J Parasit Dis (Jan-Mar 2021) 45(1):50–58
https://doi.org/10.1007/s12639-020-01276-8

REVIEW ARTICLE

# Clinical manifestation and epidemiological findings of human *linguatula serrate* infection in Iran: systematic review

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Received: 8 July 2020 / Accepted: 14 September 2020 / Published online: 23 September 2020


**Abstract** The aim of this study was to collect data and provide information on clinical diagnosis of disease, methods of dissemination, prevention and treatment of human linguatuliasis in order to increase people's awareness and health care. In this study case reports of individuals in Iran those infected with the *Linguatula serrata* were taken from the international databases (*e.g.*, Medline (PubMed), Scopus, Iranmedex, Scientific Information Database, and Irandoc) and reviewed. The review covers the case reports of human tongue worm infection published either in Persian or in English between the years 1980–2018. An individual researcher undertook the bibliographic search and evaluation of articles based on inclusion/exclusion of specific criteria. Cases of infection have been reported in eight provinces of Iran. Dietary habits play the important roles in the transmission of the parasite. Clinical diagnosis was achieved by obtaining a patient's history, then completing a clinical examination of the mentioned patients. Symptoms of infection were mainly observed in the upper respiratory tract in most reports, the patient's status was improved by removing the parasite from the infected organ. Given that viscera of slaughtered livestock plays a significant role in the transmission of this infection to humans, Careful inspection of slaughtered livestock in slaughterhouses and Preventing the slaughter of livestock illegally and unsanitary, outside the slaughterhouse, is important. Accordingly, it is very important to train the employees working in the slaughterhouses and the people who consume these organs.

**Keywords** *Linguatula serrata* · Iran · Human · Linguatulosis

**Abbreviations**

| | |
|---|---|
| SID | Scientific Information Database |
| PRISMA | Preferred Reporting Items for Systematic reviews and Meta-Analyses |

## Introduction

Linguatulosis is a rare zoonotic parasitic disease resulting from invasion of the body by wormlike parasites of the genus Linguatula (Oluwasina et al. 2014). The life cycle of this Parasite consists of four stages: eggs, larvae, nymphs and adults. The adult form lives in the upper respiratory tract, nasal passages, and frontal sinuses of carnivores, especially dogs, as the final host. The eggs, which are discharged from the main host by the nasopharyngeal secretions, are swallowed by the ruminants as intermediate hosts. In the next stage, the larvae hatch from the eggs and enter mainly the mesenteric lymph nodes and other visceral organs. The parasite can be transferred to the final host

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through consumption of meat or viscera of infected intermediate host.

Transmission to the human beings is most likely to occur accidentally when consuming raw viscera of nymph-infected sheep, goats, cows, camels, or other herbivorous animals. The entry of larvae into the body of the intermediate host causes pathological lesions and symptoms. Symptoms depend on the infected organ (Anaraki Mohammadi et al. 2008; Janbakhsh et al. 2015; Tabaripour et al. 2019).

Parasitic infection by the nymph stage causes symptoms such as sneezing, coughing, tearing, running nose, hoarseness, nausea, dizziness, vomiting, and pharyngitis (Hamid et al. 2012).

When it involves the respiratory tract, it can cause certain syndromes including nasopharyngeal linguatuliasis or Marrara syndrome which is most prevalent in the Sudan, and Halzon syndrome which is mostly prevalent in the Middle East (Anaraki Mohammadi et al. 2008; Hamid et al. 2012).

Despite the role of ruminants in the transfer of this parasite to the humans, slaughterhouses operators do not perform the necessary inspections regarding the risk of transmission of this infection to the humans, there by threatening public health.

Due to the fact that the infection of this parasite is related to the level of health and nutrition of individuals, the pattern of manifestation may be different in different countries. It is expected that in more advanced societies with higher economic and health levels, less cases of this parasitic infection have been reported, and in contrast, in undeveloped or developing societies and countries, the incidence may be higher (Tabaripour et al. 2019) and most cases have been reported in Africa, the Middle East, and southern Asia(Nagamori et al. 2019). For example in Bangladesh, many people, especially young boys and girls, love to eat fast food or junk food, in which improperly cooked meat or meat offal's are used(Islam et al. 2018).

