixic acid, 54.6% (95% CI: 38.9–69.4) to cefazidime and 76.5% (95% CI: 54.5–89.8) to cephalothin. Additionally, other antibiotic resistance patterns were as follows: clindamycin 2 (66.6%), tylosin 2 (11.7%), oxacillin 5 (100%), amikacin 3 (7.3%), ceftriaxone 9 (100%), amoxiclavc 9 (100%), penicillin 9 (100%), vancomycin 9 (100%), tobramycin 0 (0%), ofloxacin 11 (64.7%), and carbencillicin 7 (41.1%).

3.3. Characteristics of *C. coli* Antibiotic Resistance. The characteristics of the 29 studies that determined the prevalence of *C. coli* antibiotic resistance are summarized in Table 2. The prevalence of resistance of *C. coli* to different antibiotics was as follows: 24.5% (95% CI: 14.5–38.4) to ampicillin, 23.5% (95% CI: 13.7–37.2) to amoxicillin, 23.1% (95% CI: 12.1–39.5) to colistin, 25.1% (95% CI: 19.2–32.1) to enrofloxacin, 5.4% (95% CI: 2–13.5) to spectinomycin, 8.3% (95% CI: 4.7–14.1) to neomycin, 11.6% (95% CI: 5.4–23.3) to streptomycin, 9.6% (95% CI: 4.9–17.8) to chloramphenicol, 47.7% (95% CI: 35.6–60.1) to tetracycline, 67.2% (95% CI: 33.6–89.3) to trimethoprim/sulfamethoxazole, 51.5% (95% CI: 35.8–66.9) to cefotaxime, 13% (95% CI: 6.9–23) to erythromycin, 41.8% (95% CI: 31.4–53.1) to ciprofloxacin (Figure 5), 0% to imipenem, 6.8% (95% CI: 4.3–10.5) to gentamicin, 27.2% (95% CI: 1.2–92.2) to meropenem, 65.5% (95% CI: 50.1–78.2) to cephalothin, 49.2% (95% CI: 36.6–61.9) to nalidixic acid, 62.2% (95% CI: 31.8–85.2) to ceftazidime, and 73% (95% CI: 38.6–92.1) to cephalexin. Additionally, other antibiotic resistance patterns were as follows: clindamycin 2 (66.6%), tylosin 2 (11.7%), oxacillin 5 (100%), amikacin 3 (7.3%), ceftriaxone 9 (100%), amoxiclavc 9 (100%), penicillin 9 (100%), vancomycin 9 (100%), tobramycin 0 (0%), ofloxacin 11 (64.7%), and carbencillicin 7 (41.1%).

3.4. Characteristics of *C. lari* Antibiotic Resistance. A total of 4 studies investigating the prevalence of *C. lari* antibiotic resistance were included in the meta-analysis (Table 3). Antimicrobial resistance patterns of *C. lari* in Iran were as follows: 60% (95% CI: 19–90.5) to ampicillin, 93.7% (95% CI: 46.1–99.6) to amoxicillin, 14.3% (95% CI: 2–58.1) to streptomycin, 20.9% (95% CI: 10.8–36.7) to chloramphenicol, 10.5% (95% CI: 4–24.9) to tetracycline, 16.7% (95% CI: 4.2–47.7) to trimethoprim/sulfamethoxazole, 70.4% (95% CI: 51.3–84.3) to cefotaxime, 7.4% (95% CI: 2.4–20.6) to erythromycin, 0% to ciprofloxacin, 12.7% (95% CI: 5.1–28.5) to gentamicin, and 63.2% (95% CI: 32.7–85.9) to cephalexin.

**Figure 1:** A summary of the study selection processes.
Additionally, other antibiotic resistance patterns were as follows: ceftriaxone 7 (100%), amikacin 0 (0%), amoxiclav 7 (100%), penicillin 7 (100%), vancomycin 7 (100%) and tobramycin 2 (29%).

