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Status of *Linguatula serrata* infection in livestock: A systematic review with meta-analysis in Iran

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ABSTRACT

Objectives: The present systematic review attempted to determine the prevalence of *Linguatula serrata* (*L. serrata*) infection among Iranian livestock. The *L. serrata* known as tongue worm belongs to the phylum pentastomida and lives in upper respiratory system and nasal airways of carnivores. Herbivores and other ruminants are intermediate hosts.

Methods: MEDLINE, Embase, Web of Science, Google Scholar, and the Cochrane Library were searched from Nov 1996 to 22 Apr 2019 by searching terms including "*Linguatula serrata*", "linguatulosis", "pentastomida", "bovine", "cattle", "cow", "buffalo", "sheep", "ovine", "goat", "camel", "Iran", and "prevalence" alone or in combination. The search was conducted in Persian databases of Magiran, Iran doc, Barakatkns (Iran medex) and Scientific Information Database (SID) with the same keywords. After reviewing the full texts of 133 published studies, 50 studies had the eligibility criteria to enter our review.

Results: By random effects model analysis, the pooled prevalence of linguatulosis was 25% (95% CI: 18.0–33.0, $I^2 = 98.67$ % , $P < 0.001$) in goats; 15.0% (95%CI: 10.0–20.0, $I^2 = 97.95$ % , $P < 0.001$) in sheep; 12.0% (95%CI: 7.0–18.0, $I^2 = 98.05$ % , $P < 0.001$) in cattle; 7% (95%CI: 2.0–16.0, $I^2 = 97.52\%$) in buffalos and 11.0% (95%CI: 6.0–16.0%, $I^2 = 96.26$ % , $P < 0.001$) in camels. The overall prevalence in livestock was estimated to be 25%. The highest infection rate was recorded in West Azerbaijan Province (68%) and the lowest rate was in Khuzestan Province (0.23%) ($P < 0.05$).

Conclusions: We concluded that the high prevalence of *L. serrata* infection in livestock (mainly ovine linguatulosis) show the endemic status of linguatulosis in several parts of Iran and will pose a risk for inhabitants. Control strategies to reduce the parasite burden among these animals are needed.

Contents

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1. Introduction

Linguatula serrata (*L. serrata*) is one of the cosmopolitan zoonotic food-borne parasites which belongs to class pentastomida. The shape of this parasite resembles tongue and this is the reason of calling this parasite "tongue worm". The lifecycle of this parasite includes four stages: eggs, larvae, nymphs, and adults. The adults live in the upper respiratory system and nasal airways and frontal sinuses of the carnivores, especially dogs as final hosts. Eggs which discharge with nasopharyngeal secretions of the definitive host can be swallowed by herbivores (as intermediate hosts) such as cattle, buffalo, sheep, goat, etc. Then, the larvae hatch from the eggs and migrate mainly to mesenteric lymph nodes (MLNs) and other visceral organs (such as liver, lung, spleen, heart, etc.). The parasite can be transferred to the final host through consumption of meat or viscera of infected intermediate host (Soulsby, 1982; Oryan et al., 2008; Akhondzadeh Basti and Hajimohammadi, 2011; Hajipour and Tavassoli, 2019). Parasites entered in intermediate host cause pathological lesions and signs. Symptoms depend on the infected organ (Tavassoli et al., 2007a; Tavassoli et al., 2017; Shakerian et al., 2008; Dehkordi et al., 2014). Infection with this parasite causes symptoms in intermediate hosts including, emaciation, pale mucosal membranes, ascites, and serous accumulation in abdominal cavity, peritoneal inflammation, and intestinal adhesion. Important symptoms caused by the disease in sheep include: hyperplasia of pulmonary lymphatic tissue and pneumonia (Oryan et al., 2008; NourollahiFard et al., 2011). Humans can act as both intermediate and accidental final host for *L. serrata* and that means both larval and adult stages can infect humans (Koehsler et al., 2011). In humans, like other intermediate hosts, parasites mainly live in MLNs. But other organs such as liver, intestine, rarely brain, eye and prostate glands may also be affected (Islam et al., 2018). In some cases, migratory nymphs have recovered from anterior chamber of eye. In addition, other involvements like iritis and secondary glaucoma have been reported (Ryan and Durand, 2011). Human infection occurred via accidental ingestion of eggs passed from an infected dog or through consumption of raw/under-cooked infected viscera of contaminated sheep, goats, and cattle (Razavi et al., 2004). The most common form of human linguatulosis known as Halzoun syndrome (Marrara syndrome) is transmitted by ingestion of *L. serrata* nymphs (adult stage) found in intermediate host's organs and resulting in nasopharyngeal linguatulosis with signs of pharyngitis, salivation, dysphagia, and cough which all together cause type I hypersensitivity known as Halzoun syndrome. In case of visceral linguatulosis, the disease remains asymptomatic (Hajipour and Tavassoli, 2019; Shakerian et al., 2008; Meshgi and Asgarian, 2003). Detection of parasite nymphs in intermediate host is performed by biopsy, exploratory laparotomy, postmortem examination, and subsequent histopathology (Hendrix, 1998). In asymptomatic cases, there is no need for treatment as the parasite will degenerate after two years; and in symptomatic cases with high burden of parasite, surgical procedures could be useful (Hajipour and Tavassoli, 2019). It seems that visceral linguatulosis in endemic areas for *L. serrata*, like the Middle East region, is more than diagnosed cases (Oluwasina et al., 2014; Ravindran et al., 2008). In a study carried out in India, the prevalence of linguatulosis among examined animals was estimated to be about 18% (Sudan et al., 2014). Likewise, researchers in Bangladesh reported 19% in cattle (Ravindran et al., 2008) which reveals the equal prevalence in two neighborhood countries. Some researchers in Bangladesh reported that 50.7% of cattle and 31.0% of goats were diagnosed to be infected and they declared that human populations of the country are at high risk of linguatulosis (Islam et al., 2018). The results of a study conducted in Egypt in 2017 revealed that the total prevalence of linguatulosis was 22.8% in herbivorous animals with highest infection in goats (30%) and lowest in donkeys (8%) (Attia et al., 2017). Human cases have been detected in Asian countries including Turkey, Malaysia, China, India, and Bangladesh (Hajipour and Tavassoli, 2019). In Malaysia, the prevalence of 45.4% in adults has been reported (Prathap and Prathap, 1969). Also, such Middle East countries including Egypt, Tunisia, and Sudan have reported human infection cases (Hajipour and Tavassoli, 2019). Although some human cases have been reported from Iran, there is no clear estimation of the prevalence of the infection in Iranian population.

Numerous studies have been carried out on linguatulosis among the ruminants in Iran. Nonetheless, there is no exact estimation about the accurate load of this parasite in animals which is critical for economic burden evaluation and establishment of controlling strategies.

