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Review Article

Trend of toxocariasis in Iran: a review on human and animal dimensions

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Summary

One of the neglected soil and/or food-borne diseases with international public health importance is toxocariasis. Human cases are being increasingly reported from Asian, African, Oceania, European and the American countries. Hence, human toxocariasis (HT) is now considered as a major zoonosis with global and regional importance. In Iran, human and animal toxocariasis is an endemic disease with clinical and epidemiologic health problem aspects. Doubtless, understanding the epidemiology and the trend of this important parasitic disease and its affecting factors will provide the establishment of effective prevention and control programs. To better understand the trend of toxocariasis researches in Iran, this study was performed to analyze different aspects of this zoonotic disease including history, life cycle, species, human animals and environmental studies, diagnostic aspects and treatments to find out the gaps, including different aspects of clinical sings in human patients, new and specific recombinant antigens based on the native antigens, new diagnostic tools, especially rapid diagnostic tests, paratenic hosts status and new treatment procedures which is necessary to be investigated in the future studies on this important zoonotic disease.

Key words: Iran, Larva migrans, *Toxocara canis*, *Toxocara cati*, Toxocariasis

Introduction

Soil-transmitted nematodes including toxocariasis are neglected in the international public health importance in comparison with other helminthic diseases (Hotez and Wilkins, 2009). Toxocariasis is a serious zoonotic parasitic disease infecting invertebrate and vertebrate and human beings with high impact on public health worldwide. It is caused by a nematode belonging to genus *Toxocara*. A variety of animals such as dogs, cats, foxes, wolves, rodents, rats, pigeons, lambs, chickens and cattle show infection rates that may reach to 90% in some areas (Schantz, 1989). Human infection with toxocariasis was rare up until the last four decades when clinical cases were reported (Despommier, 2003). The present review article describes the lesser-known contributions of Iranian researchers to better understand the trend of toxocariasis researches analysis in Iran with emphasis on different aspects of this important zoonotic disease including history, life cycle, species, human, animals and environmental studies, diagnostic aspects and treatments to find out the gaps including investigations on the different aspects of clinical signs in human patients, making new and specific recombinant antigens based on the native antigens, new diagnostic tools especially rapid diagnostic tests, paratenic hosts status, new treatment procedures specifically non-invasive procedures and finally registration of patients which is needed to be filled with new researches in the future on this important zoonotic and food-borne disease.

History

Animal toxocariasis has been reported during intestinal worms investigations of dogs in unpublished documents; however, the first published report about animal *Toxocara* is by Sadighian in 1969 who studied helminth parasites of stray dogs and jackals in Shahsavar area, Caspian region, Iran (Sadighian, 1969). In an extensive work on helminths in wild animals *Toxocara canis* and *Toxocara cati* were shown in the north of Iran (Dalimi and Mobedi, 1992). However, the chronological order of other studies has been reflected in Table 1.

Life cycle

A wide variety of animals, including mammalian can become infected with *Toxocara* species by ingesting eggs containing larvae from contaminated soil and the consumption of contaminated raw meat or liver (Despommier, 2003). In the paratenic or transport hosts, the larvae do not develop to maturity, but migrate for months throughout host organs such as liver, lungs, kidneys, heart, brain and retina before lodging within

Table 1: Prevalence of human toxocariasis based on reports in different regions of Iran

