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REVIEW ARTICLE

A systematic review and meta-analysis on the prevalence of antibiotic-resistant *Listeria* species in food, animal and human specimens in Iran

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Abstract The aim of this study was to determine the antimicrobial resistance characteristics of *Listeria* species isolated from foods and food processing environments, animal and human specimens in Iran. A systematic review of the papers published in Persian and English languages up to 20th May 2019 and indexed in the Scientific Information Database, PubMed, Scopus and Google Scholar databases using related keywords was conducted. Eligible articles were selected based on the predefined inclusion and exclusion criteria, followed by data extraction and meta-analysis using random-effects or fixed-effects models. A total of 27 articles were found reporting antibiotic resistance patterns of different *Listeria* species using disk diffusion method. Among *Listeria* species, *Listeria monocytogenes* resistance to commonly used antibiotics i.e. penicillin, ampicillin and gentamicin was as follows: 34.5%, 26.4%, 8.9% in isolates from foods and food processing environments, 47.1%, 29.5%, 9.2% in isolates from animal specimens and 56.8%, 29.5%, 32.4% in human strains, respectively. A high prevalence of *L. monocytogenes* strains resistant to penicillin, ampicillin and gentamicin was observed in Iran. Our findings suggested that trimethoprim/sulfamethoxazole, vancomycin and ciprofloxacin can be used as alternatives in the treatment of human listeriosis in Iran due to their low resistance rates.

Keywords Antibiotic resistance · *Listeria* · Iran · Meta-analysis

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Introduction

The genus *Listeria* consists of β-hemolytic, non-spore-forming, motile (at 22–28 °C; tumbling motility), Gram-positive, facultative anaerobic rods which can be arranged as pairs or short chains (Carroll et al. 2016; Murray et al. 2015). Among 19 identified *Listeria* species, two species are considered as pathogens i.e. *Listeria monocytogenes* (*L. monocytogenes*) that regularly infects humans and *Listeria ivanovii* (*L. ivanovii*) that infects animals and rarely humans (Murray et al. 2015; Orsi and Wiedmann 2016). *L. monocytogenes* is a facultative intracellular food-borne pathogen that is widely found in nature and isolated from humans, wild and domestic animals, birds, insects, vegetation, water, food products and soil (Schuppler and Loessner 2010; Ramaswamy et al. 2007). Usually, the newborn (3.4 per 100,000), the elderly people (10 per 100,000), pregnant women (12 per 100,000) and patients with defects in cellular immunity are susceptible to *Listeria* infections which can be acquired via consumption of contaminated food products and mother to child transfer in utero or at birth (Murray et al. 2015; Olaimat et al. 2018). *L. monocytogenes* can cause neonatal diseases including early-onset listeriosis characterized by abortion, stillbirth, premature birth and high mortality rate which is acquired in utero. The pathogen can also cause late-onset listeriosis characterized by meningitis or meningoencephalitis with septicemia which is acquired 2–3 weeks after birth. The bacterium is also associated with a mild influenza-like illness and acute self-limited gastroenteritis in healthy adults, infections in pregnant women and meningitis in adults (Murray et al. 2015). In addition, the presence of *Listeria* species in food products is an important issue due to the consequent economic costs for the community in terms of consumer safety, and for the food industry (Ivanek et al. 2005). Hence, identification, control and treatment of *Listeria* infections are necessary. Combination regimens including a β-lactam alone or in combination with an aminoglycoside, i.e. either gentamicin with penicillin or gentamicin with ampicillin, are drugs of choice in the treatment of severe *Listeria* infections (Murray et al. 2015). Other antibiotics, such as trimethoprim-sulfamethoxazole, are successfully used to treat listeriosis but *Listeria* resistance to some of them has been reported, especially to fluoroquinolones, macrolides and tetracyclines (Murray et al. 2015; Olaimat et al. 2018). The prevalence of foodborne listeriosis varies between 0.1 and 11.3 cases per million persons in different countries with a mortality rate of $\leq$ 30% (Olaimat et al. 2018). In Iran, a systematic review and meta-analysis estimated the prevalence of *L. monocytogenes* to be 10%, 7% and 4% in humans, animals and food products, respectively (Ranjbar and Halaji 2018). However, no comprehensive information regarding antibiotic resistance of *Listeria* species in Iran has yet been presented. Therefore, the aim of this study was to determine the prevalence of antibiotic-resistant *Listeria* species, particularly *L. monocytogenes*, isolated from foods and food processing environments, animal and human specimens in Iran.

Methods

Search strategy

According to the PRISMA guidelines (Liberati et al. 2009), the current meta-analysis was conducted on the prevalence of *Listeria* species antibiotic resistance isolated from foods and food processing environments, animal and human specimens in Iran. For this purpose, a systematic literature search was done to find published articles until May 20, 2019 through international databases such as PubMed, Scopus and Google Scholar, as well as an Iranian national database i.e. the Scientific Information Database (SID) (https://www.sid.ir/En/Journal). We used three search terms including "antibiotic resistance", "*Listeria*" and "Iran" in both Persian and English languages. Finally, reference lists of the included eligible articles were checked for additional studies which might have been missed during databases searching.

Selection criteria

Identification of articles evaluating *Listeria* species antibiotic resistance was performed using the related keywords by two investigators independently. Retrieved articles were transferred to the EndNote reference management software. At first, the titles and abstracts and then the full texts were assessed based on inclusion and exclusion criteria. Studies with the following criteria were included in the meta-analysis: cross-sectional studies published in English or Persian languages, which were limited to Iran, *Listeria* species samples collected from foods and food processing environments, animal and human origins, and studies presenting data on the prevalence of antibiotic resistance. Non-original articles, duplicate reports, research evaluating drug resistance profiles only at the genus *Listeria* level or with insufficient data or small sample size and also articles measuring antibiotic resistance *Listeria* species isolated from mixed and non-specified samples were excluded.

Quality assessment and data extraction

The Joanna Briggs Institute (JBI) critical appraisal checklist was used to assess the quality of eligible studies (Munn et al. 2015). As shown, the main data were extracted and organized into Table 1 including the name of the first author, study publication date, *Listeria* species type, samples origins, the frequency of *Listeria* species, methods used for assessing susceptibility to different antibiotics and number of resistance to each antibiotic of *Listeria* species.