Based on numerous impacts of linguatulosis on the animal welfare, economy and public health, further considerations and research are deemed to be a desideratum for the epidemiological features and approaches for monitoring programs in Iran. Considering the widespread distribution of linguatulosis in Asian countries such as India and Bangladesh and trademark between countries, the importance of infection is more remarkable nowadays. As far as the researchers of this study investigated, there is no documented review about the exact prevalence of linguatulosis in livestock in Iran. Therefore, the current study is an attempt to fill out this gap.

2. Methods

A. Bibliography

We performed bibliographic search according to the following topics:

Articles: Complete articles, congress summaries, and unpublished data were considered.
Type of studies: All original descriptive studies (designated as cross-sectional) about animal linguatulosis were concerned.
Epidemiological parameters of interest: Prevalence of *L. serrata* infection in animals was considered.

B. Search strategy

The review was conducted according to the preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines. MEDLINE, Embase, Web of Science, Google Scholar, and the Cochrane Library were searched in English language from Nov 1996 to 22 Apr 2019 for studies on linguatulosis by search terms including "*Linguatula serrata*", "linguatulosis",

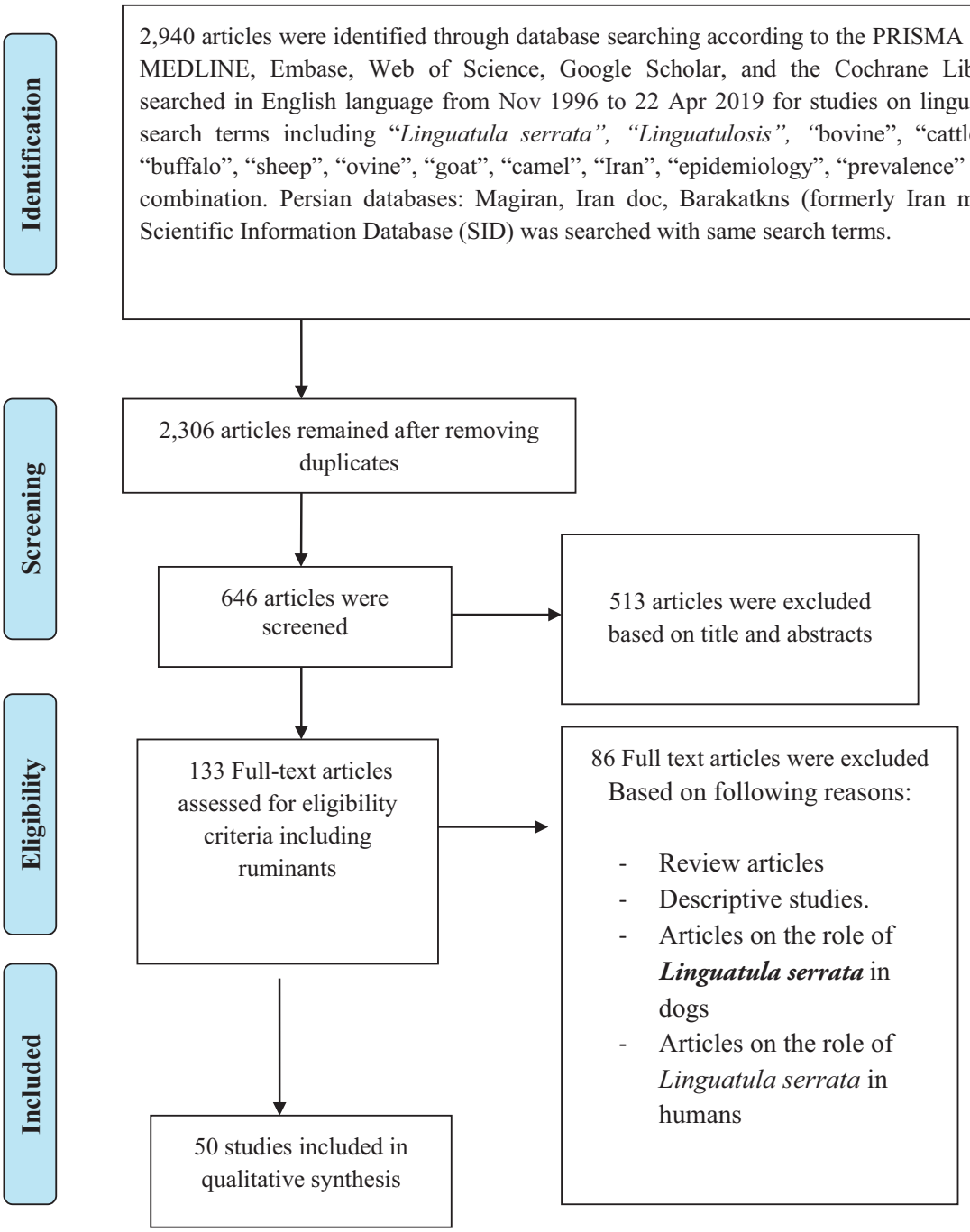

Fig. 1. Flow diagram of classification of articles for inclusion in this systematic review and meta-analysis.

"pentastomida", "bovine", "cattle", "cow", "buffalo", "sheep", "ovine", "goat", "camel", "Iran", "epidemiology", and "prevalence" alone or in combination. The flow diagram of the study design is shown in Fig. 1.

Likewise, relevant studies were extracted from Persian databases including: Magiran, Iran doc, Barakatkns (formerly Iran medex), and Scientific Information Database (SID) with the same keywords.

A. Data collection

We inclusively searched all the mentioned databases and unpublished data. The collected bibliographic references were screened carefully in order to eliminate duplicates, case reports, case series, carnivores, studies out of Iran, and human-based studies. Finally, papers with epidemiological parameters of interest were selected and 50 articles met the inclusion criteria. Those articles reporting the prevalence of linguatulosis in herbivores were included in the study (Table 1). The following data were extracted from the literature: first author, year of publication, animal's gender, prevalence rate, geographical region of study, sample size (the number of examined animals), and the year in which studies were carried out (Tables 1, 2). References of the published data were also surveyed to extend the study and to prevent missing valuable data. Eligible data were recorded in a selection sheet (Appendix).

Table 1
Baseline characteristics of included studies.

