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Review

Prevalence and associated risk factors of *Linguatula serrata* infection in definitive and intermediate hosts in Iran and other countries: A systematic review

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ABSTRACT

Linguatula serrata is known as a cosmopolitan zoonotic parasite whose adult form inhabits the upper respiratory system, nasal airways and frontal sinuses of dogs, foxes, cats and other carnivores, which are recognized as its final hosts. Its immature form resides in mesenteric lymph nodes, liver, lungs and spleen of herbivorous and other ruminants, which serve as its intermediate hosts. Both adult and nymphal stages of *L. serrata* can infect humans, which typically occurs via ingestion of eggs of infected dogs or consumption of raw or undercooked infected viscera of contaminated herbivores. The most common form of infection in human is nasopharyngeal linguatulosis, also known as *Halzoun* syndrome or *Marrara* syndrome. This paper presents a review of previous studies on *L. serrata* conducted in Iran from 1969 to 2018 and other countries. It was found that despite the fact that many studies have been conducted in Iran, the rate of infection with this parasite has not been studied in some areas of the country. In addition, the rate of infection with *L. serrata* increased with the age of ruminant animals and it was significantly higher in some areas. The prevalence of *L. serrata* nymphal infections in most areas was higher in goats in comparison to the other animals which can be an important risk factor for human infection. Although there was no significant difference in the rate of infection among male and female animals, the prevalence of *L. serrata* in male animals was typically lower than females. There was no significant difference in the seasonality of nymph infection.

1. Introduction

Linguatula serrata is a member of the phylum Pentastomida (Muller, 1975; Soulsby, 1982) and is known as a cosmopolitan zoonotic and food borne parasite. Adult stages of males and females measure 1.8–2 cm and 8–13 cm long, respectively, and they are located in nasal and respiratory passages of canids and other carnivores that are definitive hosts of this parasite. Eggs discharged from nasopharyngeal secretions of the definitive host can be ingested by herbivores, which serve as intermediate hosts, then nymphs hatch from the eggs and migrate into the mesenteric lymph nodes (MLNs), liver and lung. They are convex dorsally and flattened ventrally. The final host is infected by eating the infected viscera of intermediate hosts (Hajipour, 2016; Soulsby, 1982). In most cases, infected dogs and cats show no clinical signs, however, massive infections can cause rhinitis (nose inflammation) and nasopharngitis with chronic sneezing and/or coughing, purulent nasal discharge, nose bleeding (epistaxis), etc. In livestock, most infections with nymphs begin and remain asymptomatic but there is some evidence that proteolytic enzymes have a role in these infections (Alcala-Canto et al., 2007). In infrequent massive infections by the nymphal stage, depending on the affected organs, some clinical signs may develop. Diagnosis in dogs and other carnivores is performed based on the respiratory signs and confirmed by detection of eggs in nasal discharge or in feces. However, egg shedding is an intermittent phenomenon and can lead to false negative results. In dogs, treatment of infections with *L. serrata* is typically by the removal of the parasites from the sinuses by physical means. As well as, it may be assumed that the parasites were expelled subsequently to the ivermectin (a systemic macrocyclic lactone) treatment (Ioniță and Mitrea, 2016). In reindeer, ivermectin has been shown to be effective in killing the deer-sinus pentastomid, *Linguatula arctica* (Haugerud et al., 1993). Adult worms can be detected by rhinoscopy or rhinotomy in the nasopharynx. Diagnosis in human is usually incidental, for example, after X-rays by which cysts or granulomas can be detected, or after necropsy or during surgery for other

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Table 1
Prevalence of *L. serrata* in cattle at slaughter in Iran.