Meta-analysis

The prevalence of *Listeria* species resistant to different antibiotics was estimated as percentage and 95% confidence intervals (CIs) through pooling the data using either random-effects model (when the heterogeneity was high among included studies) or fixed-effects model (when the heterogeneity was low). In this regard, heterogeneity was estimated using the I^2 statistic and the Chi-square test with the Cochrane Q statistic (significant at $I^2 > 25\%$ and

Table 1 Extracted information from eligible studies included in the meta-analysis

References	*Listeria* species	Sample origin	Strain (n)	Antibiotic resistance (n)																		
				PEN	AMP	GEN	TMP-SMX	TET	VAN	STR	CHL	CTX	ERY	CIP	CLI	KAN	RIF	AMC	CEF	CAZ	AMK	NAL
Maktabi et al. (2016)	*L. innocua*	Food	2	0	0	0	1	1	0	0	0	ND	0	ND	ND	ND	ND	ND	ND	ND	0	ND
Rostami et al. (2015)	*L. monocytogenes*	Food	5	1	2	0	ND	0	0	ND	0	ND	1	2	ND	ND	ND	ND	ND	ND	ND	4
Rostami et al. (2015)	*L. innocua*	Food	2	1	0	0	ND	0	0	ND	0	ND	0	1	ND	ND	ND	ND	ND	ND	ND	2
Rahimi et al. (2017)	*L. monocytogenes*	Food	5	5	ND	1	ND	5	2	ND	1	ND	1	1	ND	ND	ND	ND	ND	ND	ND	0
Rahimi et al. (2017)	*L. innocua*	Food	10	10	ND	1	ND	9	4	ND	2	ND	2	3	ND	ND	ND	ND	ND	ND	ND	0
Rahimi et al. (2017)	*L. seeligeri*	Food	2	2	ND	0	ND	1	1	ND	0	ND	0	0	ND	ND	ND	ND	ND	ND	ND	0
Rahimi et al. (2010)	*L. monocytogenes*	Food	19	6	5	1	ND	3	0	ND	2	ND	3	4	ND	ND	ND	ND	ND	ND	ND	19
Rahimi et al. (2010)	*L. innocua*	Food	31	11	1	0	ND	11	0	ND	4	ND	4	6	ND	ND	ND	ND	ND	ND	ND	29
Rahimi et al. (2010)	*L. seeligeri*	Food	5	2	1	0	ND	1	0	ND	1	ND	0	1	ND	ND	ND	ND	ND	ND	ND	5
Rezai et al. (2018)	*L. monocytogenes*	Food	22	6	7	4	5	14	ND	ND	7	ND	9	15	5	ND	ND	ND	ND	ND	ND	ND
Rezai et al. (2018)	*L. ivanovii*	Food	16	5	8	4	4	11	ND	ND	4	ND	5	6	3	ND	ND	ND	ND	ND	ND	ND
Rezai et al. (2018)	*L. welshimeri*	Food	9	3	2	0	3	5	ND	ND	3	ND	3	2	2	ND	ND	ND	ND	ND	ND	ND
Rezai et al. (2018)	*L. grayi*	Food	12	5	6	2	5	7	ND	ND	2	ND	3	3	3	ND	ND	ND	ND	ND	ND	ND
Rezai et al. (2018)	*L. innocua*	Food	18	9	4	6	3	12	ND	ND	4	ND	4	5	4	ND	ND	ND	ND	ND	ND	ND
Rezai et al. (2018)	*L. seeligeri*	Food	9	3	3	2	2	5	ND	ND	1	ND	4	2	1	ND	ND	ND	ND	ND	ND	ND
Mojtahedi et al. (2004)	*L. monocytogenes*	Food	70	0	0	0	0	ND	ND	ND	ND	ND	5	ND	ND	ND	ND	ND	ND	ND	ND	ND
Mojtahedi et al. (2004)	*L. innocua*	Food	42	0	0	0	0	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
Mojtahedi et al. (2004)	*L. seeligeri*	Food	8	0	0	0	0	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
Kargar and Ghasemi (2011)	*L. monocytogenes*	Food	56	7	0	ND	ND	29	ND	ND	ND	ND	12	ND	ND	ND	ND	ND	ND	ND	11	ND

Table 1 continued

References	*Listeria* species	Sample origin	Strain (n)	Antibiotic resistance (n)																		
				PEN	AMP	GEN	TMP-SMX	TET	VAN	STR	CHL	CTX	ERY	CIP	CLI	KAN	RIF	AMC	CEF	CAZ	AMK	NAL
Zeinali et al. (2017)	*L. monocytogenes*	Food	26	2	0	5	ND	12	0	ND	5	ND	16	4	13	ND	4	ND	ND	ND	11	ND
Jamali et al. (2015)	*L. monocytogenes*	Food	43	7	9	0	5	12	3	7	1	0	6	ND	ND	0	1	ND	7	6	ND	ND
Jamali et al. (2015)	*L. innocua*	Food	47	9	5	0	5	11	4	8	1	0	9	ND	ND	0	2	ND	11	4	ND	ND
Jamali et al. (2015)	*L. seeligeri*	Food	24	2	2	0	3	5	1	3	0	0	3	ND	ND	0	2	ND	3	0	ND	ND
Jamali et al. (2015)	*L. ivanovii*	Food	19	4	0	0	1	3	0	3	0	0	1	ND	ND	0	0	ND	1	1	ND	ND
Babazadeh Naseri and Soltan Dallal (2019)	*L. monocytogenes*	Food	9	1	1	2	ND	5	ND	4	4	ND	4	4	ND	ND	ND	ND	ND	ND	ND	ND
Abdollahzadeh et al. (2016)	*L. monocytogenes*	Food	7	4	7	0	0	0	ND	0	0	7	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
Bahador et al. (2015)	*L. monocytogenes*	Food	24	12	0	ND	ND	0	ND	1	1	ND	0	0	ND	ND	ND	ND	ND	ND	ND	ND
Jamali et al. (2013)	*L. monocytogenes*	Food	18	11	ND	0	ND	13	0	ND	5	ND	2	ND	1	0	0	4	ND	ND	ND	ND
Jamali et al. (2013)	*L. welshimeri*	Food	10	4	ND	0	ND	3	0	ND	0	ND	0	ND	0	0	0	0	ND	ND	ND	ND
Jamali et al. (2013)	*L. innocua*	Food	48	18	ND	0	ND	24	0	ND	3	ND	4	ND	3	1	0	7	ND	ND	ND	ND
Jamali et al. (2013)	*L. seeligeri*	Food	7	3	ND	0	ND	1	0	ND	1	ND	0	ND	0	0	0	1	ND	ND	ND	ND
Rahimi et al. (2012a)	*L. monocytogenes*	Food	27	6	3	1	ND	3	0	ND	0	ND	2	2	ND	1	ND	ND	4	ND	ND	ND
Rahimi et al. (2012a)	*L. innocua*	Food	98	33	9	0	ND	20	0	ND	3	ND	6	14	ND	1	ND	ND	43	ND	ND	ND
Rahimi et al. (2012a)	*L. seeligeri*	Food	5	0	0	0	ND	1	0	ND	0	ND	0	0	ND	0	ND	ND	1	ND	ND	ND
Rahimi et al. (2012a)	*L. welshimeri*	Food	9	3	2	0	ND	2	0	ND	0	ND	0	2	ND	0	ND	ND	2	ND	ND	ND
Rahimi et al. (2012a)	*L. grayi*	Food	2	0	0	0	ND	0	0	ND	0	ND	0	0	ND	0	ND	ND	0	ND	ND	ND
Fallah et al. (2013)	*L. monocytogenes*	Food	278	106	107	2	7	52	58	ND	9	ND	7	49	9	ND	2	ND	ND	ND	ND	ND
Fallah et al. (2012)	*L. monocytogenes*	Food	52	41	44	10	0	34	0	ND	24	ND	15	24	8	ND	8	ND	ND	ND	ND	ND
Fallah et al. (2012)	*L. innocua*	Food	62	39	39	5	4	22	0	ND	16	ND	7	33	6	ND	5	ND	ND	ND	ND	ND

