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Review

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Status of human toxocariasis, a neglected parasitic zoonosis in Iran: a systematic review from past to current

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Abstract

Although human toxocariasis can lead to serious complications including neurological, ocular and visceral complications, there is a lack of comprehensive epidemiological information about the seroprevalence of *Toxocara* species in humans. In the present study, we analysed and reviewed the overall seroprevalence of human toxocariasis in Iran. The data collection was systematically undertaken on published articles using the PubMed, Google Scholar, ScienceDirect and Scopus databases. A total of 27 studies from the past two decades reporting seroprevalence of human toxocariasis met our eligibility criteria. The pooled proportion of *Toxocara* infection was estimated as 6.58% (95% confidence interval = 3.98–9.77). A wide variation between different studies was observed (Q statistic = 799.37, df = 26, $P < 0.0001$, and $I^2 = 96.7\%$). The seroprevalence rate of toxocariasis in the Iranian population is relatively high; contamination of the environment by eggs from the host as well as from household dogs and cats should be blamed.

Keywords

Toxocariasis, zoonosis, public health, Iran

Introduction

Toxocariasis, a neglected tropical parasitic zoonosis, is caused by the roundworm species *Toxocara canis* and *T. cati*. The nematode is frequently found in the small intestine of Canidae; however, humans can act as accidental hosts.[1] The major routes of transmission to humans are ingestion of raw vegetables, which contain embryonated eggs, close contact with infected dogs and cats, particularly in pet owners, as well as consumption of contaminated raw meat with *Toxocara* larvae. Clinical manifestations depend on the aberrant migration of second-stage larvae that result in the invasion of a wide range of organs including visceral larva migrants (VLM), ocular larva migrants, and neurologic and covert toxocariasis.[2] Significant and serious symptoms include hepatomegaly, splenomegaly, abdominal pain, hypereosinophilia, asthma, allergy, uveitis, optic papillitis, bronchitis, urticaria, behavioural disorders, vomiting, neurological, neurophysiological and occult infection.[3,4]

Human toxocariasis is diagnosed after considering epidemiological, serology, clinical, histopathological

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and laboratory findings including eosinophilia and IgE levels, imaging and serological tests.[5] Seroprevalence studies indicate that toxocariasis is cosmopolitan and can be considered one of the most common helminthic infection in humans. Human toxocariasis is increasing in prevalence according to reports from Asia, Oceania, Europe, Africa and the Americas.[6] It is higher in tropical and low- and middle-income countries, and is generally associated with low socioeconomic status. Toxocariasis, both in humans and in animals, is considered an endemic and intrinsic disease in Iran, where *Toxocara* spp. is one of the most frequent (18.8%) parasites of dogs.[7] Human toxocariasis is mainly attributed to *T. canis* rather than *T. cati*. High-risk groups for toxocariasis are children, dog owners, veterinarians and farmers, all of whom are more exposed to the eggs of *Toxocara* species. Among them, children usually have a higher tendency to inadvertently ingest *Toxocara* ova.[8] Nonetheless, toxocariasis requires more attention from public health services and research systems owing to the importance of clinical symptoms and its disease prevalence. Therefore, the major purpose of our systematic review was to elucidate and analyse the seroprevalence rate of toxocariasis in the Iranian population between 2000 and 2018 and to note the need for improving prevention and control measurements.

Methods

We included studies in English conducted on the seroprevalence of human toxocariasis in Iran from 2000 to 2018. Case reports, studies about animal toxocariasis and those using molecular methods were excluded.

The following databases were searched: PubMed; Google Scholar; ScienceDirect; and Scopus. Keywords used in combination or alone were: toxocariasis; *T. canis*; *T. cati*; seroprevalence; antibody; IgG; human; Iran; and eosinophilia. References of the articles were checked to avoid omitting any article.

A data extraction sheet was used to collect the following data from the literature: the first author; year of publication; province; residential areas (urban/rural); sample size; prevalence rate; gender for the origin of samples; age; diagnostic methods of samples; cut-off value; contact history with dog and cat; and eosinophilia.

The pooled proportions of human toxocariasis seroprevalence with a 95% confidence interval (CI) were calculated for each study. A forest plot was used to visualise heterogeneity among the included studies. Heterogeneity was expected in advance and statistical analyses including I^2 and Cochrane's Q test (with a significance level of $P < 0.1$) were used to quantify variations. The meta-analysis was performed using StatsDirectStatistal Analysis software.