Province/regions, county	Author(s), year	Subjects	Clinical aspect [β]	Infected (%)/ cases (No.)
Zabol	Farivar and Rafat, (1991)	Children under 5 years [α]	VLM	2
Chahar Mahal Bakhtiari	Yousefi *et al*., (2000)	Children under 15 years	VLM	5.3
Shiraz	Sadjjadi *et al*., (2000)	Children 6-13 years	VLM	25.6
Tehran	Rokni *et al*., (2000)	Patients 3-52 years [α]	VLM	10
Hamedan	Fallah *et al*., (2003)	Children under 10 years	VLM	5.3
Babol	Mekaniki, (2006)	Forty-year-old [α]	OLM	1
Kermanshah	Akhlaghi *et al*., (2006)	Children 2-12 years	VLM	8.5
Shiraz	Zibaei *et al*., (2008)	Child 6 years [α]	VLM	1
Zanjan	Nourian and Amiri, (2009)	Children referred to health centers and hospitals	VLM	2.7
Ahvaz	Alavi and Sephidgaran, (2009)	Children with chronic cough	VLM	34.5
Sari	Sharif *et al*., (2010)	Schoolchildren	VLM	25.0
Ahvaz	Alavi *et al*., (2011)	Schoolchildren 6-15 years	VLM	19.7
Khorramabad	Rafiee Alavi and Nayebzadeh, (2011)	Woman 57 years [α]	VLM	1
Khorramabad	Zibaei *et al*., (2013)	Epileptic patients	NT	11.8
East-Azerbaijan	Garedaghi *et al*., (2013)	Children	VLM	29.5
Khorramabad	Zibaei and Ghorbani, (2014)	Multiple sclerosis patients	NT	14.7
Shiraz	Zibaei *et al*., (2014)	Child 6 years [α]	OLM	1
Zahedan	Ghorbani-Ranjbary *et al*., (2015)	Students with cough	VLM	11.3
Isfahan	Hosseini-Safa *et al*., (2015)	Children 5-15 years	VLM	1.4
Shiraz	Sarkari *et al*., (2015)	Hypereosinophilic individuals	VLM	2.0
Babol	Ebrahimifard *et al*., (2015)	Adult eosinophilia individuals	VLM	23.5
Arak	Miladi *et al.*, (2016)	Individuals referred to lab diagnosis	VLM	4.2
Tabriz	Momeni *et al*., (2016)	30 people	VLM	29.3
Tehran	Einipour *et al*., (2016)	Uveitis patients	OLM	6.2
Mashhad	Berenji *et al*., (2016)	Owners domestic cats and dogs	VLM	20.4
Arak	Mosayebi *et al*., (2016)	Asthmatic children	VLM	1.8

[α] Case report, and [β] VLM: Visceral larva migrans, OLM: Ocular larva migrans, and NT: Neurotoxocariasis

host tissues in state of arrested development. The larvae are not encysted but remain exposed to the host environment, absorbing nutrients across the nematode cuticle (Aziz *et al*., 2007). The larvae can survive in tissue for several years despite vigorous host immunologic responses to parasite antigens (Maizels, 2013).

Toxocara species

Toxocara as a nematode is taxonomically included within the order of Ascaridida. Among a total of 21 species within the *Toxocara* genus, 2 are of significant public health concern, namely, *T. canis* and *T. cati*, for which dogs and cats are the definitive hosts, respectively, *T. canis* (Wener, 1782) and *T. cati* (Shrank, 1788) are the causative agents of toxocariasis in canidae, felidae and in humans worldwide. Molecular studies on cat nematodes in Shiraz showed that, the most prevalent one is *T. cati* (Mikaeili, 2013). *Toxocara vitulorum* (syn. *Neoascaris vituolrum*) (Goeze, 1782) is an ascarid that is frequently found in ruminants in sub-tropical regions. Its main hosts are cattle and buffalo in tropical and sub-tropical countries (Roberts, 1989; Tavassoli and Tadayon, 2000).

Human toxocariasis (HT)

Clinical cases

Human toxocariasis is a zoonotic disease caused by ingestion of embryonated eggs of *T. canis* and *T. cati*, which originate from the faeces of definitive hosts contaminating the environment and the consumption of contaminated raw and undercooked meat. Children in their first decade of life are prone to infection because of their geophagic behavior and mouthing of objects, which is linked to a higher risk of exposure at sandboxes or playgrounds contaminated with dogs and cats faeces. Human infection is mostly asymptomatic but can be associated with severe clinical syndrome due to organ injury by migrating larvae (Glickman *et al*., 1979). Depending on the organs affected and the specifity of the symptoms, the predominant clinical syndromes are classified as visceral larva migrans (VLM), ocular larva migrans (OLM), and common, neurologic, and covert toxocariasis (Magnaval *et al*., 2001). Diagnosis of HT is traditionally based on a combination of clinical, serology and histopathological interpretation (Despommier, 2003). However, sensitivity is low, as biopsy material may not always contain the larvae. Serological examination, using *in vitro* obtained excretory-secretory (ES) proteins of the larvae, is the best laboratory-based option for diagnosis (Gold-Standard test), and is considered a useful predictor of *Toxocara* spp. infection when coupled to relevant clinical data (Smith *et al*., 2009).