Ocular linguatuliasis, a very rare form, in human has also been reported from the United States, Congo, Ecuador and Austria (Mohanta and Itagaki 2017).

About the prevalence of the parasite in the final host, a recent study in Australia showed that these parasites are more common than previously thought with a 67% infection in wild dogs (Shamsi et al. 2020) Oluwasina et al. reported 37.45% of client-owned dogs were infected with *L. serrata* in Jalingo, Nigeria. In Egypt, several coprological surveys demonstrated the prevalence of *L. serrata* in dogs ranged from 0 to 25%. Feline linguatuliasis has also been reported sporadically throughout Africa. Recently, unexpectedly high prevalence of *L. serrata* in wild dogs has been reported in southeastern Australia (Hajipour et al. 2019).

Prevalence of *L. serrata* in animals slaughtered in Iran slaughterhouses: in slaughtered cows between 2006 and 2018 from 0.2 to 57%, in slaughtered camels between 2008 and 2016 from 0.9 to 21.21%, in slaughtered buffaloes between 2008 and 2013 From 0.27 to 26.26 percent, in slaughtered sheep: between 2004 to 2018 from 75.2 to 65.79 percent, in slaughtered goats between 2007 to 2018 from 46.5 to 68% and in infected dogs in Iran between 2003 and 2018 from 93.1 to 08.81 percent has been reported.(Hajipour et al. 2019; Hajipour and Tavassoli 2019).

Aim of this study was to collect data and provide information on clinical diagnosis of disease, methods of dissemination, prevention and treatment of human linguatuliasis in order to increase people's awareness and health care.

## Methods

This systematic review is limited to the years 1980 to 2018 and followed the guidelines of the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) (Moher et al. 2009) and it is conducted in four stages: (1) designation, search strategy, (2) systematic literature review and analysis, (3) evaluation of inclusion and exclusion criteria, and (4) qualitative assessment. In order to prevent bias, all search strategy development, data extraction, and quality assessment steps were performed independently by two researchers (MMS, and MZ), and the consensus of the selections confirmed by a third researcher (YM or RGH).

### Search terms and search strategy

To identify relevant studies two independent researchers (MM and MZ) undertook an online search of national and international databases: Scopus, PubMed, Science Direct, Iranmedex, Scientific Information Database (SID), and Irandoc. Researchers searched these databases manually through the reference lists and grey literature. We searched these databases from January 1980 to December 2018. The search protocol was developed based on four main roots of "*Linguatula serrata*", "Human", "Case Report", "Iran", and "linguatulosis". A Similar process was undertaken for all case reports published in Persian.

### Inclusion/exclusion

All articles those report the existence of this parasite affecting human beings in Iran were included in the study, regardless of the age or sex of the infected individual or the language of the article. Exclusion criteria includes the lack

of sufficient data or access to the full text articles, irrelevant topics, duplication, and a geographic scope outside Iran.

### Quality assessment and selection

The abstracts of all relevant articles were collected and served as an initial data set for screening the articles. The full text of the articles those were initially considered as the relevant ones were provided to the researchers, omitting the names of the journal and authors. Each article was then independently scrutinized by two researchers (HS and RG) and if the article was rejected, the reason for its rejection was recorded. The third researcher (YM) served as tie-breaker if two first researchers disagreed. In the initial search, 532 relevant articles to the topic were collected. The quality assessment of the articles assessed by the CARE Checklist which followed: title, keywords, abstract, introduction, patient information, clinical findings, timeline, diagnostic assessment, therapeutic intervention, follow-up and outcomes, discussion, patient perspective, and informed consent (Riley et al. 2017). The CARE steering group has developed a flow diagram for how a clinician should systematically collect this information during the visit a patient or performing a chart review such as the case that can be written up within CARE guidelines.

### Data extraction

The gender, age, city of residence, infected organ, symptoms of the patient, along with the method of diagnosis constitute the primary information gleaned from the full text of the articles and recorded in the form of table and graphs.

Moreover, the frequency of reported cases of infection were determined for individual cities of Iran, and illustrated on a map (Fig. 1, and Table 1).

Finally, given the considerable variety in the study methods, the extracted outcomes were summarized and reported using descriptive statistics without conducting any meta-analyses.