Infected animals (%)	Organ infected	Study area	Sex (%)	Age group (years,%)	Season (%)	Reference
			Statistical analysis*			
12.8	MLNs	Kermanshah	M (12.1), F (14) $P > 0.05$	1 > (2), 1–2 (9.16), 2–3 (13.4), > 3(30.5), $P < 0.05$	–	(Hashemnia et al., 2018)
6.9	MLNs	Sari	–	–	Spring (6.4), Summer (3.3), Autumn (4.5), Winter (12.2), P > 0.05	(Tabaripour et al., 2017)
6.9	MLNs	Babol	–	–	Spring (7), Summer (5.7), Autumn (4.8), Winter (10), $P > 0.05$	(Tabaripour et al., 2017)
6.9	MLNs	Amol	–	–	P > 0.05, Spring (8.6), Summer (4.6), Autumn (6), Winter (13)	(Tabaripour et al., 2017)
7.4	MLNs	Hamedan	M (6.7), F (7.9) P > 0.05	≤4 (7.3), > 4 (7.4), P > 0.05	–	(Gharekhani et al., 2017)
12.8	MLNs	Kermanshah	M (12.1), F (14) P > 0.05	1 > (2), 1–2 (9.16), 2–3 (13.4), > 3 (30.5), P < 0.05	–	(Hashemnia et al., 2016)
15.1	MLNs	Tabriz	M (16.2), F (22.3)	> 2 (12.06), 2–4 (16.86), > 4 (35.29), P < 0.05	Spring (17.5), Summer (20.62), Autumn (24.37),	(Nematollahi et al., 2015)
7.3	MDLNs		P > 0.05		Winter (13.12), $P < 0.05$	
16.8	MLNs	Ahvaz	M (17.4), F (16) P > 0.05	< 2 (7.9), 2– < 3 (18), 3– > 3(25.8), $P > 0.05$	–	(Alborzi et al., 2013)
17.25	MLNs	Tabriz	M (17.9), F (16.4)	< 2.5 (6.6), 2.5–5.5 (23.5), > 5.5 (26.5), P < 0.05	Spring (14), Summer (20), Autumn (16), Winter (20),	(Mirzai et al., 2012)
			P > 0.05		P > 0.05	
0.25	Liver	Tabriz	–	–	–	(Mirzai et al., 2012)
19	MLNs	Amol	–	–	–	(Youssefi et al., 2012)
35.6	MLNs	Northwest of Iran	M (28.8), F (42.6)	Under 6 month (1.3), 6–24 month (28.9),2–4 (53.4),	–	(Rezaei et al., 2011)
			P > 0.05	> 4 (49.6), P > 0.05		
16.22	MLNs	Kerman	M (13.4), F (19.6)	< 2 (7.72), 2–4 (22.4), > 4 (27.17), p < 0.05	Spring (15), Summer (18.1), Autumn (22.7), Winter	(Nourollahi et al., 2010b)
			$p > 0.05$		(9.09), $p < 0.05$	
14.8	MLNs	Babol	–	–	–	(Youssef and Hadizadeh, 2010)
57	MLNs	Urmia	M (33.14), (66.85)	> 4 (27.19), 2–4 (25.85), 2 > (4.26), $P < 0.05$	–	(Yakhchali et al., 2009)
			P < 0.05			
6.33	Liver	Urmia	M (30.37), F (69.63),	> 4 (3.57), 2–4 (2.70), 2 > (0), P < 0.05	–	(Yakhchali et al., 2009)
			P < 0.05			
0.2	Liver	Tabriz	–	–	–	(Hami et al., 2009)
44	MLNs	Urmia	–	–	–	(Tajik et al., 2006)

MLNs: Mesenteric lymph nodes, MDLNs: Mediastinal lymph nodes, HLNs: Hepatic lymph nodes, PLNs: Pulmonary lymph nodes, M: Male, F: Female, *The chi square test had used for comparison of the prevalence of *L. serrata* between males and females, the different age groups and different season. Differences were considered significant when $p < 0.05$.

Table 2
Prevalence of *L. serrata* in camels at slaughter in Iran.

Infected animals (%)	Organ infected	Study area	Sex(%)	Age group(years,%)	Season(%)	Reference
			Statistical analysis*			
15.1	MLNs	Yazd	M (14.45), F (16), $P > 0.05$	5 > (7.7), 5–10 (18.3), > 10 (24.2), $P < 0.05$	–	(Farjanikish and Shokrani, 2016)
20.5	MLNs	Rafsanjan	M (9.1), F (11.4), P > 0.05	2 > (2.3), 2–4 (6.1), 4–6 (9.1), > 6 (2.3), P < 0.05	Spring (5.4), Summer (4.5), Autumn (6.1), Winter (4.5), $P > 0.05$	(Bamorovat et al., 2014)
18.25	MLNs	Mashhad	M (19.82), F (16.07), P > 0.05	5 > (9.30), 5–10 (16.93), > 10 (20.60), $P > 0.05$	–	(Nourollahi et al., 2012)
21.12	MLNs	Isfahan	M (18.80), F (23.47), P > 0.05	6–24 month (20.75), 2–4 (20.48), > 4 (28.16), P > 0.05	–	(Rezaei et al., 2012)
12.9	MLNs	Yazd	M (13.4), F (11.8), P > 0.05	3 ≥ (18.2), 3–6 (10.6), ≥6 (13.9), P > 0.05	–	(Oryan et al., 2011)
0.9	Spleen		–	–	–	
0.9	Liver		–	–		
13.5	MLNs	Tabriz	M (10.6), F (15.6), P > 0.05	4 > (0), 4–8(8.3), > 8 (18.1), $P = 0.009$	Spring (14.8), Summer (23.5), Autumn (15.38), Winter (15), P > 0.05	(Haddadzadeh et al., 2010)
1.4	Liver		M (1.7), F (1.2)	4 > (0), 4–8 (0), > 8 (2.2)		
1.4	Lung		M (1.7), F(1.2)	4 > (0), 4–8 (0), > 8 (2.2)		
16.2	MLNs	Kerman	M (16.4), F (15.9), P > 0.05	5 > (16.4), 5–10 (25.5), > 10 (13.9), P < 0.01	–	(Radfar et al., 2010)
1.9	MDLNs		–	–		
Case Report	Lung	Tabriz	–	–	–	(Haddadzadeh et al., 2009)
21	MLNs	Najaf-Abad	M (22.2), F (18.7), $P > 0.01$	5 (0), 5–10 (13), > 10 (33), P < 0.01	–	(Shakerian et al., 2008)
4.5	Liver		M (4.6), F (4.3)			

M: Male, F: Female, MLNs: Mesenteric lymph nodes, MDLNs: Mediastinal lymph nodes. *The chi-square test had used for comparison of the prevalence of *L. serrata* between males and females, the different age groups and different seasons. Differences were considered significant when P < 0.05 or $P < 0.01$.