Visceral larva migrans

The most common, VLM, is a febrile disease of childhood, particularly affecting children between the age of one and five years old. Visceral larva migrans has been sporadically reported from different parts of Iran.

The first report on VLM in Iranian patients was reported by Jamalian (1976), followed by Farivar and Rafat (1991) who reported a 5-year-old boy admitted to a university hospital because of fever (two months), hepatomegaly, and weight loss. The serological examination was performed and the patient was strongly suspected to have suffered from visceral toxocariasis. A review of the clinical history of 10 VLM patients was published 8-years thereafter (Rokni *et al*., 2000). Zibaei *et al*. (2008) presented a case of VLM in a 6-year-old child, which was diagnosed by sonographic and biopsy finding, and subsequently confirmed by enzyme-linked immunosorbent assay (ELISA) test.

Ocular larva migrans

Ocular abnormalities are a frequent complication of toxocariasis. Ocular toxocariasis is typically a monocular disease of young children. Patients with this disease present with chronic unilateral uveitis and a marked vitreous opacification that overlies a primary eosinophilic granuloma. The first report on OLM was published in 2006 and describes the clinical history of a 40-year-old man presenting with pain and visually impaired. The acute uveitis was accompanied by a granuloma in the eye-funds (Mekaniki, 2006). Following a gap of 8 years, one case of ocular toxocariasis in a 6-year-old boy suffering from clinical manifestation suggestive of toxocarial OLM was published (Zibaei *et al*., 2014).

Exudative retinal detachment, posterior synechiae, and a cyclitic membrane may be present in the OLM. *Toxocara granuloma* is white, dome-shaped, and confined principally to the retina. Serological tests like ELISA with *Toxocara* infective larval ES antigen are the gold standard for diagnosis of ocular toxocariasis.

Covert toxocariasis

Serological studies in the past two decades indicated that HT is more prevalent in at least 3 main foci, in western and southern regions. These are, (i) the northwest areas (East Azerbaijan province); (ii) southwest (Khuzestan province), and (iii) south regions (Fars province) (Fig. 1).

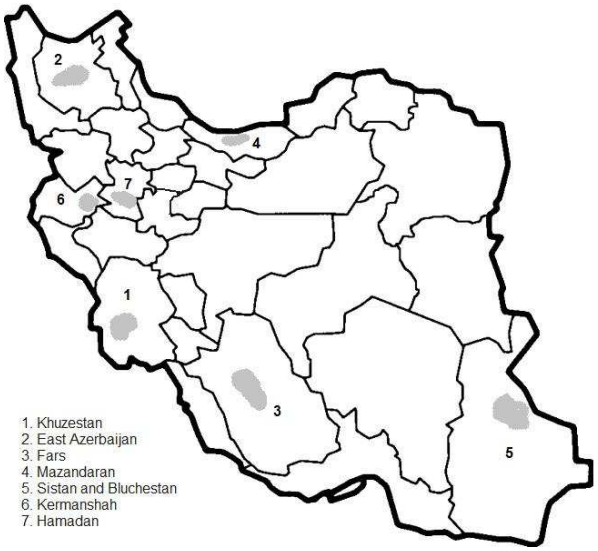

Fig. 1: Approximate distribution of human toxocariasis and *Toxocara* species in Iran. The majority of currently known HT prevalence from provinces of Khuzestan (Ahvaz, #1), East Azerbaijan (Tabriz, #2), Fars (Shiraz, #3), Mazandaran (Sari, #4), Sistan and Bluchestan (Zahedan, #5), Kermanshah (Kermanshah, #6), and Hamadan (Hamadan, #7)

The first population study based on serological tests in Iran was reported by Sadjjadi *et al*. (2000) using sera of 436 clinically healthy children. In their sample, 25.6% of subjects tested positive for *Toxocara* excretory-secretory (TES) antigens. In another study, Yousefi *et al*. (2000) demonstrated that 5.3% of children less than 15 years old possessed the IgG antibodies to TES. In a mild-scale seroepidemiological study, Garedaghi (2013) collected 336 sera from infants and tested for TES antibodies. Antibodies were confirmed in 99 individuals (29.5%). Several publications dealing with HT in Iran were identified (Akhlaghi *et al*., 2006; Mekaniki, 2006; Fallah *et al.*, 2007; Alavi and Sephidgaran, 2009; Nourian and Amiri, 2009; Sharif *et al*., 2010; Alavi *et al*., 2011; Zibaei *et al*., 2014; Ghorbani-Ranjbary *et al*., 2015; Hosseini-Safa *et al*., 2015; Momeni *et al*., 2016) (Table 1).