## Results

Our systematic review began by searching the abovementioned databases using specific keywords that resulted in 532 articles in the period of time between the years 1980 to 2019. Once duplicate items were culled, the abstracts of the remaining articles were reviewed and the irrelevant articles such as studies devoted solely to livestock, and studies of areas outside Iran were excluded. The remaining articles were identified and their full texts obtained. Finally, 15 cases which were reported in 11 case reports those provide information on patient age and gender, mode of transmission, infected organ, and methods of diagnosis and treatment, were chosen for a review (Fig. 1).

Considering 15 cases of tongue worm infections, four cases were reported in Tehran and two cases in every other below mentioned cities of Iran, namely Isfahan, Kashan and, Tabriz city. Furthermore, only one case in each of the cities of Kerman, Kermanshah, Zanjan, Arak, and Shiraz were reported. (Figure 2).

The clinical information of the cases from different regions of the country including the symptoms, infected organ, method of diagnosis, and age and gender of the patient are presented in Table 1.

In Iran individuals between the ages of 31 to 40 years showed a greater infection rate than those of other age groups (Fig. 3). The most common symptoms in Iranian individuals infected with this worm were tracheal discomfort. Between the other symptoms, the abdominal pain, weight loss, eye redness, and inner and outer ear itching have a lower frequency (Fig. 4). In this study based on the information contained in the collected articles, the items based on gender are shown in Fig. 5. According to the reported data, nasopharyngeal involvement was found more than visceral involvement and only one case of visceral involvement indicated that the individual had symptoms of abdominal pain and weight loss (Vakili et al. 2012).

## Discussion

Infection by this worm has been observed in tropical regions such as Iran (A Montazeri et al. 1997; Anaraki Mohammadi et al. 2008; Arbabi et al. 1997; Hamid et al. 2012; Janbakhsh et al. 2015; Maleky 2001; Sadjjadi et al. 1998; Siavashi et al. 2002; Vakili et al. 2012; Yazdani et al. 2014), Turkey (Gokpinar and Aydenzoz 2010; Yilmaz et al. 2011), Lebanon (Khalil et al. 2013; Schacher et al. 1969; Yagi et al. 1996), Latin America (Lazo et al. 1999), Africa (Khalil 1972; Ragab and Samuel 1955), and Europe (Koehsler et al. 2011; Pampiglione et al. 2001; Parenzan and Chieffi 1951; Tappe and Buttner 2009). Developing countries are considered as endemic areas for this parasite. In Iran it is prevalent as a result of the high consumption of nutrient-rich raw liver obtained from a livestock (Anaraki Mohammadi et al. 2008; Janbakhsh et al. 2015; Montazeri et al. 1997; Sadjjadi et al. 1998; Vakili et al. 2012; Yazdani et al. 2014). Of course, the articles published in Iran on the subject of the case report were less considered due to the passing of the treatment protocol.

The main human sources of infection by this worm pathogen are the viscera (liver, lungs, trachea, and tripe) of


**Fig. 1** Cases of human contamination with *Linguatula serrata* in different cities of Iran

herbivorous animals, especially ruminants (e.g., sheep, goats, camels, cows) followed by the nasal cavities and sinuses of dogs, foxes, and wolves (Hamid et al. 2012; Sadjjadi et al. 1998). Human infections can also be caused by the consumption of vegetables or water contaminated with pentastomida eggs. These are generally reported to bring on within one to 3 h after ingestion of the infective agent a discomfort and itching in the trachea, coughing, sneezing, yellow discharge from the nose, frontal headache, nausea, and vomiting.

Illustrating the frequency at which individual symptoms were reported in the reviewed studies, Fig. 4 shows discomfort and itching in the trachea together with coughing were the most frequently reported patient complaints. These symptoms are generally observed one to 3 h after the consumption of parasite-contaminated food. Other less common symptoms include pain in the digastric area, facial redness, and itching of the ear and Eustachian tubes.

In one case, the anemia and weight loss were observed due to a late referral to a medical practitioner (Vakili et al. 2012). In the reviewed cases, nasopharyngeal tissue was more greatly affected than intestinal tissue (93% *vs.*7%).