Abbreviations: AMP: ampicillin; AMX: amoxicillin; CST: colistin; NFX: enrofloxacin; SPT: spectinomycin; NEO: neomycin; STR: streptomycin; CHL: chloramphenicol; TET: tetracycline; TMP/SMX: trimethoprim/sulfamethoxazole; CTX: cefotaxime; ERY: erythromycin; CIP: ciprofloxacin; IPM: imipenem; GEN: gentamicin; MEM: meropenem; CEF: cephalothin; NAL: nalidixic acid; CAZ: ceftazidime; LEX: cephalaxin; AST: antimicrobial susceptibility testing; ND: not determined.

4. Discussion

Food-borne illnesses caused by *Campylobacter* species as well as other bacteria related to food poisoning can be
Figure 3: Funnel plot of the meta-analysis of the prevalence of *C. coli* resistant to ciprofloxacin in Iran.

| Study name       | Event rate | Lower limit | Upper limit | Z-value | p-value | Total |
|------------------|------------|-------------|-------------|---------|---------|-------|
| Ahvaz-1          | 0.190      | 0.073       | 0.412       | -2.604  | 0.009   | 4 / 21 |
| Ahvaz-2          | 0.200      | 0.027       | 0.691       | -1.240  | 0.215   | 1 / 5  |
| Ahvaz-Shahrekord | 0.429      | 0.144       | 0.770       | -0.377  | 0.706   | 3 / 7  |
| Hamadan-1        | 0.368      | 0.187       | 0.597       | -1.133  | 0.257   | 7 / 19 |
| Hamadan-2        | 0.667      | 0.154       | 0.957       | 0.566   | 0.571   | 2 / 3  |
| Isfahan-1        | 0.071      | 0.004       | 0.577       | -1.748  | 0.081   | 0 / 6  |
| Isfahan-2        | 0.250      | 0.034       | 0.762       | -0.951  | 0.341   | 1 / 4  |
| Isfahan-Shahrekord | 0.333   | 0.043       | 0.846       | -0.566  | 0.571   | 1 / 3  |
| Kurdistan        | 0.750      | 0.377       | 0.937       | 1.346   | 0.178   | 6 / 8  |
| Mashhad-1        | 0.444      | 0.272       | 0.631       | -0.576  | 0.565   | 12 / 27|
| Mashhad-2        | 0.556      | 0.369       | 0.728       | 0.576   | 0.565   | 15 / 27|
| Mazandaran-Golestan | 0.878   | 0.739       | 0.948       | 4.136   | 0.000   | 36 / 41|
| Rafsanjan        | 0.038      | 0.002       | 0.403       | -2.232  | 0.026   | 0 / 12 |
| Shahrekord-1     | 0.385      | 0.170       | 0.656       | -0.824  | 0.410   | 5 / 13 |
| Shahrekord-2     | 0.267      | 0.104       | 0.533       | -1.733  | 0.083   | 4 / 15 |
| Shahrekord-3     | 0.100      | 0.006       | 0.674       | -1.474  | 0.140   | 0 / 4  |
| Shiraz-1         | 0.824      | 0.573       | 0.942       | 2.421   | 0.015   | 14 / 17|
| Shiraz-2         | 0.045      | 0.003       | 0.448       | -2.103  | 0.035   | 0 / 10 |
| Shiraz-3         | 0.045      | 0.003       | 0.448       | -2.103  | 0.035   | 0 / 10 |
| Tehran-1         | 0.464      | 0.292       | 0.646       | -0.378  | 0.706   | 13 / 28|
| Tehran-2         | 0.872      | 0.727       | 0.946       | 4.002   | 0.000   | 34 / 39|
| Tehran-3         | 0.303      | 0.171       | 0.477       | -2.199  | 0.028   | 10 / 33|
| Tehran-4         | 0.652      | 0.443       | 0.816       | 1.436   | 0.151   | 15 / 23|
| Tehran-5         | 0.500      | 0.244       | 0.756       | 0.000   | 1.000   | 6 / 12 |
| Tehran-6         | 0.409      | 0.228       | 0.618       | -0.848  | 0.396   | 9 / 22 |
| Tehran-7         | 0.800      | 0.309       | 0.973       | 1.240   | 0.215   | 4 / 5  |
| Tonekabon-1      | 0.056      | 0.003       | 0.505       | -1.947  | 0.052   | 0 / 8  |
| Tonekabon-2      | 0.050      | 0.003       | 0.475       | -2.029  | 0.042   | 0 / 9  |
| Tonekabon-3      | 0.418      | 0.314       | 0.531       | -1.431  | 0.152   |       |