Table 3
Prevalence of *L. serrata* in buffalos at slaughter in Iran.

Infected animals (%)	Organ infected	Study area	Sex (%)	Age group (years, %)	Season (%)	Reference
			Statistical analysis*			
16.3	MLNs	Ahvaz	F (16.7), M (16.2), $P < 0.05$	2 > (16.1), 1- < 3 (16.3), 3- > 3 (16.7), P < 0.05	–	(Alborzi et al., 2013)
26.6	MLNs	Urmia	M (24.2), F (30.7), P ≤ 0.05	6 month > (1.5), 6–24 month (25.9), 2–4 (31.4), > 4(36.9), $P \leq 0.05$	–	(Rezaei et al., 2011)
5.73	MLNs	Urmia	M (5.33), F (6.09), $P > 0.1$	2 > (1.16), 2–5 (4.69), > 5 (16.41), $P < 0.01$	–	(Tajik and Sabet Jalali, 2010)
1.63	Liver		M (1.78), F (1.52)	2 > (0),2–5 (5.46), > 5 (8.95)		
0.27	Lung		M (0), F (0.51)	2 > (0), 2–5 (0.46), > 5 (0)		
18.75	MLNs		–	–	–	(Tajik et al., 2008)
1.66	Liver	Urmia	–	–	–	
1.92	Lung		–	–	–	

M: Male, F: Female, MLNs: Mesenteric lymph nodes. *The chi-square test had used for comparison of the prevalence of *L. serrata* between males and females, the different age groups and different seasons. Differences were considered significant when $P < 0.05$ or P < 0.01.

Table 4
Prevalence of *L. serrata* in sheep at slaughter in Iran.

Infected animals (%)	Organ infected	Study area	Sex (%)	Age group (years, %)	Season (%)	Reference
			Statistical analysis*			
19.7	MLNs	Kermanshah	M (19.04), F (20.6), $P > 0.05$	1 > (5.7), 1–2 (19), 2–3 (24.3), > 3 (30.4), $P < 0.05$	–	(Hashemnia et al., 2018)
46.66 Seropositive	Ovine sera	Fars	p > 0.05 M(47.89), F (44.26)	Seropositive, $p > 0.05$ 1 > (52.94), > 1 (42.85)	–	(Yektaseresht et al., 2017)
6.8	MLNs	Sari	–	–	Spring (3.9), Summer (9.8), Autumn (7.3), Winter (4.6), $P > 0.05$	(Tabaripour et al., 2017)
6.8	MLNs	Babol	–	–	Spring (6), Summer (9.1), Autumn (6.9), Winter (4.7), $P > 0.05$	(Tabaripour et al., 2017)
6.8	MLNs	Amol	–	–	Spring (4.4), Summer (9.7), Autumn (8.9), Winter (5.5), P > 0.05	(Tabaripour et al., 2017)
15	MLNs, MDLNs	Hamadan	M (16.7), F (13), P > 0.05	2 ≥ (17.6), > 2 (14.5), $P > 0.05$	–	(Gharekhani et al., 2017)
11.3	MLNs	Esfahan	M (10), F (12.7), p > 0.05	1 > (4.85),1–2 (21.12), 2–3 (24.24), P < 0.05	Winter (11,$P < 0.05$), Summer & Autumn (14.7), Spring (15)	(Kheirabadi et al., 2015)
2.75	MDLNs		M (2.59), F (2.95)	1 > (0), 1–2 (3.29), 2–3 (10), > 3 (24.13)		
9	MLNs, MDLNs	Shahrekord	F (15.27), M (13.28), P > 0.01	1 > (0),1–2 (11.90), 2–3 (19.23), > 3 (22.03), P < 0.01	–	(Azizi et al., 2015)
4.5						
10.2	MLNs	Hamedan	F (21.05), M (9.70), p < 0.05	1 > (12.93), 1–2 (7), > 2 (11.11), p > 0.05,	–	(Dehkordi et al., 2014)
17	MLNs	Amol	–	–	–	(Youssefi et al., 2012)
38.57	MLNs	Tabriz	M (30.17), F (45.10), p < 0.05	1 > (35.52),1–2 (48.14), 2–3 (67.16), > 3 (77.08), P < 0.05	Spring (47.61), Summer (49.52), Autumn (61.90), Winter (40.95), P > 0.05	(Mirzaei et al., 2011)
10.23	MDLNs		M (9.72), F (10.06)	1 > (0),1–2 (0), 2–3 (2.7), > 3 (4.1)		
0.71	Liver		M (0.54), F (0.85)			
23.7	MLNs	Kerman	M (12.5), F (20.9), P > 0.05	1 > (10.8), 1–2 (16.7), 2–3 (22.2), > 3 (23.4), $P < 0.001$	Spring (18.8), Summer (13), Autumn (18.8), Winter (14.7), $P > 0.05$	(Nourollahi et al., 2011)
8.9	MDLNs					
16.1						
42.69	MLNs	North West of Iran	Mal (40.5), F (44.8), P ≤ 0.05	6 month > (3.4), 6–2 (44.4), 2–4 (58.3), > 4 (58.7), $P \leq 0.05$	–	(Rezaei et al., 2011)
30.9	MLNs	Urmia	–	–	–	(Yakhchali and Tehrani, 2011)
65.79	MLNs	Urmia	M (34.32), F (65.68), p < 0.05	1 > (3.93),1–3 (24.66), > 3 (10.45), $p < 0.05$	–	(Yakhchali et al., 2009)
32.28	Liver		M (32.53),F (67.47)	1 > (0),1–3 (12.5), > 3 (2.42)		
52.5	MLNs	Urmia	–	–	–	(Tavassoli et al., 2007a)
11.5	MLNs	Shiraz	M (4.3), F (17.6), P < 0.01	1 > (0), 1–1.5 (8.3), 1.5–2 (37.5), 2.5–3 (33.3), ≥3.5 (18.8), P < 0.01	–	(Shekarforoush et al., 2004)
3	Liver					