According to Fig. 1, the spatial distribution of the parasite indicates that infections in the western and central regions of the country are more prevalent which probably dues to the cultural norms of local diets and the frequency of stray dogs. For instance, there is a high incidence of tongue worm among the stray dogs of Shahrekord (Meshgi and Asgarian 2003) while the highest number of reports arising in Tehran and Isfahan provinces (Fig. 1).

The point that a significant number of cases were reported from single Families indicates the role of the

**Table 1** Specifications of reported cases of human infection with *Linguatula serrata* in Iran

| First author | Cites | Years of study | Publication | Sex (M/F) | Age (Year) | Implicated organ | Diagnostic method |
|---|---|---|---|---|---|---|---|
| Anaraki G (4) | Shahriar | 2007 | 2007 | M | 10 | Naso-pharyngeal | Clinical |
| Sajjadi M(3) | Shiraz | 1998 | 1998 | F | 35 | Naso-pharyngeal (throat) | FALL method |
| Vakili S (7) | Zanjan | 2012 | 2012 | M | 55 | Small intestine | Ultra sound colonoscopy angiography |
| Yazdani R(8) | Kerman | 2013 | 2014 | F | 32 | Naso-pharyngeal | Naso pharyngo-scopy and broncho-scopy |
| Janbakhsh Alireza (2) | Kermanshah | 2015 | 2015 | M | 34 | Naso-pharyngeal | Clinical |
| Montazeri A (9) | Tabriz | 1996 | 1996 | F | 28 | Nasopharyngeal | Clinical |
| | | | | F | 11 | | |
| Yeganeh Moghadam A (10) | Hasan Abad of Kashan | 2001 | 2001 | F | 30 | Nasopharyngeal | Clinical and Glycerin gel application |
| Siavashi M (11) | Tehran | 2002 | 2002 | M | 27 | Nasopharyngeal | Clinical |
| | | | | F | 23 | | |
| | | | | F | 43 | | |
| Arbabi M (12) | Kashan | 1997 | 1997 | M | 32 | Nasopharyngeal | Clinical |
| Tabibian H (1) | Isfahan | 2012 | 2012 | F | 34 | Nasopharyngeal | forceps |
| | | | | | 12 | | |
| Sarmadian H | Shazand | 2017 | Unpublished | M | 13 | Nasopharyngeal | Clinical |

individual's nutritional culture in getting infected by this parasite. (Tabaripour et al. 2019).

The reported age of the infected individuals showed a distribution of 1, 3, 4, 5, 1, and 1 for the 1st to 6th decade of life, respectively. The majority of the reported cases were therefore in individuals between the ages of 30 to 40 years (Fig. 3). The case studies under review showed a greater incidence of tongue worm infection among women than men (60% *vs.* 40%). The local belief that the consumption of raw liver contributes to promoting human hematopoiesis may explain this difference.

A diagnostic tongue worm infection often relies on the patient's clinical symptoms, the history of consuming food contaminated with the parasite, and contact with pets those are likely to be infected. The most efficient method for diagnosis is achieved when both an evaluation of clinical symptoms and patient history are considered.

The diagnosis is confirmed through microscopic investigation of pathogen morphology. This process includes the removal of white spots from the patient's larynx or mouth, preparing a slurry of the excised material, fixing it with ethanol, and then staining it appropriately (e.g. using hematoxylin) (Moghadam and Dehghan 2001). In some reported cases of visceral infection, further examination may include magnetic resonance imaging (MRI) and CT-SCAN of the chest and abdomen, bronchoscopy, abdominal and pelvic ultrasonography, laparoscopy, and even biopsy and histopathology (Vakili et al. 2012; Yazdani et al. 2014).

The treatment of tongue worm infection is not specific but rather mainly treats the symptoms and instantly the antihistamines (Cetirizine and others) may be administered. Some cases may also involve parasite removal using forceps (Janbakhsh et al. 2015; Moghadam and Dehghan 2001). Disease symptoms are eliminated with the removal of the parasite or using the supportive medications (Moghadam and Dehghan 2001; Sadjjadi et al. 1998; Yazdani et al. 2014).