Table 1 continued

References	*Listeria* species	Sample origin	Strain (n)	Antibiotic resistance (n)																		
				PEN	AMP	GEN	TMP-SMX	TET	VAN	STR	CHL	CTX	ERY	CIP	CLI	KAN	RIF	AMC	CEF	CAZ	AMK	NAL
Fallah et al. (2012)	*L. ivanovii*	Food	13	7	7	0	0	2	0	ND	5	ND	0	5	0	ND	0	ND	ND	ND	ND	ND
Fallah et al. (2012)	*L. seeligeri*	Food	7	0	0	0	0	1	0	ND	0	ND	0	0	0	ND	0	ND	ND	ND	ND	ND
Khalili Borujeni et al. (2013)	*L. ivanovii*	Food	5	5	0	0	0	0	ND	ND	0	ND	0	ND	ND	ND	ND	ND	ND	ND	NA	ND
Rahimi et al. (2012b)	*L. monocytogenes*	Food	5	3	2	0	ND	3	0	ND	1	ND	3	1	ND	ND	ND	ND	ND	ND	ND	3
Rahimi et al. (2012b)	*L. innocua*	Food	14	7	0	0	ND	4	0	ND	2	ND	0	4	ND	ND	ND	ND	ND	ND	ND	13
Abbasinejad et al. (2015)	*L. monocytogenes*	Food	3	0	ND	0	ND	0	ND	ND	0	ND	0	ND	ND	ND	ND	ND	ND	ND	ND	ND
Akrami-Mohajeri et al. (2018)	*L. monocytogenes*	Food	22	17	ND	4	0	19	0	10	17	ND	8	ND	5	2	1	3	ND	ND	ND	ND
Akrami-Mohajeri et al. (2018)	*L. innocua*	Food	31	25	ND	0	0	20	0	4	23	ND	4	ND	2	0	0	1	ND	ND	ND	ND
Akrami-Mohajeri et al. (2018)	*L. seeligeri*	Food	10	4	ND	0	0	5	0	5	3	ND	2	ND	0	0	1	1	ND	ND	ND	ND
Soleymani Najaf Ababdi et al. (2017)	*L. monocytogenes*	Food	104	30	44	10	10	40	3	ND	25	ND	3	20	8	ND	7	ND	ND	ND	ND	ND
Heidarzadeh et al. (2018)	*L. monocytogenes*	Human	22	10	10	8	ND	10	ND	10	12	ND	10	4	ND	ND	ND	ND	ND	ND	ND	ND
Abdollahzadeh et al. (2016)	*L. monocytogenes*	Human	7	5	7	1	0	0	ND	4	0	7	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
Kalani et al. (2015)	*L. monocytogenes*	Human	14	8	0	ND	ND	2	ND	0	4	ND	3	0	ND	ND	ND	ND	ND	ND	ND	ND
Lotfollahi et al. (2011)	*L. monocytogenes*	Human	9	7	0	ND	ND	0	ND	1	1	7	0	0	ND	ND	ND	ND	ND	ND	ND	ND
Dehkordi et al. (2013)	*L. monocytogenes*	Animal	227	99	67	77	ND	162	ND	79	68	ND	75	27	ND	ND	ND	ND	36	ND	ND	ND
Jamali et al. (2014)	*L. monocytogenes*	Animal	19	6	ND	0	ND	11	0	ND	0	ND	2	ND	2	0	0	1	ND	ND	ND	ND
Jamali et al. (2014)	*L. innocua*	Animal	5	0	ND	0	ND	1	0	ND	0	ND	0	ND	0	0	0	0	ND	ND	ND	ND

Table 1 continued

References	*Listeria* species	Sample origin	Strain (n)	Antibiotic resistance (n)																		
				PEN	AMP	GEN	TMP-SMX	TET	VAN	STR	CHL	CTX	ERY	CIP	CLI	KAN	RIF	AMC	CEF	CAZ	AMK	NAL
Jamali et al. (2014)	*L. seeligeri*	Animal	9	1	ND	0	ND	2	0	ND	0	ND	0	ND	0	0	0	0	ND	ND	ND	ND
Jamali et al. (2014)	*L. ivanovii*	Animal	25	7	ND	0	ND	14	0	ND	0	ND	5	ND	4	0	0	3	ND	ND	ND	ND
Jamali and Radmehr (2013)	*L. monocytogenes*	Animal	17	12	ND	0	ND	10	0	ND	4	ND	1	ND	0	0	0	5	ND	ND	ND	ND
Jamali and Radmehr (2013)	*L. innocua*	Animal	3	1	ND	0	ND	1	0	ND	0	ND	0	ND	0	0	0	0	ND	ND	ND	ND

PEN penicillin, *AMP* ampicillin, *GEN* gentamicin, *TMP/SMX* trimethoprim/sulfamethoxazole, *TET* tetracycline, *VAN* vancomycin, *STR* streptomycin, *CHL* chloramphenicol, *CTX* cefotaxime, *ERY* erythromycin, *CIP* ciprofloxacin, *CLI* clindamycin, *KAN* kanamycin, *RIF* rifampin, *AMC* amoxicillin-clavulanic acid, *CEF* cephalothin, *CAZ* ceftazidime, *AMK* amikacin, *NAL* nalidixic acid, *ND* not determined

$p < 0.1$). Asymmetry of funnel plots was explored as an indicator of potential publication bias. Meta-analysis was performed using the Comprehensive Meta-Analysis (CMA) software version 2.2 (Biostat, Englewood, NJ).

Results

Literature search and study characteristics

Of 1069 collected reports after searching in national and international databases, a total of 27 articles met predefined inclusion and exclusion criteria and were found to be eligible for the analysis of *Listeria* species antibiotic resistance (Fig. 1). Included studies were reported from Ahvaz, Bandar Torkaman, Chahar Mahal & Bakhtiyari, Isfahan, Karaj, Kurdistan, Lorestan, Marvdasht, Mashhad, Mazandaran, Shiraz, Tehran, Urmia and Yazd. As shown in Table 1, 20, 4 and 3 the research papers assessed antibiotic resistance profiles of *Listeria* species isolated from foods and food processing environments, human and animal origins, respectively. Food products as raw, ready-to-cook and ready-to-eat included seafood products, milk and traditional dairy products, processed meat, poultry products as well as market and processing environments which have been used for food products. Clinical specimens were collected from pregnant women with vaginitis (vaginal swab) and woman with spontaneous abortion (blood, urine, placental tissue, fecal and vaginal swabs). Also, animal specimens were obtained from ducks, geese, bovine, ovine, caprine, buffalo and camel species. *L. monocytogenes* was the most common *Listeria* species isolated from foods and food processing environments (57.9% samples), human (100% samples) and animal (86.2% samples) specimens.