Just as in other parasitic infections, direct demonstration is the only way to make definite diagnosis of visceral toxocariasis. However, it is difficult to find the larva in either tissue biopsies or autopsies due to its very small size. Based on improvements in the field of serology, diagnosis of VLM is usually made by detection of the specific antibodies to TES, along with clinical manifestations such as eosinophilia, eosinophilic pneumonia.

Neurological toxocariasis

The sites of central nervous system (CNS) invasion by *Toxocara* larvae include the spinal cord and brain. Neurotoxocariasis (NT) is a CNS manifestation of *Toxocara* infection that is influenced by multiple factors, such as the number of ingested eggs, previous exposure, and host genetic factors, all of which contribute to the complex pathogenesis of NT (Xinou *et al*., 2003). Zibaei and Ghorbani (2014) conducted a case-control study and found a significant association between *Toxocara* seropositivity and multiple sclerosis. The results showed that from 68 multiple sclerosis patients who participated in the study, 14.7% had positive anti-*Toxocara* antibodies.

Epilepsy is considered an important health problem in the developing countries such as Iran. A possible association between toxocariasis and epilepsy has been hypothesized and *Toxocara* infection has been suggested as cofactor for epilepsy. In a study by Zibaei *et al.* (2013), frequency of *Toxocara* infection in epileptic patients was 11.8% (n=10 out of 85).

Animal toxocariasis

Toxocara infection in the dogs: *T. canis*

Published papers on animal toxocariasis in peer-reviewed journals have been reviewed (Table 2). The first paper of animal toxocariasis in Iran has been published by Sadighian (1969) in stray dogs (35%) and jackal (10%) of Caspian Sea region in Iran, although unpublished documents show earlier reports of animal toxocariasis in Iran (Table 1). Similarly, Mirzaians *et al.* (1972) reported that 16.6% of domestic dogs were infected with *T. canis* in Tehran.

In a study in Gilan and Mazandaran provinces on dogs, jackals, cats, badgers, foxes, and wild cat in the provinces, provided by the Provincial Institute of

Table 2: Prevalence of animals *Toxocara* spp. infection in different Iranian governorates according to reports