Cases of tongue worm infection in humans have been reported in Africa (5), East Asia (6), South America (Lazo et al. 1999), the United States (Baird et al. 1988; Gardiner et al. 1984), and the Middle East (Janbakhsh et al. 2015) while the latter representing the majority of the reports (Janbakhsh et al. 2015).

In the Sudan, the infection known locally as Marrara syndrome was found to occur after eating liver, lungs, trachea, and rumen, (Yagi et al. 1996). Similar causative conditions were observed by eating raw sheep liver in a case reported in Lebanon where the infection was termed Halzoun syndrome due to the involvement of the respiratory system and nasopharynx. Halzoun is a rare infection that can also be caused by the nymph stage of *Linguatula serrata* (Hamid et al. 2012; Moghadam and Dehghan 2001; Siavashi et al. 2002).

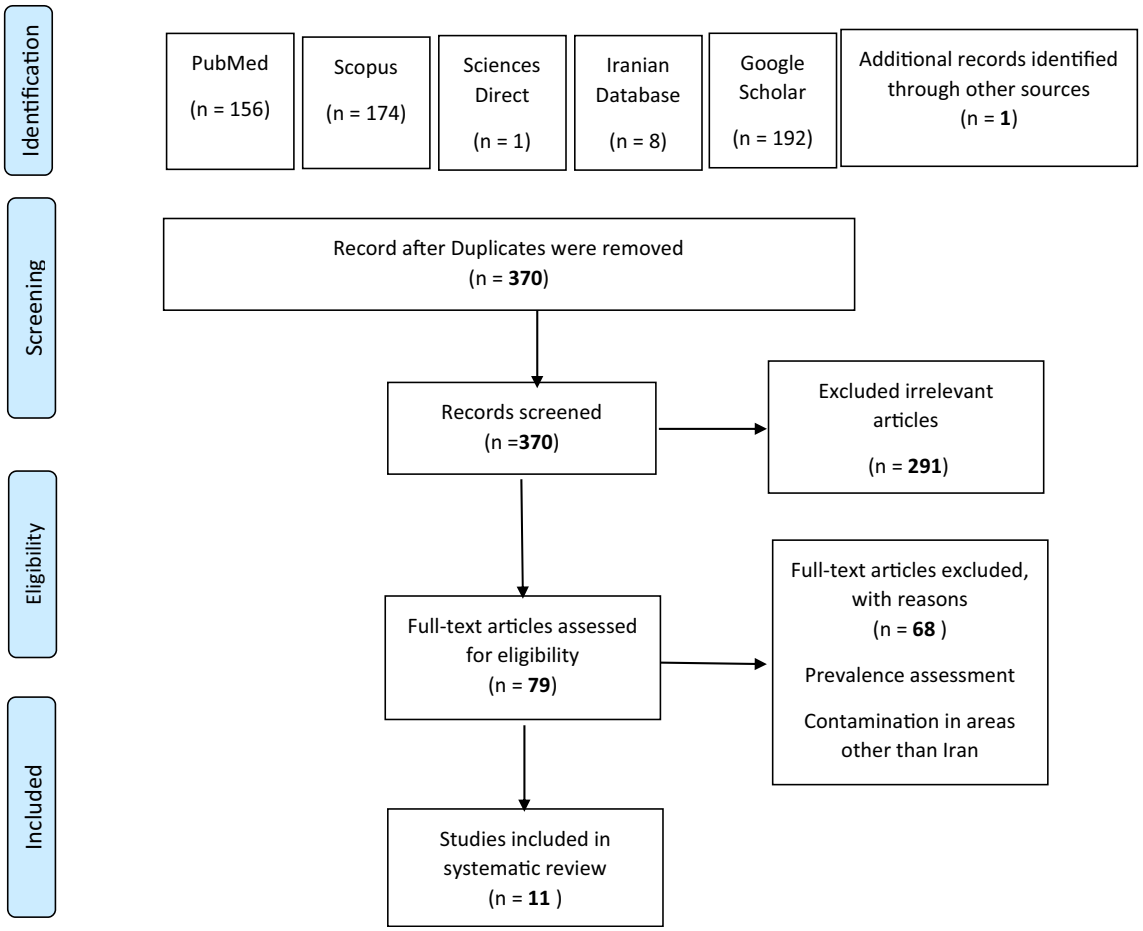


**Fig. 2** Flow diagram of the literature search and study selection

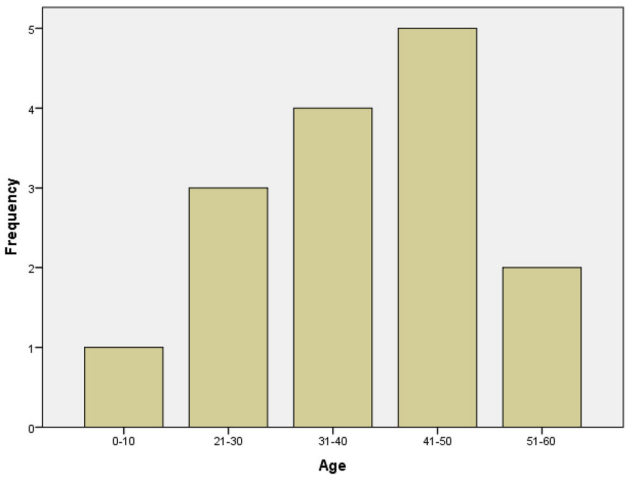


**Fig. 3** Age distribution of human cases infected by *Linguatula Serrata*

The presence of cysts of this parasite in human organs has been widely reported around the world. This parasite has been found in the nose and throat of a 20-year-old Iranian man (Morsy et al. 1999), in an anterior chamber of the eyes of an 8-year-old girl in Mississippi, USA (Rendtorff et al. 1962), in the eyes of a 34-year-old woman in Guayaquil, Ecuador (Lazo et al. 1999), in the lime liver nodules of a 62-year-old man in northern Carolina, USA (Baird et al. 1988), in the liver of a 15-year-old boy in Bashkortostan, Russia (Montazeri et al. 1997), in the lung nodules of a 42-year-old man with AIDS in Apulia, Italy (Pampiglione et al. 2001), and in the parenchymal tubercles in the small intestine wall of a 3-year-old girl in Zhejiang, China (Lai et al. 2010).

The actual number of patients with pentastomiasis is unknown as some of them are asymptomatic. Autopsy investigations in Nigeria, and western Malaysia indicated incidence rates of 33% to 45%, respectively (Sulyok et al. 2014). In a study conducted in two Lebanese hospitals between the years 2005 and 2007, all 32 cases presenting with itchy noses and throat congestion referred within a few minutes to 12 h after consuming raw liver (Lai et al. 2010). These two hospitals were selected for their vicinity to restaurants which served raw sheep liver. The average age of the 32 patients was 35 years old. Half of the individuals having eaten the same type of food had similar