M: Male, F: Female, MLNs: Mesenteric lymph nodes, MDLNs: Mediastinal lymph nodes. The chi-square test had used for comparison of the prevalence of *L. serrata* between males and females, the different age groups and different seasons. Differences were considered significant when $P < 0.05$or $P < 0.01$.

Table 5
Prevalence of *L. serrata* in goats at slaughter in Iran.

Infected animals (%)	Organ infected	Study area	Sex (%)	Age group (years, %)	Season (%)	Reference
			Statistical analysis*			
25.1	MLNs	Kermanshah	M (23.7), F (26.7), P > 0.05	1 > (5.4), 1–2(24.5), 2–3(26.9), > 3(46.1), *P* < 0.05	–	(Hashemnia et al., 2018)
58.2	MLNs	Tabriz	M (46.98), F (73.45), P < 0.05	1 > (41.92), 1–2 (56.28), > 2 (75.57), P < 0.05	Spring (45.40), Summer (47.84), Autumn (78.42), Winter (61.16), *P* > 0.05	(Hajipour et al., 2018a)
16.8	MLNs	Sari	–	–	Spring (16.7), Summer (18.9), Autumn (18), Winter (15.8), P > 0.05	(Tabaripour et al., 2017)
16.8	MLNs	Babol	–	–	Spring (15), Summer (18), Autumn (17), Winter (36), P > 0.05	(Tabaripour et al., 2017)
16.8	MLNs	Amol	–	–	Spring (15.7), Summer (19.8), Autumn (16.7), Winter (16), P > 0.05	(Tabaripour et al., 2017)
25.1	MLNs	Kermanshah	M (23.7), F (26.7), P > 0.05	1 > (5.4), 1–2 (24.5), 2–3 (26.9), > 3 (46.1), P < 0.05	–	(Hashemnia et al., 2016)
24	MLNs	Hamadan	M (27.39), F (100), p < 0.05	1 > (40.6), 1–2 (17.5), > 2 (0), p > 0.05	–	(Dehkordi et al., 2014)
6.60	Lung					
	Liver					
69.15	MLNs	Amol	–	–	–	(Youssefi et al., 2012)
50.75	MLNs	North West of Iran	M (50.3), F (51.2), P ≤ 0.05	6 > month (4.7), 6–24 month (36.6),2–4 (63), > 4 (63.8), P ≤ 0.05	–	(Rezaei et al., 2011)
49.1	MLNs & MDLNs	Kerman	M (46.1), F (54.3), P > 0.05	< 1 (47.45),1–2 (47 0.91), 2–3 (51.94), > 3 (66.6), P < 0.05	Spring (50), Summer (38.6), Autumn (76.4), Winter (31.8), P < 0.05	(Nourollahi et al., 2010a)
59.78	MLNs	Urmia	M (38.72), F (61.28) P < 0.05	2 > (0), 2–4 (24.76), > 4 (47.5) P < 0.05	–	(Yakhchali et al., 2009)
5.46	Liver		M (28.86), F (71.74)	3 > (0),2–4 (8.8), > 4 (1.33)		
68	MLN	Urmia	–	–	–	(Tavassoli et al., 2007b)

M: Male, F: Female, MLNs: Mesenteric lymph nodes, MDLNs: Mediastinal lymph nodes. The chi-square test had used for comparison of the prevalence of *L. serrata* between males and females, the different age groups and different seasons. Differences were considered significant when P < 0.05.

Table 6
Prevalence of *L. serrata* infection in dogs and cats in Iran.

Animal	Infected animals (%)	Organ infected	Study area	Sex (%)	Age group (years, %)	Season	Reference
				Statistical analysis*			
Dog	1.93	Frontal sinuses	Urmia	Female	3-year-old	–	(Hajipour et al., 2018b)
	40.62	Nasal cavities	Ilam	–	2 years old dogs were infected rather than 2 <	–	(Bahrami et al., 2011)
	27.83	Frontal sinuses	North west of Iran	M (30.8), F (24.4), P < 0.05	< 6 month (0), 6–24 month (26.1), 2–4 (31.6), > 4 (37.5), P < 0.05	–	(Rezaei et al., 2011)
	81.08	Frontal sinuses	Urmia	M (81.81), F (80), *P* > 0.05	< 8 month (23 0.33), > 8 month (76.66), P > 0.05	–	(Rasoli et al., 2010)
	76.5	Nasal tubinates	Shiraz	M (72.9), F (81.08), P > 0.05	8 month > (60), > 8 month (80)	–	(Oryan et al., 2008)
	53.22	Nasal cavities	Marand	–	–	–	(Razmaraei et al., 2007)
	62.2	Nasal cavities	Shahrekord	M (67.4), F (53.7), P > 0.01	< 2 (44), 3–4 (76.7), 5 (70.8), P < 0.01	–	(Meshgi and Asgarian, 2003)
Cat	Case report	Diaphragmatic Lobes of lung	Ahvaz	Female	1.5 years old	–	(Esmaeilzadeh et al., 2008)

M: Male, F: Female. ·The Chi Square or Backward elimination tests (SPSS version 17.0) had used for comparison of the prevalence of *L. serrata* between males and females, the different age groups and different seasons. Differences were considered significant when P < 0.05 or P < 0.01.