Governorates	Author(s), year	Animals	Species	Infected (%)
Tehran	Makarechian, (1955)	Dogs	*T. canis*	76.0
Tehran	Mobedi, (1968)	Dogs	*T. canis*	66.0
Mazandaran	Sadighian, (1969)	Stray dogs	*T. canis*	35.0
Mazandaran	Sadighian, (1969)	Jackals	*T. canis*	10.0
Tehran	Mirzayans, (1971)	Domestic cats	*T. cati*	31.4
Tehran	Mirzayans *et al*., (1972)	Domestic dogs	*T. canis*	16.6
Gilan and Mazandaran	Arfaa, (1972)	Dogs	*T. canis*	35.0
Gilan and Mazandaran	Arfaa, (1972)	Jackal	*T. canis*	10.0
Mazandaran and Gilan	Dalimi and Mobedi, (1992)	Wild cats	*T. cati*	13.0
Mazandaran	Gholami *et al*., (1999)	Dogs and Jackals	*T. canis*	13.3
Fars	Sadjjadi *et al*., (2001)	Stray cats	*T. cati*	52.8
Fars	Mehrabani *et al*., (2002)	Stray dogs	*T. canis*	3.9
Fars	Zibaei *et al*., (2007)	Stray cats	*T. cati*	42.6
Mazandaran	Sharif *et al*., (2007)	Stray cats	*T. cati*	60.0
West-Azerbaijan	Tavassoli *et al*., (2008)	Dairy calves	*T. vitulorum*	8.1
Iran	Meshgi *et al*., (2009)	Golden Jackal (*Canis aureus*)	*T. canis*	32.4
Isfahan	Arbabi and Hooshyar, (2009)	Stray cats	*T. cati*	13.3
Khorasan Razavi	Razmi, (2009)	Dogs	*T. canis*	17.9
North Iran	Daryani *et al*., (2009)	Stray dogs	*T. canis*	60.0
Iran	Meshgi *et al*., (2009)	Red fox (*Vulpes vulpes*)	*T. canis*	10.8
Zanjan	Esmaeilzadeh *et al*., (2009)	Stray cats	*T. cati*	8.0
East-Azerbaijan	Shirzadi *et al*., (2010b)	Persian cats	*T. cati*	20.0
Semnan	Eslami *et al*., (2010)	Stray dogs	*T. canis*	22.0
East-Azerbaijan	Shirzadi *et al*., (2010a)	Stray cats	*T. cati*	39.0
Ilam	Bahrami *et al*., (2011)	Stray dogs	*T. canis*	36.6
Khorasan Razavi	Borji *et al*., (2011)	Stray cats	*T. cati*	28.8
Tabriz	Garedaghi and Safar Mashaei, (2011)	Pet and stray dogs	*T. canis*	12.0
Golestan	Ghaemi *et al*., (2011)	Persian leopard (*Panthera pardus saxicolor*)	*T. cati*	2.0[†]
Ilam	Bahrami *et al*., (2011)	Stray cats	*T. cati*	20.7
Isfahan	Pestehchian *et al*., (2012)	Stray dogs	*T. canis*	6.3
Kerman	Mirzaei and Fooladi, (2012)	Owned dogs	*T. canis*	4.3
West-Azerbaijan	Tavassoli *et al*., (2012)	Sheep and pet dogs	*T. canis*	9.7
Fars	Mikaeili *et al*., (2013)	Stray cats	*T. cati*	26.7
Khorasan Razavi	Adinezadeh *et al*., (2013)	Stray dogs	*T. canis*	7.3
Khorasan Razavi	Beiromvand, *et al*., (2013)	Domestic and stray dogs	*T. canis*	25.0
Khorasan Razavi	Shemshadi *et al*., (2014)	Carnivores	*T. canis*	75.0
Tehran	Meshgi *et al*., (2014)	Stray cats	*T. cati*	52.7
East-Azerbaijan	Garedaghi *et al*., (2014)	Stray dogs	*T. canis*	12.0
Hamadan	Sardarian *et al*., (2015)	Household dogs	*T. canis*	41.8
Ardebil	Zare-Bidaki *et al*., (2015)	Dogs	*T. canis*	43.5
Khorasan-Razavi	Emampour *et al*., (2015)	Stray dogs	*T. canis*	29.0
Hamadan	Sardarian *et al*., (2015)	Stray dogs	*T. canis*	22.1
Golestan	Geraili *et al*., (2016)	Persian leopard	*T. canis*	23.3
East-Azerbaijan	Hajipour *et al*., (2016)	Stray cats	*T. cati*	78.8
Mazandaran	Savari *et al*., (2016)	Dogs	*T. canis*	27.0
Golestan	Geraili *et al*., (2016)	Persian leopard	*T. cati*	3.3

[†] *T. cati* isolated from two leopards

Veterinary Medicine, a total sample size of 152 was assessed. Intestines were collected and direct examination was conducted. Parasite adults of *T. canis* were detected in dogs (6.2%) and jackals (15.5%) (Dalimi and Mobedi, 1992).

Another Iranian investigation on *T. canis* infection in dogs originates from 1992 and was a cross-sectional study conducted to determine the prevalence in stray dogs of Mazandaran province (Gholami *et al*., 1999). Intestines of the animals were sampled from 75 randomly selected in each of the cities of Mazandaran province. Adult worms in the dogs' intestine were detected by stereomicroscope and direct microscope. The overall prevalence of infected dogs was 13.3% (n=10 out of 75).

A more recent study carried out in 2015 focused on the detection of intestinal helminths of stray dogs in Mashhad, in the northeast of Iran (Emampour *et al*., 2015). In this study, the prevalence of *T. canis* was determined by the detection of adult worms in the intestine of animals, and not by the detection of eggs in eggs in faeces. Adult worms of *T. canis* were detected in 24.0% of the dogs surveyed (n=29 out of 100). In accordance with the above survey, the significant differences in prevalence were not observed between male (n=14, 22.9%) and female (n=15, 38.4%). Moreover, the prevalence was higher in dogs younger's than 1 year (n=21, 25.6%) versus dogs below or above 1 year of age (n=8, 44.1%).