No.	Province	Total number of examined	Number of positives (%)	Reference
1	Khuzestan	3958	9(0.23)	Saiyari et al. (1996)
2	Chaharmahal and Bakhtiari	222	1(0.45)	Shekarforoush and ArzaniShahni (2001)
3	Fars	204	74(36.27)	Razavi et al. (2004)
4	Fars	200	29(14.5)	Shekarforoush et al. (2004)
5	East Azarbaijan	1920	537(27.96)	Nematollahi et al. (2005)
6	WestAzarbaijan	110	48(43.63)	Tajik et al. (2006)
7	West Azarbaijan	200	105(52.5)	Tavassoli et al. (2007a)
8	WestAzarbaijan	100	68(68)	Tavassoli et al. (2007b)
9	Isfahan	400	102(25.5)	Shakerian et al. (2008)
10	West Azarbaijan	80	15(18.75)	Tajik et al. (2008)
11	Kohgiluyeh and Boyer-Ahmar	139	73(52.51)	Alborzi and Darakhshandeh (2008)
12	WestAzarbaijan	600	5(0.83)	Rasouli et al. (2009)
13	East Azarbaijan	800	3(0.37)	Hami et al. (2009)
14	Kerman	407	263(64.61)	NourollahiFard et al. (2010a)
15	Kerman	210	38(18.09)	Radfar et al. (2010)
16	West Azarbaijan	366	28(7.65)	Tajik and Sabet Jalali (2010)
17	Kerman	450	103(22.88)	NourollahiFard et al. (2010b)
18	East Azarbaijan	140	23(16.42)	Haddadzadeh et al. (2010)
19	Mazandaran	135	24(17.77)	Youssefi and Haddadzadeh Moalem (2010)
20	East Azarbaijan	420	223(53.09)	Mirzaei et al. (2011)
21	West Azarbaijan	1663	646(38.84)	Rezaei et al. (2011)
22	East Azarbaijan	280	92(32.85)	Garedaghi (2011)
23	Tehran	100	64(64)	Rajabloo et al. (2011)
24	Kerman	808	132(16.33)	NourollahiFard et al. (2011)
25	West Azarbaijan	136	42(30.9)	Yakhchali and Tehrani (2011)
26	Yazd	101	13(12.9)	Oryan et al. (2011)
27	Mazandaran	307	107(34.8)	Youssefi et al. (2012)
28	Razavi Khorasan	400	73(18.25)	NourollahiFard et al. (2012)
29	Isfahan	232	49(21.12)	Rezaei and Tavassoli (2012)
30	East Azarbaijan	740	444(60)	Rezaei et al. (2012)
31	East Azarbaijan	400	70(17.5)	Mirzaei et al. (2012)
32	East Azarbaijan	185	22(11.89)	Mirzaei et al. (2013)
33	Khozestan	223	37(16.6)	Alborzi et al. (2013)
34	Hamedan	300	46(15.33)	Sadeghi Dehkordi et al. (2014)
35	Tehran	799	258(32.3)	Bokaie et al. (2014)
36	Isfahan	620	337(54.35)	Pirali Kheirabadi et al. (2014)
37	Kerman	132	27(20.5)	Bamorovat et al. (2014)
38	Tehran	774	198(25.58)	HasanzadehKhanbaghi et al. (2014)
39	Isfahan	506	71(14.03)	PiraliKheirabadi et al. (2015)
40	East Azarbaijan	640	144(22.5)	Nematollahi et al. (2015)
41	Chaharmahal and Bakhtiari	200	27(13.5)	Azizi et al. (2015)
42	East Azarbaijan	200	13(6.5)	Alipourazar and Garedaghi (2015)
43	Mazandaran	50	20(4)	Youssefi et al. (2016)
44	Kermanshah	1258	241(19.15)	Hashemnia et al. (2018)
45	Yazd	272	50(18.38)	Farjanikish and Shokrani (2016)
46	Hamedan	1080	163(15.09)	Gharekhani et al. (2017)
47	Mazandaran	6249	568(9.08)	Tabaripour et al. (2017)
48	Razavi Khorasan	400	76(19%)	Farshchi et al. (2018)
49	Tehran	767	66(8.6%)	Bokaie et al. (2018)
50	West Azarbaijan	104	63(60.6%)	Tavassoli et al. (2018)

Table 2
Pooled prevalence (95%CI) of *Linguatula serrata* in different provinces of Iran.

Province	Goat	Sheep	Cattle	Buffalo	Camel
Tehran	53.0(46.0–60.0)	NES	NES	NES	NES
Fars	16.0(13.0–20.0)	7.0(4.0–9.0)	NES	NES	NES
East Azarbaijan	17.0(6.0–32.0)	22.0(11.0–36.0)	6.0(1.0–14.0)	1.0(0.0–2.0)	5.0(1.0–10.0)
West Azarbaijan	35.0(2.0–80.0)	27.0(5.0–57.0)	21.0(1.0–58.0)	8.0(1.0–21.0)	NES
Kerman	31.0(28.0–34.0)	16.0(13.0–18.0)	11.0(9.0–13.0)	NES	11.0(2.0–27.0)
Mazandaran	41.0(2.0–78.0)	7.0(6.0–8.0)	7.0(3.0–13.0)	NES	NES
Hamedan	20.0(7.0–37.0)	13.0(11.0–18.0)	NES	NES	NES
Isfahan	26.0(24.0–28.0)	6.0(5.0–8.0)	NES	NES	14.0(4.0–29.0)
Kermanshah	25.0(22.0–28.0)	NES	13.0(11.0–15.0)	NES	NES
Chaharmahal and Bakh	NES	4.0(0.0–11.0)	NES	NES	NES
Kohgiluyeh and Boyer	NES	23.0(18.0–28.0)	NES	NES	NES
Yazd	NES	NES	NES	NES	7.0(1.0–15.0)
Heterogeneity (I^2, P)	99.3%, p < 0.001	98.1%, p < 0.001	97%, p < 0.001	97.5%, p < 0.001	96.3%, p < 0.001

NES=No enough sample.

B. Paper collection

Three independent reviewers (R. Tabaripour, M. Keighobadi and S. HosseiniTeshnizi) screened the studies for their qualifications for inclusion in this study (Kapp index showed an agreement of 91% between four reviewers). Disagreements were resolved by M. Fakhar and A. Shokri.

C. Quality of studies

The quality of meta-analysis was evaluated with STROBE checklist. A checklist including 22 items was considered for well reporting of observational studies. These items were related to the article's title, abstract, introduction, methods, results, and discussion sections. The score under 7.75 was considered a poor quality, between 7.76 and 15.5 low, between 15.6 and 23.5 moderate, and >23.6 high (Von Elm et al., 2007).

D. Statistical analysis

In this meta-analysis, the number of examined and the number of positive cases were extracted from each study and then standard error (SE) was calculated using the following equation: $SE_p = \sqrt{\frac{p(1-p)}{n}}$ (where n and p are the sample size and prevalence of study, respectively). Cochran's heterogeneity statistic ($p < 0.1$) and the I-squared index (25%: low; 50%: medium and 75%: high) were used to evaluate heterogeneity across effect sizes (ESs).

The prevalence for each study and pooled estimate of prevalence were presented in a forest plot in which we reported the results as ES with 95% confidence intervals (CI). When heterogeneity was present, we used a random effects model (DerSimonian–Laird method); otherwise we applied a fixed effects model (Mantel–Haenszel method) to estimate pooled effects size. Subgroup analysis was used to evaluate source of heterogeneity among studies. Potential publication bias was explored using Egger's test ($P < 0.1$ as significant). The meta-analysis was performed with the trial version of Stata MP Version 14 statistical software.