Table 7
Prevalence of *L. serrata* in rabbits and Indian crested porcupines (intermediate hosts) in Iran.

Sample	Area study	Infected organ	Infected animals (%)	Reference
European hare	Urmia	Small intestine contents	3.33	(Tavassoli and Bakht, 2014)
Indian crested porcupines	Southwest of Iran	MLNs	50	(Rajabloo et al., 2014)

reasons. An important aspect in diagnosis of linguatulosis is the identification of antigens which are specific and highly immunogenic for the infected host. Because the nymphal stages of *L. serrata* isolated from different animals have different strains, their somatic proteins can be different (Ghorashi et al., 2016; Hajipour et al., 2016; Tavassoli et al., 2014). Linguatulosis can appear as a nasopharyngeal or visceral disease in humans. Nasopharyngeal infection in humans can occur by ingesting the nymphal stages of *L. serrata* found in undercooked infected liver, lungs, lymph nodes, or other infected organs of the intermediate herbivore hosts. The nymphs emerge from their cysts in the stomach and migrate up to the nasopharynx, where they anchor to the mucosal epithelium by their prominent hooks. In this case, humans can serve as a definitive host with nymph and/or mature parasites found in the nasopharyngeal tract and frontal sinuses. A range of more or less severe symptoms can occur such as: inflammation of the upper respiratory tract; swelling of submaxillary and cervical lymph nodes; salivation; dysphagia; coughing; itchy throat; temporary conductive deafness due to the blockage of the eustachian tube by edema or by nymphs; and suppurative otitis media because of secondary bacterial infections. The clinical signs collectively cause a syndrome of type I hypersensitivity, also known as Marrara or Halazoun syndrome (Khalil and Schacher, 1965; Yagi et al., 1996). Visceral pentastomiasis occurs after ingesting infective eggs of *L. serrata* excreted from nasopharyngeal secretions or feces of infected dogs or other carnivores. In this case human serves as intermediate hosts and infected dogs or other carnivores serve as definitive hosts which can contaminate water resources, vegetables, and fruits (Fain, 1975; Tappe and Buttner, 2009). There are no published studies assessing antiparasitic treatment of human linguatuliasis; however, the use of ivermectin, praziquantel and mebendazole have been suggested (Warrell, 2010). In asymptomatic patients no treatment is necessary, since the parasites degenerate after approximately two years (Lazo et al., 1999). Only in symptomatic infections with numerous parasites may a surgical approach have to be considered (Tappe and Buttner, 2009). Many factors are involved in the prevalence of this disease including: nymphs escaping from eggs and traversing the intestine; variety of definitive and intermediate hosts including wild carnivores, methods of slaughtering and sanitation of slaughterhouses; methods of meat cooking; sanitation rate of water for human consumption and water resources for definitive hosts, and methods of disinfecting vegetables and fruits (Fain, 1975; Tappe and Buttner, 2009). It is also proposed that eating raw or undercooked offal, especially liver of farm animals (cattle, goats or sheep), is a suitable way of promoting the fetus growth during pregnancy, because it has high contents of iron and vitamins. After religious feasts, in Middle East, in which sheep or goats are often served as uncooked, Halzoun can occur (Oluwasina et al., 2014; Tavassoli et al., 2014), so physicians should be aware of this and should consider *L. serrata* infection in patients that report respiratory tract symptoms, especially upper tracts in endemic regions, where people consume raw or uncooked liver or in patients who are in close contact with domestic and home-reared animals. The prevalence of *L. serrata* infections in final and intermediate hosts varies in different regions of Iran and can be influenced by these factors. To highlight the importance of *L. serrata* infections and assess some factors that could influence prevalence and aid scholars, researchers and veterinarians investigating means of decreasing prevalence, this review of the literature was performed.

2. Materials and methods

A systematic review of the literature was performed using online databases from various fields and in Iran and other regions of world in 2017. Databases included: Pub Med, Science Direct, Elsevier, SID, Magiran, Irandoc, Google Scholar and the World Health Organization. Key words included: “pantastomid” and “*Linguatula serrata*”, “parasites” and “Iran”. Conferences abstracts and articles published in national and international journals were included. Based on the principles of systematic review studies, non-related documents were excluded and, after screening the publications, all documents whose contexts were in concordance with the aim of the present study were selected for final review. Data extracted from each included publication were: “infected animals”, “infected organ”, “study areas”, “sex”, “age group” and “season”. All data were summarized in tabular form.

3. Results

After collecting the documents related to the prevalence of

Table 8
Linguatuliasis in humans in Iran.