The reported data suggest that prevalence of infection in dogs, ranges from 4.3% to 43.5% in Iran, depending both on the method used and on the location. One of the best options for reducing toxocariasis in dogs is preventive chemotherapy (Dalimi and Mobedi, 1992). To be effective, this intervention should reach both stray and owner dogs.

Toxocara infection in the cats: *T. cati*

A large number of studies have been conducted for infection of definitive animal hosts with *T. cati*. In the case of feline infection, a variety of different methods have been used for identification of feline infection with

some measuring coproantigen positivity, some identifying worms following arecoline purgation, and some attempting to adjust these estimates in order to estimate the true infection status. However, the prevalence of infection with toxocariasis in cat in different regions of Iran is shown in Table 2 (Mirzayan, 1971; Arbabi and Hooshyar, 2009).

The early citation for feline toxocariasis in Iran was in 1971; it was mentioned that *T. cati* occurred in 31.4% of the domestic cats (Mirzayan, 1971). In 1992, a study in Gilan and Mazandaran provinces showed that the prevalence of toxocariasis in examined cats was 13.0% (Dalimi and Mobedi, 1992). The highest (78.0%) and lowest (8.0%) rate of infection were in cities of Azarshahr (East Azerbaijan province) and Zanjan (Zanjan province), respectively (Sharif *et al*., 2007; Esmaeilzadeh *et al*., 2009). Accordingly, all these animals having the label of final hosts can be regarded as the source of infection. The public health authorities have established a monitoring system to decrease the risk of infection.

Epidemiological picture of *Toxocara* spp. in paratenic host

Post-mortem examination (necropsy) of the tissues and organs for presence of larvae is the gold standard examination for the detection of infection in paratenic hosts. Beaver (1969) hypothesized that organs or tissues of infected animals can serve as sources of *Toxocara* infection for humans.

In Iran, several studies have reported that gerbils, rats, chicken, and partridge as paratenic hosts infected with *Toxocara* spp. (Azizi *et al*., 2007; Oryan *et al*., 2009; Oryan *et al*., 2010; Zibaei *et al*., 2010d; Ebrahimi *et al*., 2013; Zibaei *et al*., 2017b) (Table 3). Azizi *et al*. (2007) experimentally inoculated *T. cati* eggs into the gizzard of chickens and observed migrating larvae in the liver. More recently, a study on naturally infected broiler chickens revealed that the frequencies of the species in the chickens were *T. canis* larvae (83.3%, n=5 out of 33) and *T. cati* larvae (16.7%, n=1 out of 33) (Zibaei *et al*., 2017b).

Contamination with *Toxocara* species eggs in environment

Soil-transmitted and helminths are still one of the most important health problems in the world, even in developing countries (Alonso *et al*., 2001). Although dogs and cats are definitive hosts, but expelled eggs should remain in the soil until larva develops within 6 weeks (Coelho *et al*., 2001; Chorazy and Richardson, 2005). We found eleven reports conducted in Iran from 2006 (Tavassoli *et al*., 2008; Maraghi *et al*., 2014) (Table 4). The first Iranian study dealing with environmental

Table 3: *Toxocara* species identified in the paratenic hosts according to the technique applied

Host	Author(s), Year	Infection	Method	Species
Chickens	Oryan *et al*., (2009)	Experimentally	D [η]	*T. cati*
Chickens	Oryan *et al*., (2009)	Experimentally	D	*T. cati*
Chickens	Azizi *et al*., (2007)	Experimentally	D	*T. cati*
Partridges	Ebrahimi *et al*., (2013)	Naturally	D	-
Gerbils and rats	Zibaei *et al*., (2010d)	Experimentally	D	*T. cati*
Chickens	Zibaei *et al*., (2017b)	Naturally	D & M [γ]	*T. canis* and *T. cati*

[η] D: Digestion, and [γ] M: Molecular

Table 4: Soil and vegetables contamination with eggs of *Toxocara* spp. in different regions of Iran