3. Results

Among all databases searched from 1996 to 2019 (~24 years), a total of 50 articles were appropriate to be included in this systematic review and meta-analysis study. All the articles were cross-sectional which had been designated to evaluate the prevalence of *L. serrata* in herbivores including sheep, goat, cattle, buffalo, and camel in Iran. Totally, 11,807 sheep, 14,084 goats, 8037 cattle, 2188 buffaloes and 3791 camels were examined, respectively (Table 1).

The pooled prevalence of *L. serrata* in goats under a random-effects model was estimated 25.0 (95%CI: 18.0–33.0, $I^2 = 98.67$ % , $P < 0.001$). The pooled prevalence was significantly higher than zero (ES = 0: z = 10.77 $P < 0.001$) (Fig. 2). Also the pooled prevalence of *L. serrata* in sheep under a random-effects model was estimated 15.0 (95%CI: 10.0–20.0, $I^2 = 97.95$ % , $P < 0.001$) and the pooled prevalence was significantly higher than zero (ES = 0: z = 10.36, $P < 0.001$) (Fig. 3).

In the same way, random effect model showed the prevalence of *L. serrata* in cattle 12.0 (95%CI: 7.0–18.0, $I^2 = 98.05$ % , $P < 0.001$) which was significantly higher than zero (ES = 0: z = 11.23 $P < 0.001$) (Fig. 4). The pooled prevalence of *L. serrata* in buffaloes was estimated 7.0% (95%CI: 2.0–16.0, $I^2 = 97.52$ % , $P < 0.001$) and was significantly higher than zero (ES = 0: z = 3.41 $P < 0.001$) (Fig. 5). By same model, the pooled prevalence of *L. serrata* in camels was estimated 11.0% (95%CI: 6.0–16.0%, $I^2 = 96.26$ % , $P < 0.001$) being significantly higher than zero (ES = 0: z = 3.41 $P < 0.001$) (Fig. 6).

The forest plot diagram of this review is shown in Figs. 2–6. The highest infection rate was in goats (25%) and then in sheep (15%), cattle (12%), camels (11%) and the lowest infection rate was in buffaloes (7%), respectively. Most of the studies about goats

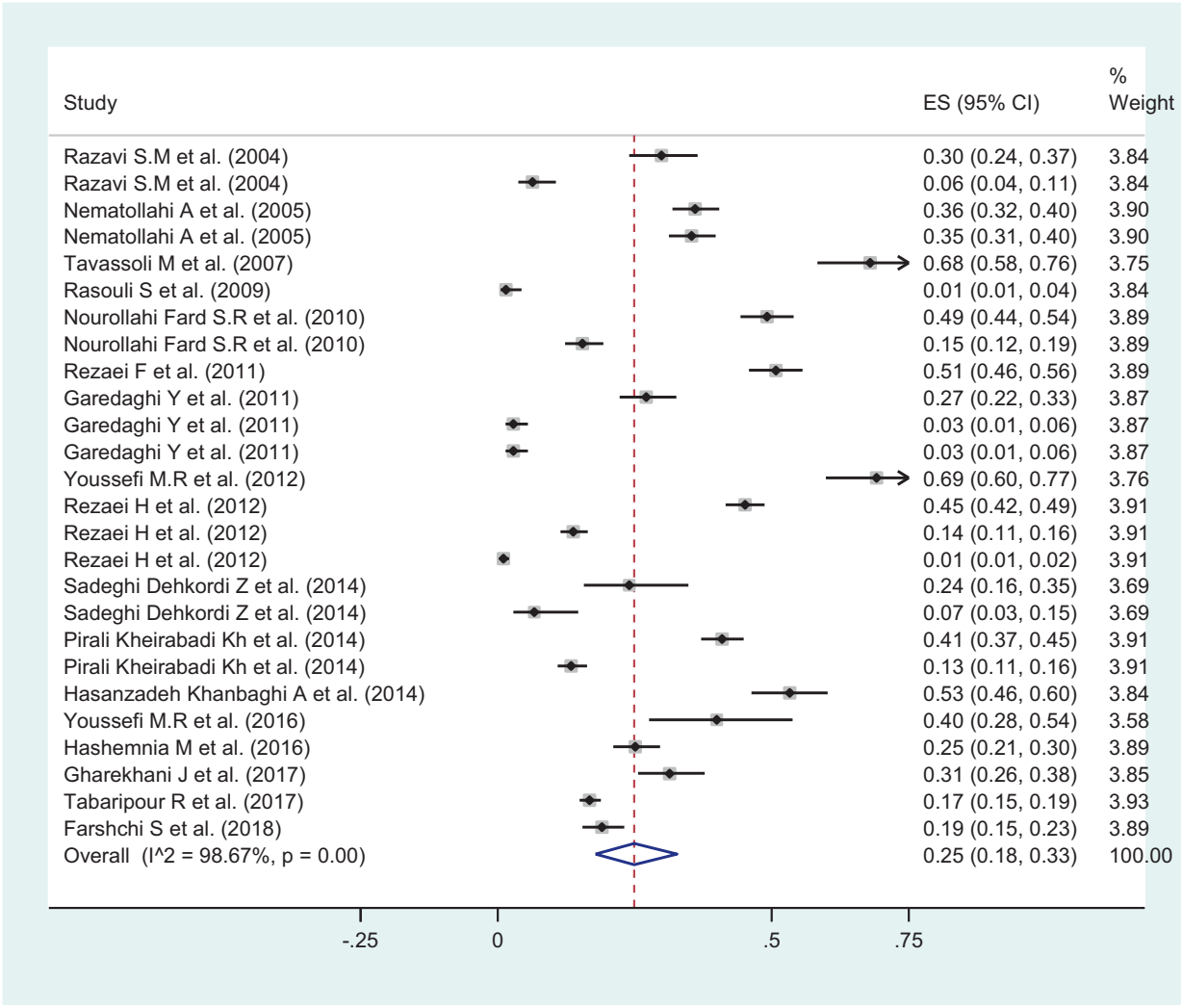

Fig. 2. Schematic graph showing proportion meta-analysis plot of *Linguatula serrata* in goats in Iran (random-effects).

belonged to Tehran Province [53.0(46.0–60.0)] and West Azerbaijan had the highest number of studies conducted on sheep [27.0 (5.0–57.0)], cattle [21.0(1.0–58.0)], and buffaloes [8.0(1.0–21.0)], respectively. In addition, Kerman Province had the most records in camels [11.0(2.0–27.0)] (Table 2).

The subgroup analysis showed that the infection rate in male animals was significantly more than females ($p = 0.00$) except for the sheep (Table 3). Moreover, as data analysis showed, the highest prevalence of 56% was seen in mediastinal lymph nodes in goats while the maximum prevalence of 23% of mesenteric lymph nodes (MLNs) was seen in sheep and the lowest prevalence was about 0.01% in the liver of cattle (Table 3). There was a publication bias according the Egger's test which revealed the significant bias in the studies related to buffaloes ($p = 0.009$) (Table 4). This result might be due to the fewer publications about buffaloes (8 studies).