Characteristics of *Listeria* species antibiotic resistance in Iran

All eligible studies used disk diffusion technique to determine antimicrobial susceptibility of *Listeria* species isolated in Iran. The results of antibiotic resistance according to the type of sample are shown in Table 2 for *L. monocytogenes*, *L. ivanovii*, *L. innocua*, *L. seeligeri*, *L. grayi* and *L. welshimeri*. As shown in Table 2, there is a heterogeneity among some studies in determining the prevalence of antibiotic resistance in *Listeria* species. In this case, random-effects model was used for pooling the data. Also, funnel plots were asymmetric suggesting potential publication bias in estimating the percentage of resistance for some antibiotics (Fig. 2).

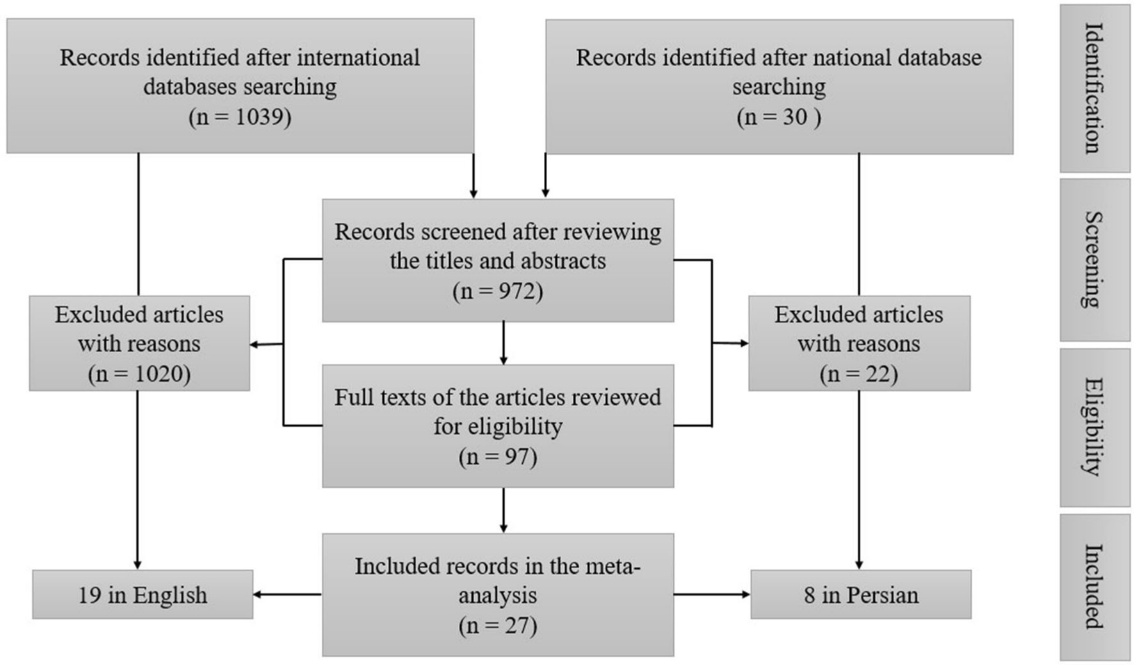

Fig. 1 Flowchart of literature search and study selection for meta-analysis

Discussion

Listeria together with other pathogens including *Campylobacter*, *Vibrio*, *Salmonella*, *Shigella*, *Escherichia*, *Yersinia*, *Staphylococcus*, *Clostridium* and *Bacillus* are causative agent for more than 90% of food poisonings (Jalalpour 2012). It has been suggested that antibiotic therapy is necessary in severe cases of infection but drug resistance has increased among food-borne pathogens during the past few decades. Drug-resistant microbial species are a significant threat to public health, food security and treatment of diseases, and account for long-term hospitalization, increased mortality rates and enormous medical costs in the world (Olaimat et al. 2018; Jamali et al. 2014). One of the main food-borne microbes associated with major public health concern, especially in the food industry, is *L. monocytogenes* (Olaimat et al. 2018). In the present study, resistance rates of *L. monocytogenes* as well as other *Listeria* species in food products were high against some antibiotics (Table 1). Antibiotic resistance of food-borne *L. monocytogenes* pathogen may be either intrinsic or acquired due to genetic alterations or adaptation to environmental stresses including physical (e.g., heat and high pressure), chemical (e.g., acids and salts) and biological (e.g., microbial antagonism) stressors during food production and in the food processing environments (Olaimat et al. 2018; Lungu et al. 2011). Studies have also shown that factors such as the use of antimicrobial compounds in food preservation (via inducing efflux pumps), as well as sublethal exposure to disinfectants in food processing environments may contribute to the emergence of antibiotic-resistant food isolates of *L. monocytogenes* (Olaimat et al. 2018). Since *L. monocytogenes* is isolated from ubiquitous sources, the food chain can play an important role in transferring antibiotic resistant strains between animals and humans (Olaimat et al. 2018). In this study, antimicrobial resistance of *L. monocytogenes* isolated from human specimens against antibiotics used in primary therapy of *Listeria* infections i.e. penicillin, ampicillin and gentamicin was found to be 56.8%, 29.5% and 32.4% (Fig. 3), respectively. These prevalence rates are higher than the results of *L. monocytogenes* isolated from food (34.5%, 26.4% and 8.9%) and animal (47.1%, 29.5% and 9.2%) origin specimens. Frequent use of these antibiotics as the first-line drugs in listeriosis treatment as well as acquisition of resistance genes from the commensal unrelated bacterial species in foods and food processing environments through mobile genetic elements and efflux pumps can justify the high levels of *L. monocytogenes* resistance in human samples (Olaimat et al.

Table 2 Characteristics of *Listeria* species antibiotic resistance isolated in Iran