Area examined	Author(s), year	Subjects	Prevalence (%)
Shiraz	Motazedian *et al*., (2006)	Public area	6.3
Urmia	Tavassoli *et al*., (2008)	Public parks	7.8
Shiraz	Zibaei and Sadjjadi, (2010b)	Public area	Let. to Editor
Khorramabad	Zibaei *et al*., (2010a)	Public parks	63.3
Tehran	Tavalla *et al*., (2012)	Public parks	38.0
Tabriz	Garedaghi *et al*., (2012)	Public parks	9.3
Tehran	Khazan *et al*., (2012)	Public area	10.0
Qazvin	Saraei *et al*., (2012)	Public parks	3.6
Southern Iran	Olyaei and Hajivandi, (2013)	Leafy vegetables plants	16.0
Amol	Siyadatpanah *et al*., (2013)	Applied vegetables	3.2
Abadan	Maraghi *et al*., (2014)	Public parks	29.2
Shiraz	Ghorbani Ranjbary *et al*., (2014)	Public parks	15.0
Ahvaz	Khademvatan *et al*., (2014)	Public area	46.3
Mashhad	Berenji *et al*., (2015)	Public parks	7.7
Isfahan	Ghomashlooyan *et al*., (2015)	Public parks	28.6
Khaf	Berenji *et al*., (2015)	Public parks	10.3
Shahrekord	Fallah *et al*., (2016)	Vegetables	3.9
Mazandaran	Rostami *et al*., (2016)	Salad vegetables	1.7
Kermanshah	Ghashghaei *et al*., (2016)	Public parks	18.0
Karaj	Zibaei *et al*., (2017a)	Public parks	36.4

contamination detected *Toxocara* spp. eggs in 12 out of 112 soil samples collected by cluster random sampling from the uppermost centimeter of soil in 26 public places and children's playground in 4 regions of Shiraz, southern Iran, reported an overall prevalence of 6.3% with *T. cati* ova infected regions (Motazedian *et al*., 2006). The highest contamination rate was in downtown public places in the 3rd (22.2%) and the 4th (20.0%) regions from four regions. Contamination was not observed during the dry seasons. However, due to their applied methodology, it was argued that the conclusions reported by them was not entirely supported by their results (Zibaei and Sadjjadi, 2010b).

Recently, the contamination level of public parks samples was assumed in the Mashhad and Khaf cites, in the northeast of Iran (Berenji *et al*., 2015). Three-hundred and forty soil samples of Mashhad (n=195) samples and Khaf (n=145) parks samples, using simple random method were collected and examined with flotation technique and direct smear, and were evaluated using a light microscope. *Toxocara* spp. eggs were present in 7.7% and 10.3% of public parks of Mashhad and Khaf, respectively. The authorities of cities should pay considerable attention to disease control of these zoonotic infections. This can be achieved by increasing the hygiene education of people and pet owners and controlling the number of stray cats and dogs.

Diagnostic aspects

The diagnosis of *Toxocara* infection in human is mainly based on clinical, epidemiological, and laboratory information, which include imagining finding, blood tests, eosinoplilia, immunoglobulin E level, and serological tests (Fillaux and Magnaval, 2013). Enzyme-linked immunosorbent assay and Western blotting are two types of tests that are available for the immunodiagnosis of toxocariasis, both using TES antigens (Magnaval *et al*., 1991; Ishiyama *et al*., 2009; Roldan and Espinoza, 2009; Maraghi *et al*., 2012). It has long been considered that ES proteins secreted by nematodes hold the key to their success as parasites (Stirewalt, 1963). The first report by de Savigny (1975) demonstrated that *T. canis* larvae could be cultured for long periods of time, and that these culture supernatants contained antigens that were specific in diagnosing HT. The nature of TES was extensively studied by Maizels *et al*. (1984, 2000), and Maizels and Page (1990).