Patient	Area study	Infected organ	Source of the infection	Clinical symptoms	Reference
34-years old man	Kermanshah,	Pharynx	Consumed raw liver of goat	Coughing, sneezing and runny nose	(Janbakhsh et al., 2015)
32-year-old woman	Kerman,	Nasopharyngeal region and throat	Consumed raw liver of sheep	Sneezing, coughing and respiratory discharges appeared, progressively	(Yazdani et al., 2014)
55-year-old man	Zanjan	Small bowel	–	Fever, abdominal pain, abdominal distension, and weight loss.	(Taba Taba et al., 2012)
34 years old mother and her 12 years old daughter	Isfahan	Pharynx	Consumed raw liver of goat	Coughing, sneezing, yellow nasal and ear discharges	(Hamid et al., 2012)
10-year-old boy	Tehran	–	Consumption of hamburger and undercooked sheep liver	Prickling sensation in the throat, sneezing, coughing and nasal discharges	(Anaraki Mohammadi et al., 2008)
27-year-old man and two women aged 23 and 43 years (family)	Iran	Larynx, nose and gums	Consumption of barbecued liver (Kabab)	Sneezing, coughing and nasal dis-charge, dyspnea, dysphagia and frontal headache	(Siavoshi et al., 2002)
28 years old woman	Tehran	Throat	–	Discharge had without any further complaining	(Maleky, 2001)
35 year old woman	Shiraz	Pharynx	Consumed raw liver of sheep	Itching of the nose, palate and throat with copious nasal and lacrimal discharge and redness of the eyes and face	(Sadjjadi et al., 1998)
28 years old mother and her 11 years old daughter	Tabriz	Nose and mouth	Consumed raw gut of sheep	Nasal, ear, frontal, and throat pruritus, oral and nasal discharge, cough, headache, vertigo	(Montazeri et al., 1997)

linguatulosis in definitive and intermediate hosts from online available and credible databases, a total of 120 documents were obtained. The results of the present study showed that many studies have been conducted on the prevalence of *L. serrata* infection in definitive and intermediate hosts in Iran; however, some areas have not yet been studied with information on the epidemiology of this parasite not available. Based on the results, listed in Tables 1–10, prevalence varies between locations and hosts.

4. Discussion

Based on this literature review, prevalence differs among animals depending on the location. This probably indicates that geographic and climatic factors affect the survival of the eggs. The highest infection of ruminants with *L. serrata* nymphs was observed in Amol (69.15%) (Youssefi et al., 2012), Urmia (65.79–68%) (Tavassoli et al., 2007b; Yakhchali et al., 2009), Tabriz (58.2%) (Hajipour et al., 2018a) and northwest of Iran (42.69%) (Rezaei et al., 2011) which indicated the climatic parameters (more humid and mild climate) that can enhance the egg survival in the environment (e.g., on vegetables and fruits, in water resources), and also showed that suitable temperature and humidity can play important roles in the epidemiology of this infection. In some areas such as; Tabriz (58.2%) (Hajipour et al., 2018b), Amol (69.15%) (Youssefi et al., 2012), north west of Iran (50.75%) (Rezaei et al., 2011), Urmia (59.78–69%) (Tavassoli et al., 2007b; Yakhchali et al., 2009), the prevalence of infection with *L. serrata* nymphs are higher in goats than in cattle, sheep, buffaloes and camels. The reason is not clear but it may relate to different forage habitats of goats, geographical climate or high exposure to dogs, which serve as definitive hosts. Close contact between dogs and intermediate hosts like goats can also play an important role in *L. serrata* transmission. On the other hand, goats grazing ahead of the flocks can be another reason for the observed increase in the risk of infection (Hajipour, 2012, 2016; Tavassoli et al., 2007b). Another reason for the high infection rate of nymphs in goats could potentially be attributed to *L. serrata* strain differences, with some strains being more adapted to certain hosts (Tavassoli et al., 2014). In their study on *L. serrata* isolated from different farm animals of Iran, Tavassoli et al. (2014) found molecular differences among the parasite by amplifying and sequencing of 18S rRNA. Based on the reported results, the lowest diversity of nucleotide sequences (98.8%) was observed in sheep, cattle, and dogs, while the highest one (100%) was recorded in camels and goats. However, studies on phylogenetic relationships among *L. serrata* isolates from Iran based on 18S rRNA and mitochondrial cox1 gene sequence by Ghorashi et al. (2016) showed a higher sequence diversity and intraspecies variation in the cox1 gene compared to 18S rRNA sequences and there was no association between genetic variations and host species or geographical location, perhaps due to the small sample size. Genomic DNA was isolated from a *L. serrata* female expelled from a dog imported to Norway from Romania and from four *L.arctica* females collected from semi-domesticated reindeer from northern Norway and subjected to PCR amplification of the complete nuclear 18S rRNA gene and a 1045-bp portion of the mitochondrial cytochrome c oxidase subunit I gene (cox1) (Gjerde, 2013). First report of molecular characterization and sequence phylogenetic analysis of *L. serrata* from India was presented by Sudan et al. (2018). The highest prevalence of infection in dogs was in Urmia (81.08%) (Rasoli et al., 2010), Shiraz (76.5%) (Oryan et al., 2008), and Shahrekord (62.2%) (Meshgi and Asgarian, 2003). The major reason for this high prevalence of linguatulosis in dogs is the offal of domestic ruminants and ingestion of raw viscera of sheep, goats, and other herbivores. There are many stray dogs that live as scavengers and have access to slaughterhouse offal or the carcasses of infected herbivores, such as goats, sheep, and cattle; this facilitates the spread of the parasite to dogs. Many stray dogs that live as scavengers have access to offal or carcasses of infected herbivores, such as goats, sheep, and cattle, which facilitates the spread of the parasite among man and

Table 9
Prevalence of *L. serrata* in animals as intermediate and definitive hosts in other countries.