Listeria species	Sample origin		Antibiotic resistance (n)									
			PEN	AMP	GEN	TMP-SMX	TET	VAN	STR	CHL	CTX	ERY
L. monocytogenes	Food	%	**34.5**	**26.4**	**8.9**	**5.9**	**40.5**	**5.8**	**22**	**17.7**	**29.2**	**17.6**
		95% CI	24.4–46.2	16.2–39.8	5.3–14.6	2.6–12.8	28.3–54	2.5–13.1	9–44.6	9.7–30.3	0–99.8	10.2–28.6
		I^2	81.9	83.3	54.6	69.6	85.2	69	69.4	83.9	91.9	83.3
		Q	99.8	84	35.2	23	115.2	35.5	13	99.7	12.3	101.9
		p	0.00	0.00	0.00	0.00	0.00	0.00	0.01	0.00	0.00	0.00
	Human	%	**56.8**	**29.5**	**32.4**	**6.3**	**18.3**	–	**28.7**	**27.8**	**83.1**	**26.8**
		95% CI	42.7–69.9	4.3–79.6	17.6–51.7	0.4–53.9	5.2–47.8	–	9.7–60.1	10.6–55.8	55.3–95.1	9.4–56.2
		I^2	6.7	75.2	10.2	0	60.7	–	61.5	60.1	0	57.3
		Q	3.2	12.1	1.1	0	7.6	–	7.7	7.5	0.76	4.6
		p	0.36	0.00	0.29	1.0	0.05	–	0.05	0.05	0.38	0.09
	Animal	%	**47.1**	**29.5**	**9.2**	–	**69.5**	**2.6**	**34.8**	**23.3**	–	**16.5**
		95% CI	30.3–64.6	23.9–35.8	0.9–52.1	–	63.6–74.8	0.4–16.5	28.9–41.2	11.2–42.2	–	4.8–43.4
		I^2	64	0	75.8	–	18.4	0	0	51	–	72.6
		Q	5.5	0	8.2	–	2.4	0	0	4	–	7.3
		p	0.06	1.0	0.01	–	0.29	0.95	1.0	0.13	–	0.02
L. ivanovii	Food	%	**41.5**	**29.5**	**10.5**	**14.4**	**25.7**	**3**	**15.8**	**20.9**	**2.5**	**12**
		95% CI	19.9–67	9.6–62.4	3–30.9	6.5–28.9	6.8–62.1	0.4–18.4	5.2–39.2	8.1–44.4	0.2–29.8	3.3–34.9
		I^2	60.7	64.9	31.8	21.9	76.9	0	0	42.2	0	45.3
		Q	7.6	8.5	4.4	3.8	13	0	0	5.1	0	5.4
		p	0.05	0.03	0.22	0.27	0.00	0.85	1.0	0.15	1.0	0.13
	Human	%	–	–	–	–	–	–	–	–	–	–
		95% CI	–	–	–	–	–	–	–	–	–	–
		I^2	–	–	–	–	–	–	–	–	–	–
		Q	–	–	–	–	–	–	–	–	–	–
		p	–	–	–	–	–	–	–	–	–	–
	Animal	%	**28**	–	**1.9**	–	**56**	**1.9**	–	**1.9**	–	**20**
		95% CI	14–48.2	–	0.1–24.4	–	36.6–73.7	0.1–24.4	–	0.1–24.4	–	8.6–40
		I^2	0	–	0	–	0	0	–	0	–	0
		Q	0	–	0	–	0	0	–	0	–	0
		p	1.0	–	1.0	–	1.0	1.0	–	1.0	–	1.0
L. innocua	Food	%	**43.7**	**12**	**4.8**	**9**	**41.5**	**4.7**	**15.5**	**15.3**	**1**	**12.4**
		95% CI	30.3–58.1	3.9–31.4	1.9–11.5	4.1–18.3	29.6–54.5	1.5–13.2	9.1–25.2	6.8–30.9	0.1–14.6	9.3–16.5
		I^2	79.3	88.1	58.4	40.6	75.5	60.7	0	83.5	0	0
		Q	53.3	67.7	26.4	8.4	40.8	22.9	0.2	60.7	0	9.2
		p	0.00	0.00	0.00	0.13	0.00	0.00	0.88	0.00	1.0	0.51

Table 2 continued

Listeria species	Sample origin		Antibiotic resistance (n)									
			PEN	AMP	GEN	TMP-SMX	TET	VAN	STR	CHL	CTX	ERY
	Human	%	–	–	–	–	–	–	–	–	–	–
		95% CI	–	–	–	–	–	–	–	–	–	–
		I^2	–	–	–	–	–	–	–	–	–	–
		Q	–	–	–	–	–	–	–	–	–	–
		p	–	–	–	–	–	–	–	–	–	–
	Animal	%	**20**	–	**10.2**	–	**25.5**	**10.2**	–	**10.2**	–	**10.2**
		95% CI	3.8–61.3	–	1.4–47.3	–	6.4–63.3	1.4–47.3	–	1.4–47.3	–	1.4–47.3
		I^2	0	–	0	–	0	0	–	0	–	0
		Q	0.7	–	0	–	0.1	0	–	0	–	0
		p	0.37	–	0.83	–	0.67	0.83	–	0.83	–	0.83
L. seeligeri	Food	%	**26.1**	**14.7**	**9.2**	**12.1**	**30.9**	**8.1**	**27.3**	**15**	**2**	**18**
		95% CI	13.9–43.7	7.2–27.7	4.1–19.2	5.7–23.9	20.4–43.7	3.1–19.5	5.3–71.7	7.6–27.7	0.1–25.1	10.1–29.9
		I^2	36.4	0	0	0	8	0	79.3	0	0	0
		Q	12.5	4.2	3.7	1.9	7.6	3.6	4.8	4.7	0	6.2
		p	0.12	0.50	0.88	0.74	0.36	0.71	0.02	0.68	1.0	0.50
	Human	%	–	–	–	–	–	–	–	–	–	–
		95% CI	–	–	–	–	–	–	–	–	–	–
		I^2	–	–	–	–	–	–	–	–	–	–
		Q	–	–	–	–	–	–	–	–	–	–
		p	–	–	–	–	–	–	–	–	–	–
	Animal	%	**11.1**	–	**5**	–	**22.2**	**5**	–	**5**	–	**5**
		95% CI	1.5–50	–	0.3–47.5	–	5.6–57.9	0.3–47.5	–	0.3–47.5	–	0.3–47.5
		I^2	0	–	0	–	0	0	–	0	–	0
		Q	0	–	0	–	0	0	–	0	–	0
		p	1.0	–	1.0	–	1.0	1.0	–	1.0	–	1.0
L. grayi	Food	%	**37.9**	**45.1**	**16.7**	**41.7**	**47.3**	**16.7**	–	**16.7**	–	**23.5**
		95% CI	17.2–64.1	22.2–70.4	4.9–43.7	18.5–69.2	15.3–81.7	1–80.6	–	4.9–43.7	–	8.5–50.5
		I^2	0	0	0	0	27.5	0	–	0	–	0
		Q	0.5	0.9	0	0	1.3	0	–	0	–	0
		p	0.44	0.33	1.0	1.0	0.24	1.0	–	1.0	–	0.76
	Human	%	–	–	–	–	–	–	–	–	–	–
		95% CI	–	–	–	–	–	–	–	–	–	–
		I^2	–	–	–	–	–	–	–	–	–	–
		Q	–	–	–	–	–	–	–	–	–	–
		p	–	–	–	–	–	–	–	–	–	–

Table 2 continued

Listeria species	Sample origin		Antibiotic resistance (n)									
			PEN	AMP	GEN	TMP-SMX	TET	VAN	STR	CHL	CTX	ERY
	Animal	%	–	–	–	–	–	–	–	–	–	–
		95% CI	–	–	–	–	–	–	–	–	–	–
		I^2	–	–	–	–	–	–	–	–	–	–
		Q	–	–	–	–	–	–	–	–	–	–
		p	–	–	–	–	–	–	–	–	–	–
L. welshimeri	Food	%	**35.8**	**22.2**	**4.8**	**33.3**	**36.6**	**4.8**	–	**13.9**	–	**13.9**
		95% CI	20.4–54.7	8.6–46.5	1–20.8	11.1–66.7	20.5–56.4	0.7–27.2	–	2.9–47.1	–	2.9–47.1
		I^2	0	0	0	0	12.3	0	–	41.5	–	41.5
		Q	0.1	0	0	0	2.2	0	–	3.4	–	3.4
		p	0.94	1.0	0.99	1.0	0.31	0.96	–	0.18	–	0.18
	Human	%	–	–	–	–	–	–	–	–	–	–
		95% CI	–	–	–	–	–	–	–	–	–	–
		I^2	–	–	–	–	–	–	–	–	–	–
		Q	–	–	–	–	–	–	–	–	–	–
		p	–	–	–	–	–	–	–	–	–	–
	Animal	%	–	–	–	–	–	–	–	–	–	–
		95% CI	–	–	–	–	–	–	–	–	–	–
		I^2	–	–	–	–	–	–	–	–	–	–
		Q	–	–	–	–	–	–	–	–	–	–
		p	–	–	–	–	–	–	–	–	–	–