In Iran, research primarily at the Tehran University of Medical Sciences investigated the use of TES from second-stage larvae for detection of serum antibodies to *T. canis* (Jahani *et al*., 1996). In a study by Maleky and Massoud (1997) ES antigen of *T. canis* and *T. cati* were demonstrated to have fractions with molecular weight between 30-120 kDa. Finding showed that the common fraction is 67 kDa. Zibaei *et al*. (2016) studied the ES antigens of *T. cati* larvae using ELISA and also Western blotting for serodiagnosis of HT and determined that the ELISA analyses using *T. cati* ES antigens has a good sensitivity (96.7%) compared to *T. canis* ES as antigens for diagnosis HT. Electrophoretic analyses of *T. cati* ES antigens revealed a range of 20-150 kDa fractions and application of Western blotting based on 42 and 50 kDa fractions of ES antigens can be recommended for the acute diagnosis of toxocariasis. Production of monoclonal antibodies against *T. cati* has been reported by Zibaei *et al*. (2010c) for diagnosis of toxocariasis which verified that capture-ELISA is sensitive enough to detection of 5 ng/ml of *T. cati* antigen.

Although the antigenicity and specifity of TES is fairly high, cross-reaction to other parasite, especially nematode parasites have been observed (Yamasaki *et al*., 2000). To overcome this problem, Zahabiun *et al*. (2015) cloned *T. cati* recombinant TES-120 (rTES-120), expressed and compared with its *T. canis* homolog in an IgG4-Western blotting. The findings showed that the diagnostic sensitivity and specifity of *T. cati*, rTES-120 were 70% and 100%, respectively, and about *T. canis* rTES-120 were 57.4% sensitivity and 94.4% specifity. The results revealed that the serodiagnosis sensitivity was 76% when using rTES-120 for both species considered.

Treatment

Anthelmintics eliminate worms in the intestines of definitive hosts. Piperazine, Pyrantel pamoate, Fenbendazole have been used for treatment of *T. canis* in dogs and Piperazine, Pyrantel pamoate, Selamectin, for *T. cati* infection in cats (Ballweber, 2001).

Although hypobiotic larvae are thought to be difficult to kill in dogs and cats, Selamectin has been used as a preventive against *Toxocara* in dogs and cats (Taylor *et al*., 2016). Anyhow, the efficacy against larvae in different hosts, at different body sites, or at different stages of larval development, is still not completely understood (Oryan *et al*., 2009). In paratenic hosts the larva tend to migrate to the brain as their final site which is difficult for drug exposure (Oryan *et al*., 2008).

Patients with severe toxocariasis, particularly if there is CNS involvement, can be treated with systemic acting and larvicidal anthelminthics. Effective results have been reported with use of albendazole, mebendazole, fenbendazole, and diethylcarbamazine (Magnaval, 1995; Oryan *et al*., 2009; Oryan and Alabadi, 2015). Most of these results are obtained from experimental studies on mice as one of the animal models where administration of higher doses of anthelminthic started directly after inoculation with *Toxocara* larvae and continued for several days (Overgaauw and van Knapen, 2013). The anthelminthic dose should be increased gradually over a period of days and covered by concomitant administration of steroids. The best results and a low rate of side effects in man are reported for mebendazole at a daily dose of 20-25 mg/kg for 3 weeks or albendazole 400 mg twice daily for 7 days administered concomitantly with prednisone 0.5-1.0 mg/kg daily in cases of visceral or ocular toxocariasis (Zibaei *et al*., 2008; Zibaei *et al*., 2014; Allahdin *et al*., 2015).

The literature search on toxocariasis (caused by *T.*

canis and *T. cati*) in Iranian people yielded only a limited number of reports. Data from studies and case reports were predominantly conducted in Iran, hampering a reliable estimation of the importance of toxocariasis in Iranian people. Yet, the information suggests that *Toxocara* infection of the cats and dogs hosts, and environmental contamination with *Toxocara* species eggs is remarkable. Information from HT is less conclusive. However, data is limited and scatted across different fields and over time. There is a clear need for more new data including the investigations on the different clinical views in human patients, i.e. VLM, OLM, covert and neurological toxocariasis epidemiology, making new and specific recombinant antigens based on the native *Toxocara* species, new diagnostic tools, especially lateral flow tests or rapid diagnostic tests, paratenic hosts status especially those as food sources, new treatment procedures specifically non-invasive procedures and finally registration of patients in different health centers which need to be filled with new researches in the future on this important zoonotic and food-borne disease. Dedicated studies including human, animal and environmental health data should be conducted in different geographical areas. The outcome of such studies will allow policy makers to set proprieties and design strategies, combining accurate surveillance and prevention of this zoonotic and food-borne disease.

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