In addition, distribution of *L. serrata* in 13 provinces of Iran is shown in (Table 1). The highest infection rate of *L. serrata* in herbivores was recorded in West Azerbaijan Province (68%), then Kerman (64.61%), followed by Tehran (64%), East Azerbaijan (60%), Isfahan (54.35%), and Kohgiluyeh and Boyer-Ahmar (52.51%); meanwhile, the lowest rate belonged to Khuzestan (0.23%) with a significant difference among them (Table 1).

4. Discussion

Several studies have been carried out to determine the prevalence of *L. serrata* among herbivores in Iran, but there is no documented exact estimation about this subject.

As the parasite involves the ruminants, the rate of infection is high in regions with farming animal activities. The highest infection rate was reported in goats and in all provinces; Mazandaran with 69.15% infection rate had the highest rate in Iran. This

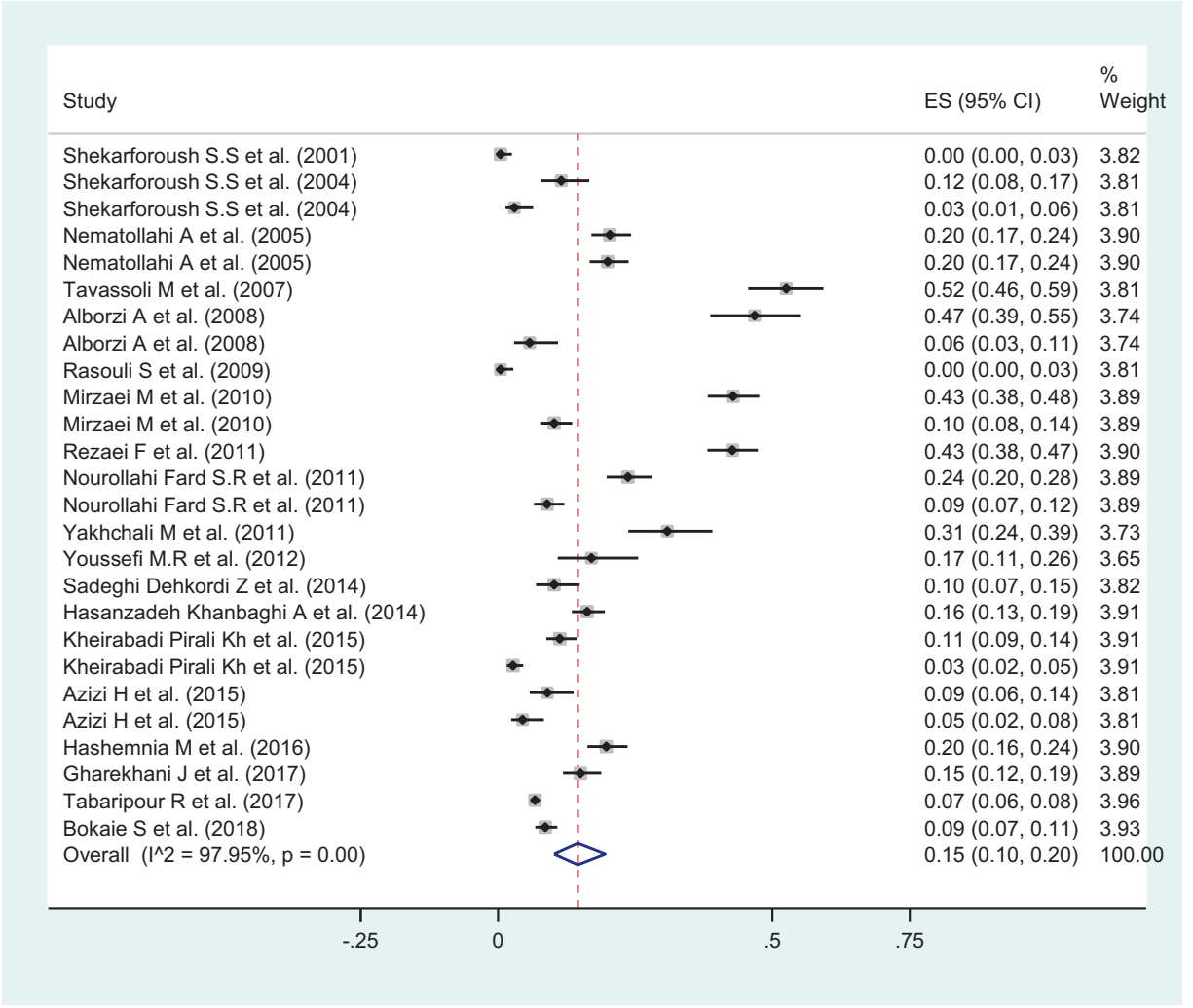

Fig. 3. Schematic graph showing proportion meta-analysis plot of *Linguatula serrata* in sheep in Iran (random-effects).

may be related to the climatic condition and humidity, different forage habitats of goats, or more exposure to dogs (Hajipour and Tavassoli, 2019). Overall, Tabriz in East Azerbaijan (68%) and Urmia in West Azerbaijan (60%) had the highest prevalence rates of infection. The reason for high prevalence of infection in these regions may be related to the climatic parameters and high humidity which create optimum condition for parasite eggs survival in the environment. Also, infection with *L. serrata* seems to be higher in mediastinal and mesenteric regions because the mesenteric lymph nodes, located in the way of portal circulation formerly than other organs. In a study carried out by NourollahiFard in 2010, they examined mesenteric and mediastinal lymph nodes of 450 cattle at different sexes and age groups. In this study, they found that 16.22% of mesenteric lymph nodes were infected with this parasite and the infection rate was increased with age as the higher prevalence of infection was observed in animals aged above four years. Also, the prevalence of *L. serrata* nymphs in different seasons differed significantly ($p < 0.05$) and the infection rate was higher in autumn season which may be due to humidity or climatic variations (NourollahiFard et al., 2010a). Rezaei et al. (2011) studied the prevalence of *L. serrata* infection among dogs (definitive host) and domestic ruminants (intermediate host) in the northwestern parts of Iran. They examined upper respiratory tract of 97 dogs (45 females and 52 males) and the mesenteric lymph nodes (MLNs) of 396 goats (203 females and 193 males), 406 buffaloes (166 females and 240 males), 421 cattle (209 females and 212 males), and 438 sheep (223 females and 215 males) for *L. serrata* infection. They categorized the animals into four age groups, including younger than six months, six to 24 months, two to four years, and older than four years old. Their results showed that 27.83% of dogs were infected with *L. serrata*. The infection rate for goats, buffaloes, cattle and sheep was 50.75%, 26.6%, 36.62% and 42.69%, respectively.