Animal	Infected animals (%)	Organ infected	Study area	Sex (%)	Age group (years, %)	Season (%)	Reference
				Statistical analysis*			
Cattle	50.7	MLNs HLNs PLNs	Bangladesh	M (45), F (57.1), P < 0.05	–	P > 0.05 -	(Islam et al., 2018)
	13.8	Liver	Talca, Chile	– –	*p* = 0.187		(Parraguez et al., 2017)
	5.97	MLNs	Lima, Peru	–	4–5 >	–	(Castro et al., 2015)
	19	MLNs	Kalpetta, India	–	–	–	(Ravindran et al., 2008)
	14.47	Spleen	Mosul, Iraq	–	–	–	(Al-Sadi and Ridha, 1994)
	7.89	MLNs					
Camel	25	MLNs	Egypt	M (23.7), F (30), P > 0.05	6–12 month (0), > 1–2 (18.8), > 2 (29.2), *P* > 0.05	–	(Attia et al., 2017)
	Case report	Lung	South American	–	–	–	(Gomez-Puerta et al., 2017)
	1.25	Liver	Sudan	–	–	–	(Mohammed et al., 2016)
	10%	MLNs	Egypt	–	–	–	(Khalil, 1976)
Buffalo	18.3	MLNs	Mathura, India	M (51.5), F (48.5), P > 0.05	1 > (0), 1–3 (51.5), > 3 (48.5), P > 0.05		(Sudan et al., 2014)
	*8	MLNs	Kalpetta, India	–	–	–	(Ravindran et al., 2008)
	2	MLNs	North India	–	–	–	(Sisakumar et al., 2005)
Goat	31	MLNs HLNs PLNs	Bangladesh	P < 0.05 –	–	P > 0.05 –	(Islam et al., 2018)
Sheep	15.19	MLNs	Van, Turkey	–	–	–	(Gul et al., 2009)
	0	Lung					
	11	MLNs	Romania	–	–	–	(Miclaus et al., 2008)
	5.4	MLNs	Kirikkale, Turkey	M (14.81), F (4.32), P > 0.05	P > 0.05, –	–	(Aydenizoz et al., 2012)
Rabbit	19.04	Gastrointestinal tracts	Macedonia, Greece	–	–	–	(Diakou et al., 2014)
	2	Mesenteric intestinal	Southeastern united states	–	–	–	(Andrews et al., 1980)
	40	Mesenteric ganglia, Lung	Auburn, Alabama	–	–	–	(Moore and Moore, 1947)
Dog	Case report		UK, Imported from Romania	–	–	–	(Villedieu et al., 2017)
	Case report	Frontal sinuses	Romania	–	–	–	(Ioniță and Mitrea, 2016)
	Case report	Nasal cavities	United Kingdom	–	–	–	(Mitchell et al., 2016)
	35.67	–	Jalingo, Nigeria	M (39.41), F (30.77), P > 0.05	0–10 week (49.69), 11–20 week (19.42), P < 0.05	–	(Oluwasina et al., 2014)
	38.57	–	Jalingo, Nigeria	M (41.19), F (34.09), P > 0.05	0–10 week (50.19), 11–20 week (24.77), *P* < 0.05	–	(Oluwasina et al., 2014)
	Case report	Nasal mucosa	Italy	–	–	–	(Bordicchia et al., 2014)
	1.76	Fecal (larve)	Nile Delta, Egypt	–	–	–	(Khalafalla, 2011)
	0.87	Fecal	Neuquen, Argentina	–	–	–	(Soriano et al., 2010)
	8.33	Nasal cavity	Erzurum, Turkey	M (3.84), F(13.63)	–	–	(Aldemir, 2004)
	2	Nasal cavity	Bursa, Turkey	M (25.8), F (10.5)	–	–	(Akyol et al., 1995)
	Case report	Nasal cavity	Turkey	–	–	–	(Gothe et al., 1991)
	0.4	Nasal cavity	Thessaloniki, Greece	M(0.4), F(0)	–	–	(Haralabidis et al., 1988)
	3.5	–	Rabat, Morocco	–	–	–	(Pandey et al., 1987)
	53	Nasal cavity	Elazığ, Turkey	–	–	–	(Taşan, 1987)
	8.33	Head	Cairo, Mongrel	M (58.97), F (30.77)	–	Spring & Summer (66.67), Autumn & Winter (33.33)	(Khalil, 1970)
Cat	Case report	Lung (larve)	Tembladera, Peru	–	-	-	(Ibanez, 1969)
Red fox	1.3	Nasal cavity	Bosnia and Herzegovina	–	–	–	(Hodžić et al., 2016)

M: Male, F: Female, MLNs: Mesenteric lymph nodes, MDLNs: Mediastinal lymph nodes. *The Chi Square or *t*-tests (SPSS) had used for comparison of the prevalence of *L. serrata* between males and females, the different age groups and different seasons. Differences were considered significant when P < 0.05.