Figure 4: Forest plot of the meta-analysis of the prevalence of *C. jejuni* resistant to ciprofloxacin in Iran.
prevented by avoiding food contamination and growth of bacteria through proper food preparation and proper cooking as well as avoidance of contamination of water sources and consuming pasteurized dairy products [2, 45]. However, the main problem is food contamination with drug-resistant pathogens, which is a major threat to public health [46]. Antibiotic resistance genes can be transferred among food-borne pathogens, and this makes the treatment of severe infections difficult [46]. Today, fluoroquinolone-resistant *Campylobacter* species have turned into a global concern [9]. Fluoroquinolones are selective drugs in the treatment of campylobacteriosis; however, an increasing trend of resistance in *Campylobacter* species is involved from human and animal origins has been reported in the USA and Canada (19–47%), European countries (17–99%), and Africa and Asia (>80%) [5]. According to the present study, the resistance of *Campylobacter* species isolated from human and animal origins to quinolones and fluoroquinolones including ciprofloxacin, nalidixic acid, enrofloxacin, and ofloxacin was also prevalent in Iran and varied from 0% to 87.3% (Tables 1–3). Efflux pumps, CmeABC, and single point mutations in DNA gyrase A (GyrA) such as C257T mutation, the most frequent mutation, are involved in chromosomally mediated quinolone resistance in *Campylobacter* species [5].

Macrolides are also recommended as another selective antibiotic class for the treatment of campylobacteriosis [2, 5]. The resistance rate to erythromycin in *Campylobacter* species isolated from human and animal samples in Iran was low (6.4%, 13%, and 7.4% for *C. jejuni*, *C. coli*, and *C. lari*, respectively). The frequency of erythromycin resistance in Iran was higher than that in Turkey [47], Ethiopia [48], Canada [49], Australia [50], and the Czech Republic [51] and lower than that of South Africa [52], Malaysia [53], Italy [54], China [55], South Korea [56], and Poland [57]. Noteworthy, the determination of *Campylobacter* species susceptibility patterns against other antibiotics has received less attention. One reason could be attributed to the high sensitivity of bacteria to these antibiotics. For example, in the current study, antibiotic resistance pattern to protein synthesis inhibitors was low. On the other hand, resistance to protein synthesis inhibitors was lower than cell growth inhibitors and folic acid metabolism inhibitors.

As shown in other studies, the efficacy of cell growth inhibitor antibiotics against *Campylobacter* species is limited [5]. Our study also showed that among the three evaluated *Campylobacter* species, antibiotic resistance to β-lactam antibiotics, especially penicillins and cephalosporins, was high. On the other hand, the resistance rate to imipenem was lower than meropenem. The intrinsic resistance and β-lactamase enzymes are two main mechanisms of resistance to β-lactam antibiotics in *Campylobacter* species [5]. The intrinsic resistance is also the main resistance mechanism of *Campylobacter* species against vancomycin and folic acid metabolism inhibitors [5]. Our results confirmed high resistance rates to these antibiotics probably due to intrinsic resistance.

**5. Conclusion**

In accordance with the WHO report on fluoroquinolone-resistant *Campylobacter* species in the world and the urgent need to develop new antibiotics, our meta-analysis showed a high prevalence of resistance of *Campylobacter* species isolated from human and animal origins to quinolones and fluoroquinolones in Iran. On the other hand, compared to penicillins, cephalosporins, and sulfonamides,
Campylobacter species were susceptible or showed low resistance rates to aminoglycosides, chloramphenicol, and imipenem. Therefore, these antibiotics could be recommended for the treatment of campylobacteriosis in Iran. We recommend monitoring antibiotic-resistant Campylobacter species through continuous drug sensitivity monitoring and investigating resistance mechanisms, especially against fluoroquinolones, to prevent further expansion of resistant species in Iran.

Data Availability
There are no original data associated with this review.

Conflicts of Interest
The authors declare that there are no conflicts of interest.

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