The results revealed that there was a significant correlation between prevalence rate with age and sex in all animals ($P \leq 0.05$). The highest prevalence rate was found in goats ($P \leq 0.05$) (Rezaei et al., 2011). In a study carried out in Urmia in 2006 by Tajik et al., the rate of 44% infection with *L. serrata* was reported in MLNs of examined cattle while in 2009, Yakhchali and Tehrani, 2011 reported the prevalence rate of 57% in MLNs of cattle in the same city (Tajik et al., 2006; Yakhchali and Tehrani, 2011).

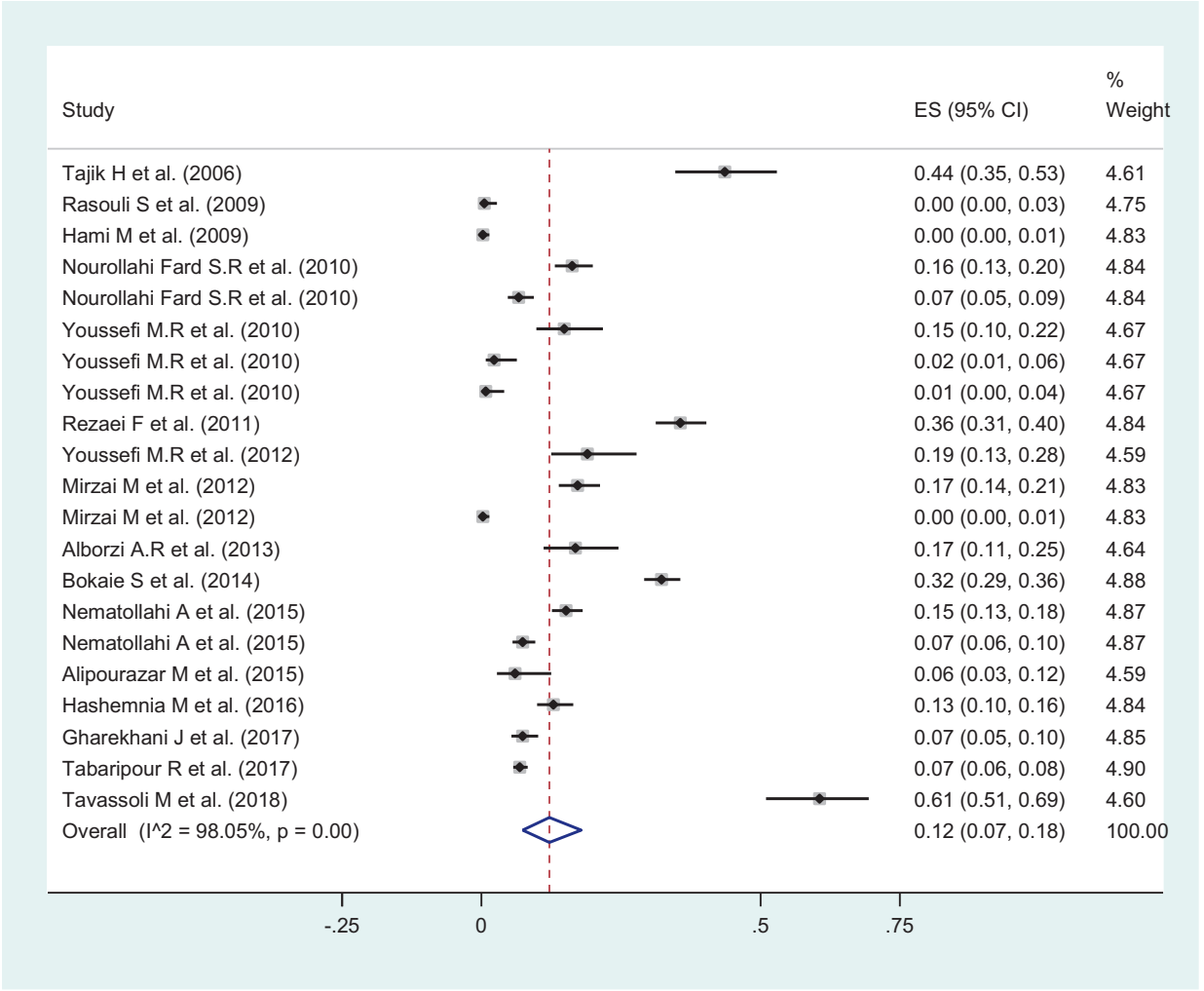

Fig. 4. Schematic graph showing proportion meta-analysis plot of *Linguatula serrata* in cattle in Iran (random-effects).

Furthermore, Mirzai et al. reported the prevalence rate of 17.25% infection in MLNs of cattle in Tabriz and the prevalence rate of 16.8% was reported in Ahvaz in 2013 by Alborzi et al. (Mirzaei et al., 2012; Alborzi et al., 2013). Only 8 studies are available about buffaloes' linguatulosis in Iran and the highest prevalence of 26.6% was reported from MLNs by Rezaei et al. (2011) in Urmia and the rate of 18.75% by Tajik et al. (Tajik et al., 2008; Sinclair, 1954). Sheep were the most studied herbivores in Iran and the highest rate of infection with *L. serrata* (52.5%) was reported in 2007 by Tavassoli et al. in Urmia (Tavassoli et al., 2007b) followed with 42.69% reported by Rezaei et al. in 2011 in the same region (Rezaei et al., 2011). The high prevalence of linguatulosis in dogs and domestic ruminants revealed that there is a high risk of this infection as an endemic disease in the northwestern region of Iran. Also, the study with serological method carried out by Yektaseresht et al. in 2017 in Fars Province revealed the seropositivity of 46.66% in sheep (Yektaseresht et al., 2017). Since this province is one of the most important foci of animal husbandry, preventive measurements and control of infection with *L. serrata* should be seriously considered in this province.

Prevalence studies of *L. serrata* from different regions in domestic animals have shown that the infection has a global distribution. The reports indicating the prevalence of 43% in Beirut (Khalil and Schacher, 1965), 72% in certain areas of Britain (Sinclair, 1954), 50.7% in Bangladesh cattle (Islam et al., 2018), 13.8% in Talca, Chile (Parraguez et al., 2017), 14.47% in Iraqi cattle (A1-Sadi and Ridha, 1994), and 25% in Egyptian camels (Khalil, 1973). These data show the wide range of infection among animals in the world.PF.