Table 10
Linguatuliasis in human in other country.

Patient	Area study	Infected organ	Source of the infection	Clinical symptoms	Reference
25-year-old woman	India	Anterior chamber of the eye	–	Diminution of vision, pain, redness and watering.	(Bhende et al., 2014)
9-year-old boy	Bulgaria	M.L.Ns	–	Palpatory pain the ilo-coecal region and enlarged liver	(Mateva et al., 2013)
26 years old woman	Van, Turkey	Oral cavity	–	Coughing, a burning sensation in the nasopharyngeal mucous membranes, sore throat, loss of voice, vomiting and fatigue	(Yilmaz et al., 2011)
5-year-old boy	India	Anterior chamber of the eye	–	Diminution of vision and a gradually enlarging white dot in the right eye since 2 months,	(Saumya Pal et al., 2011)
14-year-old girl	Austria	Eye	Contact with dog	Redness, pain, and progressive visual loss in the right eye	(Koehsler et al., 2011)
42-year-old, HIV-seropositive man	Bari, Italy	Lung	–	Lung cancer	(Pampiglione et al., 2001)
20 years old man	Egypt	–	–	Fever, urticaria (face and neck), coughing, vomiting	(Morsy et al., 1999)
34-year old woman	Ecuador	Eye	–	Ocular pain on the right side, with conjunctivitis and visual difficulties due to the presence of a shadow	(Lazo et al., 1999)
28 years old woman	Khartoum	Nose	Eating marrara prepared from a female goat	Itching of the nose, palate and throat, and running from the nose	(El-Hassan et al., 1991)
37-year old woman	Tunisia	Nasal discharge	Improperly cooked meat	Severe cough, hoarseness and dysphagia, frontal headache	(Buslau et al., 1990)
62-year-old man	North Carolina, USA	Liver	–	Lymphocytic lymphoma, Laparotomy for gastric resection of an extranodal lymphoma and cholecystectomy revealed a 6-mm nodule on the surface of the liver	(Baird et al., 1988)

animals. High rates of contact with livestock and dogs and feeding dogs with raw viscera of home-slaughtered sheep, goat, cattle, and camel can create an excellent condition for perpetuating the parasites' life cycle. No significant difference in rates of infection between male and female animals were seen in most studies; however, the prevalence of *L. serrata* was lower in males in comparison to females. The results of studies conducted by Alborzi et al. (2013), Rezaei et al. (2011), Dehkordi et al. (2014), Mirzaei et al. (2011), and Shekarforoush et al. (2004) did indicate that the prevalence of *L. serrata* nymphs in females was significantly ($P < 0.05$) higher in comparison to males. This finding may be due to the higher mean age of females than males, with females being slaughtered at an older age. Significant differences were also found among different ages of animals. The prevalence was lower in young dogs (< 6 month) compared to older ones (> 6 month) (Rezaei et al., 2012; Rezaei et al., 2011). Normally, young dogs, up to about 6 months, feed on their mother's milk and have less access to infected herbivores offal. High rate of infection among these old animals (> 6 month) suggested their easy access to the source of infection and also indicated the hyperendemicity of *L. serrata* in those area. Infection rate showed an increase with the age of ruminant animals and it is highly significant in some areas. Nymphs can develop within 5 to 6 months, according to the lower prevalence in younger groups. The rates of *L. serrataL. serrata* prevalence in mediastinal lymph nodes were reported to be lower than that of mesenteric lymph nodes or liver (Azizi et al., 2015; Kheirabadi et al., 2015; Nematollahi et al., 2015; Mirzaei et al., 2011; Nourollahi et al., 2011; Radfar et al., 2010). Giving the life cycle of *L. serrata* and route of circulation within the host, they likely reach and infect the mesenteric lymph nodes before the other organs. In comparison to Iran, the infection rate of *L. serrata* in ruminants and dogs is low in most other countries where prevalence studies have been conducted. Reasons for this difference include fewer stray dogs, potentially healthier dogs, and not feeding infected viscera to dogs. The highest prevalence of *L. serrata* found in other countries was in cattle (50.7%) and goats (31%) in Bangladesh (Islam et al., 2018). The higher prevalence in cattle may be due to genetic makeup of the animal breeds, which usually contributes to the host specificity of animals to a particular pathogen. However, feeding habits of cattle, bottom feeder grazers, and goats, browsers, may also play a key role in the significant variation of the infection rate between the two species studied in Bangladesh.

5. Conclusion

Although the diagnosis of linguatulosis is difficult, one cannot ignore it and a strict control program should be developed and implemented by authorities, as well as a monitoring program. Also, increasing the awareness of *L. serrata* and providing education about transmission is needed. The high prevalence of *L. serrata* infection in MLNs of goats must be considered an important risk factor for human infection within Iran. Some specific measures that should be implemented to break the life-cycle and infections include:

- Prevention programs for nymph MLN infections in ruminants, the intermediate hosts, focused on hygiene
- Avoiding feeding dogs, the definitive hosts, raw MLNs or other offal
- Avoiding contact with canine saliva and drinking water used by dogs or wild canids to prevent the infection in people
- Use of ivermectin to treat infected dogs.

Conflict of interest

There is no conflict of interest.

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