Listeria species	Sample origin		Antibiotic resistance (n)								
			CIP	CLI	KAN	RIF	AMC	CEF	CAZ	AMK	NAL
L. monocytogenes	Food	%	**25.4**	**14.2**	**4.7**	**5.4**	**17.9**	**15.7**	**14**	**29.3**	**68.6**
		95% CI	16.3–37.4	6–30	1.8–12	2.3–12.3	8.8–33.1	8.9–26.2	6.4–27.8	12.4–54.9	21.7–94.5
		I^2	77.4	88	0	70.8	0	0	0	77.5	67.1
		Q	48.7	50.1	2.1	20.6	0.4	0	0	4.4	9.1
		p	0.00	0.00	0.53	0.00	0.48	0.87	1.0	0.03	0.02
	Human	%	**13.3**	–	–	–	–	–	–	–	–
		95% CI	5.6–28.4	–	–	–	–	–	–	–	–
		I^2	3.3	–	–	–	–	–	–	–	–
		Q	2	–	–	–	–	–	–	–	–
		p	0.35	–	–	–	–	–	–	–	–

Table 2 continued

Listeria species	Sample origin		Antibiotic resistance (n)								
			CIP	CLI	KAN	RIF	AMC	CEF	CAZ	AMK	NAL
Animal	%	**11.9**	**8**	**2.6**	**2.6**	**15.6**	**15.9**	–	–	–	
	95% CI	8.3–16.8	2.3–24.2	0.4–16.5	0.4–16.5	2.6–56.1	11.7–21.2	–	–	–	
	I^2	0	0	0	0	67	0	–	–	–	
	Q	0	0.76	0	0	3	0	–	–	–	
	p	1.0	0.38	0.95	0.95	0.08	1.0	–	–	–	
L. ivanovii	Food	%	**37.9**	**12.7**	**2.5**	**3**	–	**5.3**	**5.3**	–	–
		95% CI	22.4–56.4	3–40.8	0.2–29.8	0.4–18.4	–	0.7–29.4	0.7–29.4	–	–
		I^2	0	25.7	0	0	–	0	0	–	–
		Q	0	1.3	0	0	–	0	0	–	–
		p	0.95	0.24	1.0	0.85	–	1.0	1.0	–	–
	Human	%	–	–	–	–	–	–	–	–	–
		95% CI	–	–	–	–	–	–	–	–	–
		I^2	–	–	–	–	–	–	–	–	–
		Q	–	–	–	–	–	–	–	–	–
		p	–	–	–	–	–	–	–	–	–
	Animal	%	–	**16**	**1.9**	**1.9**	**12**	–	–	–	–
		95% CI	–	6.1–35.7	0.1–24.4	0.1–24.4	3.9–31.3	–	–	–	–
		I^2	–	0	0	0	0	–	–	–	–
		Q	–	0	0	0	0	–	–	–	–
		p	–	1.0	1.0	1.0	1.0	–	–	–	–
L. innocua	Food	%	**28.7**	**10.3**	**1.4**	**5.4**	**9**	**33.7**	**8.5**	**16.7**	**75.8**
		95% CI	16–45.9	6.3–16.4	0.4–4.2	2.7–10.5	2.1–30.9	16.9–56	3.2–20.6	1–80.6	23.3–97
		I^2	78.1	23.6	0	6.9	55	81.8	0	0	77.2
		Q	27.4	3.9	0.31	3.2	2.2	5.5	0	0	13.1
		p	0.00	0.26	0.95	0.35	0.13	0.01	1.0	1.0	0.00
	Human	%	–	–	–	–	–	–	–	–	–
		95% CI	–	–	–	–	–	–	–	–	–
		I^2	–	–	–	–	–	–	–	–	–
		Q	–	–	–	–	–	–	–	–	–
		p	–	–	–	–	–	–	–	–	–
	Animal	%	–	**10.2**	**10.2**	**10.2**	**10.2**	–	–	–	–
		95% CI	–	1.4–47.3	1.4–47.3	1.4–47.3	1.4–47.3	–	–	–	–
		I^2	–	0	0	0	0	–	–	–	–
		Q	–	0	0	0	0	–	–	–	–
		p	–	0.83	0.83	0.83	0.83	–	–	–	–

Table 2 continued

Listeria species	Sample origin		Antibiotic resistance (n)								
			CIP	CLI	KAN	RIF	AMC	CEF	CAZ	AMK	NAL
L. seeligeri	Food	%	**16.1**	**7.3**	**4.6**	**8.1**	**11.9**	**14**	**2**	–	**60.4**
		95% CI	6.5–34.8	2.1–22.4	1.2–16.8	3.1–19.7	3–37.3	5.3–31.9	0.1–25.1	–	2.9–98.7
		I^2	0	0	0	0	0	0	0	–	71.4
		Q	1	0.33	0.5	0.1	0	0.1	0	–	3.5
		p	0.89	0.95	0.89	0.98	0.78	0.66	1.0	–	0.06
	Human	%	–	–	–	–	–	–	–	–	–
		95% CI	–	–	–	–	–	–	–	–	–
		I^2	–	–	–	–	–	–	–	–	–
		Q	–	–	–	–	–	–	–	–	–
		p	–	–	–	–	–	–	–	–	–
	Animal	%	–	**5**	**5**	**5**	**5**	–	–	–	–
		95% CI	–	0.3–47.5	0.3–47.5	0.3–47.5	0.3–47.5	–	–	–	–
		I^2	–	0	0	0	0	–	–	–	–
		Q	–	0	0	0	0	–	–	–	–
		p	–	1.0	1.0	1.0	1.0	–	–	–	–
L. grayi	Food	%	**23.5**	**25**	**16.7**	–	–	**16.7**	–	–	–
		95% CI	8.5–50.5	8.3–55.2	1–80.6	–	–	1–80.6	–	–	–
		I^2	0	0	0	–	–	0	–	–	–
		Q	0	0	0	–	–	0	–	–	–
		p	0.76	1.0	1.0	–	–	1.0	–	–	–
	Human	%	–	–	–	–	–	–	–	–	–
		95% CI	–	–	–	–	–	–	–	–	–
		I^2	–	–	–	–	–	–	–	–	–
		Q	–	–	–	–	–	–	–	–	–
		p	–	–	–	–	–	–	–	–	–
	Animal	%	–	–	–	–	–	–	–	–	–
		95% CI	–	–	–	–	–	–	–	–	–
		I^2	–	–	–	–	–	–	–	–	–
		Q	–	–	–	–	–	–	–	–	–
		p	–	–	–	–	–	–	–	–	–
L. welshimeri	Food	%	**22.2**	**15.8**	**4.8**	**4.5**	**4.5**	**22.2**	–	–	–
		95% CI	8.6–46.5	4.5–42.6	0.7–27.2	0.3–44.8	0.3–44.8	5.6–57.9	–	–	–
		I^2	0	14.7	0	0	0	0	–	–	–
		Q	0	1.1	0	0	0	0	–	–	–
		p	1.0	0.27	0.96	1.0	1.0	1.0	–	–	–