In a study carried out in 2017 in Australia by Shamsi et al., the researchers chose a number of definitive hosts for infection, including red foxes, feral cats, wild dogs, and intermediate hosts including cattle, sheep, feral pigs, rabbits, goats, and a European hare from the hilltops of south-eastern Australia for detecting *L. serrata* among them. Their results showed that totally 14.5% of red foxes (n = 55), 67.6% of wild dogs (n = 37), and 4.3% of cattle (n = 164) were infected. They concluded that common occurrence of the parasite in wild dogs, and less frequently in foxes, suggests that these wild canids can act as a potential reservoir for infection of livestock, wildlife, domestic dogs, and possibly humans. The high rate of linguatulosis in

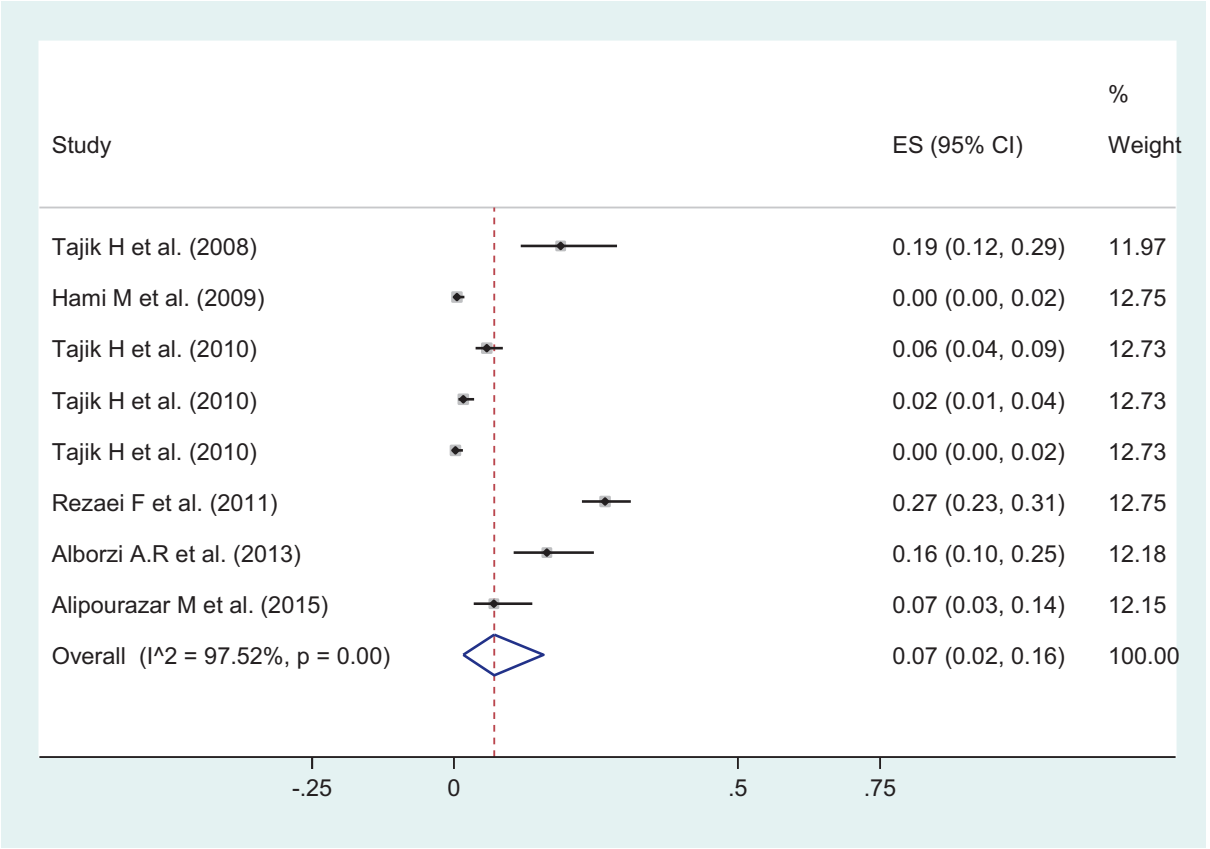

Fig. 5. Schematic graph showing proportion meta-analysis plot of *Linguatula serrata* in buffaloes in Iran (random-effects).

wild dogs and foxes in south-eastern Australia suggests that this parasite is more common than what it was previously estimated. Among all potential intermediate hosts in the area, only 4.3% of cattle were infected with parasites' nymphs which suggest that the search for the host(s) acting as the main intermediate host in the region should be continued (Shamsi et al., 2017). There is a correlation between animal husbandry and canine linguatulosis. Eating the raw offal, especially liver of farm animals, is the main source of canine infection. In the mentioned study, stray dogs were more infected than owned dogs which can be justified with better veterinary cares and feeding in the second group (Oluwasina et al., 2014).

Reports from Asian countries, and especially the Middle East region and Iran confirm that linguatulosis poses veterinary and public health importance. In addition, in the Middle East, Halzoun also occurs after consuming uncooked sheep/goats in some religious feasts. Also, a new intermediate host named crested porcupines (*Hystrix indica*) which consumes meat and viscera has been reported from southwest of Iran (Rajabloo et al., 2014). Several human nasopharyngeal involvement cases have been reported from Iran following the consumption of barbecued liver (Tabibian et al., 2012; Maleky, 2001; Siavashi et al., 2002; Mohammadi et al., 2008). It is believed that some unhealthy mindsets, such as the belief that eating raw liver is nutritionally more efficient, play an important role in human linguatulosis in Iran. In this regard, Montazeri et al. reported two cases of linguatulosis in the nose and mouth of a 28 year old woman and her 11 year old daughter who had a history of eating the raw gut of sheep and complained of coughing, headache, oral and nasal discharge (Montazeri et al., 1997). In addition, Sadjjadi et al. reported a case of pharyngeal linguatulosis in a 35 year old woman in Shiraz (Sadjjadi et al., 1998).

In a study carried out in Kerman by Yazdani et al., a 32-year-old woman with history of eating raw liver and complaining of upper respiratory symptoms was reported (Yazdani et al., 2014). Maleky et al. in Tehran reported a 25 year old woman with throat pentastomiasis (Maleky, 2001). Also, two cases of Halzoun syndrome were reported in 2012 from Isfahan by Tabibian et al. They reported an Afghan mother and daughter (aged 34 and 23) in Isfahan with history of eating raw goat liver (Hamid et al., 2012). Siavoshi et al. reported three cases of Halzoun syndrome including a man and two women with history of consuming raw liver (Siavoshi et al., 2002). The latest report of pharyngeal linguatulosis was released by Jahanbakhsh et al. in Kermanshah about a 34 year old man with history of consuming raw goat liver (Janbakhsh et al., 2015).