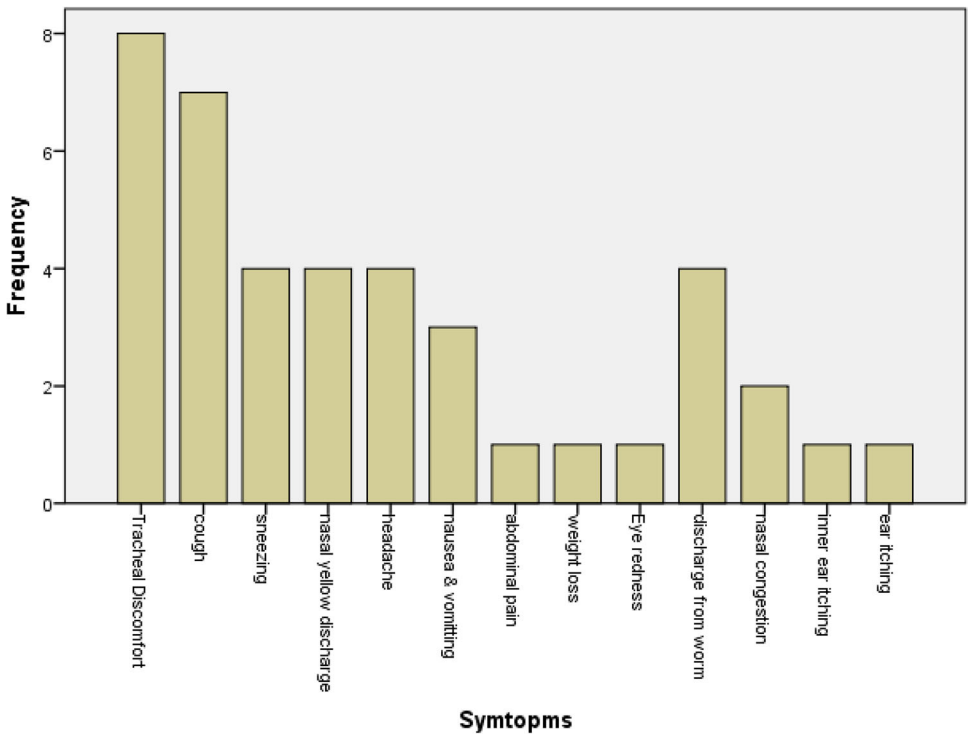


**Fig. 4** Distribution of symptoms among individuals infected by *Linguatula Serrata*

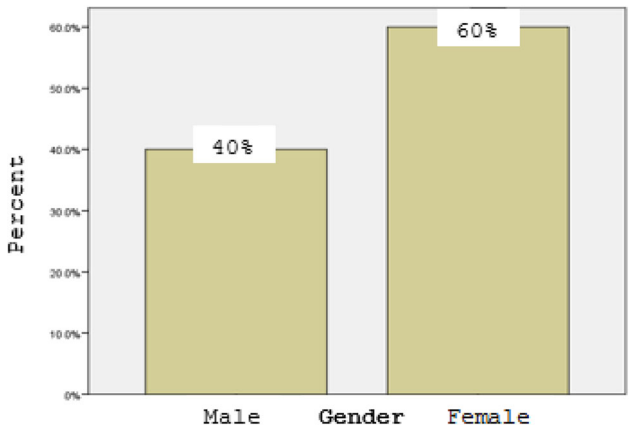


**Fig. 5** Gender distribution of patients by percentage

symptoms. Sheep, and goats comprised respectively 78%, and 22% of the sources of infected liver (Khalil et al. 2013).

In a study conducted in Congo, 12 men, and 6 women existed between the 19 examined cases and the sex of one patient was not reported. The average age of the cases when they were diagnosed was 14 years. In another study, most of the cases were reported from sub-Saharan African countries (11 cases) and the rest from the United States, Europe, India, Israel, and South America (Sulyok et al. 2014). Therefore, this parasitic infection is not associated with any particular country but the presence of the mentioned risk factors predisposes an individual to get infected with this parasite.

## Conclusion

Considering the patient's symptoms including respiratory tract itching, coughing, sneezing, in some cases visible worms and getting a full history on consumption of semi-cooked or raw ruminants' visceral organs, work and workplace allows a better diagnosis by physicians especially in the endemic areas. In addition, educating and enhancing the knowledge of people and health workers as well as improving hygiene play the important roles in preventing the infection.

Given that viscera of slaughtered livestock plays a significant role in the transmission of this infection to humans, Careful inspection of slaughtered livestock in slaughterhouses and Preventing the slaughter of livestock illegally and unsanitary, outside the slaughterhouse, is important.

**Acknowledgements** The authors thank the Infectious Diseases Research Center of Arak University of Medical Sciences.

**Authors' Contributions** HS, ZN and RG conceptualized the idea for this review, formulated the review question, and objectives, assisted with the development of the final search strategy, contributed to the data analysis/interpretation, and writing the manuscript. RG, SS, MZ, MMS, YM, MKH and BE contributed to the conceptualization of the final review question, formulation of the review objectives, data analysis/interpretation, and writing the manuscript. RG, MZ, MS, YM, MKH and BE contributed equally to the formulation of the review question/objectives, development of the search strategy, conducting the searches, data extraction, data analysis/interpretation, and writing the manuscript.

**Funding** The present study was registered at Arak University of Medical Sciences (Grant No. 3113).

**Compliance with ethical standards**

**Conflict of interest** There was not any conflict of interests by all authors.

**Ethical standard** All experimental procedures were approved by the Ethics Committee of Arak University of Medical Sciences, Iran. (Ethical Code: IR.Arakmu.rec.1397.58).

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