Table 2 continued

Listeria species	Sample origin		Antibiotic resistance (n)								
			CIP	CLI	KAN	RIF	AMC	CEF	CAZ	AMK	NAL
	Human	%	–	–	–	–	–	–	–	–	–
		95% CI	–	–	–	–	–	–	–	–	–
		I^2	–	–	–	–	–	–	–	–	–
		Q	–	–	–	–	–	–	–	–	–
		p	–	–	–	–	–	–	–	–	–
	Animal	%	–	–	–	–	–	–	–	–	–
		95% CI	–	–	–	–	–	–	–	–	–
		I^2	–	–	–	–	–	–	–	–	–
		Q	–	–	–	–	–	–	–	–	–
		p	–	–	–	–	–	–	–	–	–

PEN penicillin, *AMP* ampicillin, *GEN* gentamicin, *TMP/SMX* trimethoprim/sulfamethoxazole, *TET* tetracycline, *VAN* vancomycin, *STR* streptomycin, *CHL* chloramphenicol, *CTX* cefotaxime, *ERY* erythromycin, *CIP* ciprofloxacin, *CLI* clindamycin, *KAN* kanamycin, *RIF* rifampin, *AMC* amoxicillin-clavulanic acid, *CEF* cephalothin, *CAZ* ceftazidime, *AMK* amikacin, *NAL* nalidixic acid

Bold indicates total resistance rate to each antibiotic

2018; Abdollahzadeh et al. 2016). Additionally, in penicillin-allergic individuals, vancomycin or trimethoprim/sulfamethoxazole are recommended for the treatment of invasive listeriosis (Abdollahzadeh et al. 2016). The prevalence of vancomycin- and trimethoprim/sulfamethoxazole-resistant *L. monocytogenes* isolated from different origins was as follow: 5.9% to trimethoprim/sulfamethoxazole and 5.8% to vancomycin in food specimens, 6.3% to trimethoprim/sulfamethoxazole in human specimens and 2.6% to vancomycin in animal specimens (Table 2). The antibiotic resistance of *L. monocytogenes* isolated from food products in different countries was as follows: 100% to penicillin, 4.8% to gentamicin, 57.1% to vancomycin and 4.8% to trimethoprim/sulfamethoxazole in India, 93.8% to penicillin, 3.1% to gentamicin, 46.8% to vancomycin and 6.3% to trimethoprim/sulfamethoxazole in Egypt, and 100% to penicillin, 7.8% to gentamicin, 45.1% to vancomycin and 11.7% to trimethoprim/sulfamethoxazole in Yemen (Obaidat et al. 2015). Another study from Turkey showed 66.7% resistance to penicillin, 75% to ampicillin, 8.3% to gentamicin, 0% to vancomycin and 50% to trimethoprim/sulfamethoxazole (Aras and Ardiç 2015). Also, Ha et al. in a study in South Korea indicated that ampicillin, gentamicin, vancomycin and trimethoprim/sulfamethoxazole resistance rates of *L. monocytogenes* isolated from food products were 97%, 0%, 0% and 0%, respectively, (Ha et al. 2017). On the other hand, it is necessary to monitor the extensive use of antibiotics as supplements to enhance the growth or prevent, control and treat diseases in animals or as pesticide on fruits, and also use of sub-inhibitory concentrations of antibiotics in human diseases treatment which can lead to the emergence of the antibiotic resistance and effect on human infection therapy (Olaimat et al. 2018). It is worth noting that tetracycline is frequently used for treating animal infections in Iran (Akrami-Mohajeri et al. 2018). This drug is also used in treating human infections (Olaimat et al. 2018). Our results indicated that *L. monocytogenes* strains isolated from food products (40.5%), animal (69.5%) and human (18.3%) samples exhibited a high resistance rate to tetracycline. Similar results were observed for other *Listeria* species (Table 2). However, 3% and 6% of *L. monocytogenes* isolates from food products in Italy and Canada were resistant to tetracycline, respectively (Abdollahzadeh et al. 2016). In pregnant women, erythromycin is an antibiotic of choice to treat listeriosis (Olaimat et al. 2018). However, the current study showed that 26.8% of human isolates of *L. monocytogenes* were resistant to erythromycin. Other antibiotics used to treat listeriosis are rifampicin, chloramphenicol and fluoroquinolones (Olaimat et al. 2018). Among them, chloramphenicol-resistant *L. monocytogenes* strains isolated from food (17.7%), animal (27.8%) and human (23.3%) origins and