In Turkey, human infestation with *L. serrata* has also been reported. Yilmaz et al. reported a 26 year old woman in Van Province complaining of coughing Yilmaz et al. (2011). Also, a pentastomiasis case in a 70 year old native farmer from Keningau,

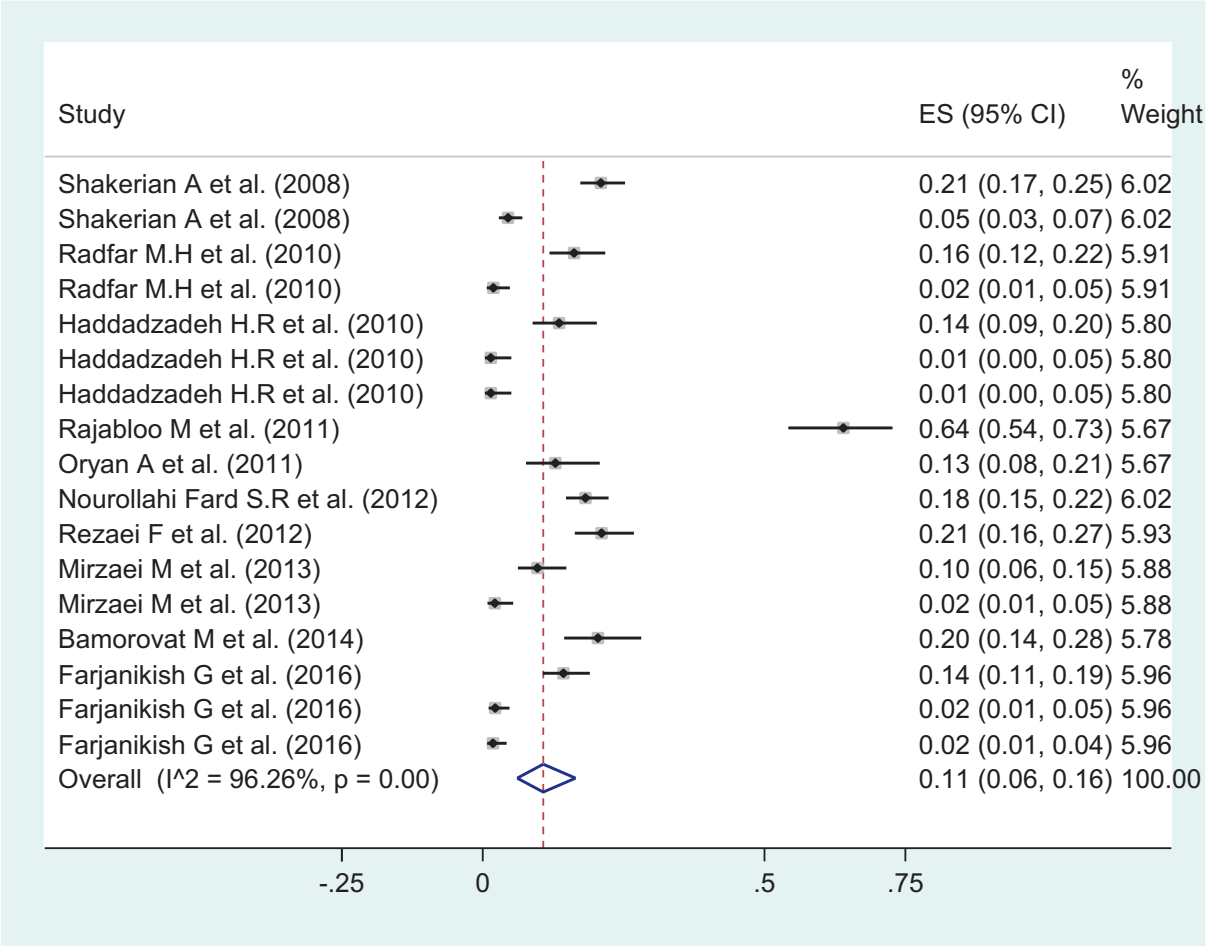

Fig. 6. Schematic graph showing proportion meta-analysis plot of *Linguatula serrata* in camels in Iran (random-effects).

Sabah, East Malaysia was reported in 2011 with a one-month history of upper abdominal discomfort, weight loss, anorexia, jaundice, and dark urine. After using the Whipple procedure and doing some histopathological examinations, the parasite was diagnosed as a nymph stage of *Armillifer moniliformis* (Latif et al., 2011). Overall, these results show that special attention should be paid to the public health and animal care in order to prevent the infection in Asian and African countries.

In conclusion, the high prevalence of *L. serrata* infection in the Iranian livestock (mainly ovine linguatulosis) shows the endemic status of linguatulosis in Iran and will pose a risk for the inhabitants. In developing countries, the main reason of getting infected among individuals with low economical income is consuming offal (and especially raw offal) such as tongue, brain, liver, kidney, intestine, and heart. Therefore, an exact inspection of visceral organs and particularly lymph nodes is needed in the slaughter houses to prevent human linguatulosis. Accordingly, people should be aware of the disadvantages and risks of eating

Table 3
Pooled prevalence (95%CI) of *Linguatula serrata* according sex and involved organ.

		Goat	Sheep	Cattle	Buffalo	Camel
Sex	Male	27.0(15.0–40.0)	12.0(4.0–20.0)	18.0(12.0–25.0)	NES	16.0(8.0–24.00)
	Female	23.0(16.0–31.0)	20.0(7.0–33.0)	12.0(8.0–16.0)	13.0(5.0–22.0)	15.0(8.0–22)
	p-Value	<0.001	<0.001	<0.001	–	0.091
Involved organ	Mesenteric lymph nod	15.0(8.0–24.0)	23.0(14.0–34.0)	20.0(13.0–28.0)	16.0(6.0–30.0)	16.0(13.0–19.0)
	Liver	22.0(7.0–43.0)	7.0(0.0–25.0)	0.01(0.00–1.0)	NES	3.0(1.0–5.0)
	Mediastinal lymph nodes	52.0(48.0–56.0)	6.0(3.0–11.0)	NES	NES	2.0(1.0–3.0)
	Lung	52.0(35.0–68.0)	NES	4.0(1.0–7.0)	1.0(0.0–2.0)	NES
	Mesenteric and Media	17.0(15.0–19.0)	16.0(14.0–18.0)	NES	NES	NES
	Spleen	NES	NES	NES	NES	NES
	Lymph nodes (LN)	NES	NES	NES	NES	NES

NES=No enough sample.

Table 4
The results of *Egger's test* to assess publication bias among studies.

Animals	Coef	Std. Err.	t	p-Value
Goat	1.97	1.91	1.03	0.32
Sheep	2.03	1.19	1.70	0.11
Cattle	0.06	1.44	0.03	0.83
Buffalo	6.10	1.59	3.83	0.009
Camel	1.38	2.04	0.68	0.51

raw / undercooked liver or other internal organs of herbivores. Meanwhile, physicians should also be aware of the illness and consider *L. serrata* infestation in patients with complains of upper respiratory tract symptoms in endemic areas. Altogether, our data provide some valuable information regarding the epidemiology of linguatulosis in domestic ruminants in Iran which will likely be very favorable for management and control programs of this disease. Therefore, feeding dogs with the offal of infected animals should be prevented in order to control the infection in ruminants.

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Declaration of Competing Interest

The authors declare that there is no conflict of interests.

Appendix A. Article information sheet

Article type……

Title……

Author(s)……

Date……

Journal……

Year, Volume, Pages……

Study design……

Methodology……

Sample size……

Diagnostic test……

Test relevance ……

Test cut off ……

Study region ……

Results……

After contact with investigators: Include/ Exclude

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