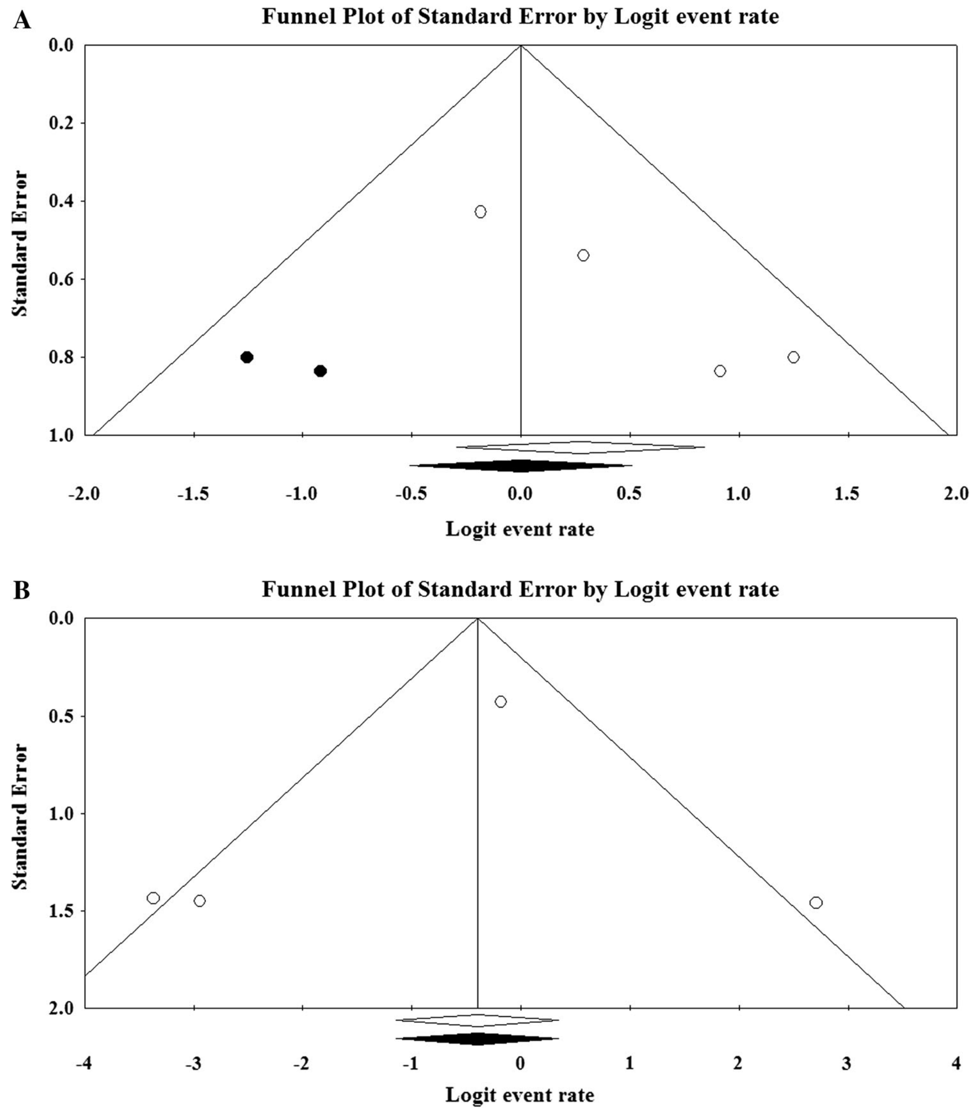

Fig. 2 Funnel plots depicting publication bias of studies reporting the prevalence antibiotic resistance of *L. monocytogenes* to penicillin (**a**) and ampicillin (**b**) in human specimens

ciprofloxacin-resistant *L. monocytogenes* strains isolated from food origin (25.4%) showed high resistance rates. However, rifampin-resistant *L. monocytogenes* strains isolated from food (5.4%) and animal (2.6%) origins had low resistance rates. In addition to the pathogen source, other species of the genus *Listeria* can affect the emergence of *L. monocytogenes* antibiotic resistance in through genetic material exchange (Allen et al. 2016). Therefore, investigation of the antibiotic resistance of other *Listeria* species is also important. Our study showed that resistance of *Listeria* species isolated from foods and food processing environments and animal sources in Iran was high to some antibiotics (Table 2).

Conclusion

The present systematic review and meta-analysis warns about the emergence of *Listeria* species resistant to different antibiotics in different pathogen sources in Iran. For example, a high prevalence of *L. monocytogenes* strains resistant to commonly used antibiotics in treating human listeriosis i.e. penicillin, ampicillin and gentamicin was observed in Iran. In addition, other species of the genus *Listeria* indicated high resistance rates to some antibiotics. Therefore, to reduce the spread of *Listeria* drug resistance in Iran, excessive use of antibiotics either in the treatment of human infections or in animal feeding as growth supplements and prophylaxis should be controlled and limited. Nonetheless, our findings suggest that trimethoprim/sulfamethoxazole, vancomycin and ciprofloxacin can be

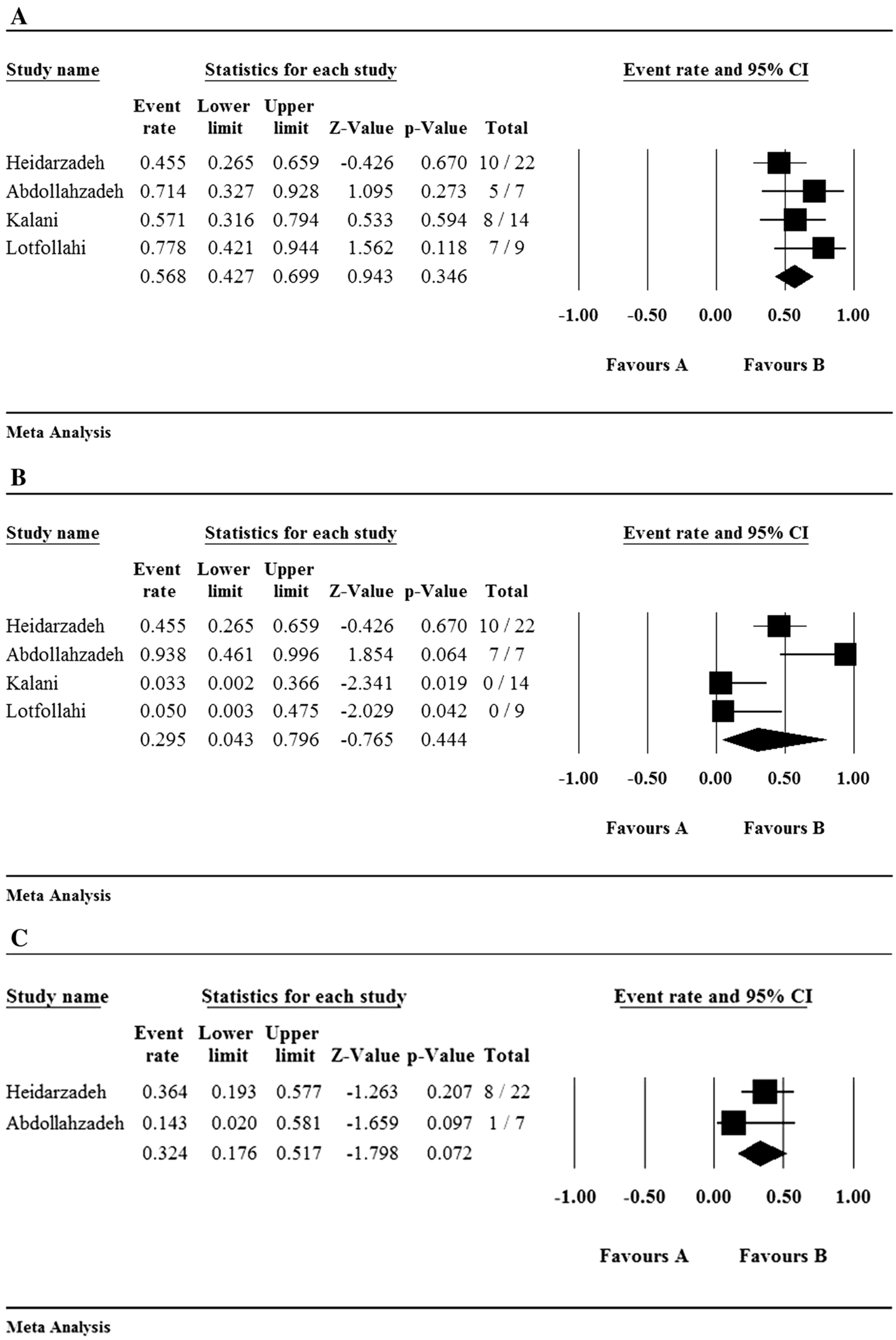

Fig. 3 Forest plots depicting the prevalence of antibiotic resistance of *L. monocytogenes* to penicillin (**a**), ampicillin (**b**) and gentamicin (**c**) in human specimens

alterative antibiotics, due to their low resistance rates, in the treatment of human listeriosis in Iran. Finally, we recommend evaluating mechanisms of antibiotic resistance in *Listeria* species, especially *L. monocytogenes* in Iran.

Compliance with ethical standards

Conflict of interest The authors declare that there is no conflict of interest.

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