Results

In the first phase of database search (using PubMed, Google Scholar, ScienceDirect and Scopus), 1763 records were identified. In the next step, 52 duplicate papers were removed and 1543 records were excluded based on their title and abstract. Full texts of the remaining 168 articles were assessed for eligibility criteria based on their sample size, being reviewed articles or case series reports, animal studies and sufficient data numbers. A total of 27 studies met the eligibility criteria in our meta-analysis. We accumulated 9490 individuals evaluated for toxocariasis using serological diagnostic methods in different areas of Iran, of whom 821 were positive (Table 1). Enzyme-linked immunosorbent assay (ELISA; 25 studies) was the most common serological employed method for diagnosis of anti-*Toxocara* IgG antibody in humans. The pooled proportion of toxocariasis among the studied Iranian people from 2000 to 2018, considering the model of random effects, was estimated as 6.58% (95% CI = 3.98–9.77). Figure 1 shows a forest plot of our systematic review. A wide variation in the seroprevalence estimates of different studies was observed (Q statistic = 799.37, df = 26, $P < 0.0001$ and $I^2 = 96.7\%$).

The prevalence of human toxocariasis infection in various regions of Iran was in the range of 0%–29.4%, the distribution in different areas of Iran is shown in Figure 2. The age range of the individuals was 1 month–80 years; however, 70% of studies were conducted in children aged ≤15 years.

Discussion

Human toxocariasis is considered one of the most prevalent neglected tropical zoonotic helminthic infections owing to the man–soil–dog cycle in rural and urban areas in both low- and high-income countries.[9] A similar systematic review reported that the overall prevalence of *Toxocara* spp. contaminating soil samples from Iran is 16%.[10] Different rates of human toxocariasis have been reported from areas in the world, including Spain (1%), Brazil (3.6%), Turkey (15.7%), Iraq (20.6%) and Argentina (37.9%–39%).[11–15]

Diagnosis of *Toxocara* infection is usually determined via ELISA using excretory-secretory antigens of *Toxocara* spp. Among different serological diagnostic assays, ELISA was utilised in the majority of toxocariasis studies in humans to determine sera for anti-Toxocara antibodies. owing to its high and reliable sensitivity, specificity and availability.[16–18] However, a single seropositivity could have limited pathological

Table 1. Publications of human toxocaraisis included in the current systematic review.

No.	Author and reference	Year	Province	Method	Total individuals	Positive individuals
1	Yousefi et al.[29]	2000	Chaharmahal and Bakhtiari	IFA	64	13
2	Sadjjadi et al.[22]	2000	Fars	ELISA	519	133
3	Akhlaghi et al.[30]	2006	Tehran	ELISA	260	22
4	Fallah et al.[31]	2007	Hamadan	Immunosorbent assay	544	29
5	Nourian et al.[32]	2008	Zanjan	ELISA	810	22
6	Sharif et al.[23]	2010	Mazandaran	ELISA	1210	302
7	Alavi et al.[33]	2011	Khozestan	ELISA	203	4
8	Maraghi et al.[34]	2012	Khozestan	ELISA	100	1
9	Zibaei et al.[35]	2013	Lorestan	ELISA	85	3
10	Yagoob et al.[24]	2014	East Azerbaijan	ELISA	336	99
11	Khademvatan et al.[36]	2014	Khozestan	ELISA	95	4
12	Berenji et al.[37]	2015	Razavi Khorasan	ELISA	40	1
13	Hosseini-safa et al.[38]	2015	Isfahan	ELISA	427	6
14	Sarkari et al.[39]	2015	Fars	ELISA	100	3
15	Allahdin et al.[40]	2015	Khozestan	ELISA	144	2
16	Ghafari et al.[41]	2016	Chaharmahal and Bakhtiari	ELISA	552	11
17	Mosayebi et al.[42]	2016	Markari	ELISA	70	0
18	Momeni et al.[43]	2016	West Azerbaijan	ELISA	397	12
19	Berenji et al.[44]	2016	Razavi Khorasan	ELISA	93	1
20	Shahraki et al.[45]	2017	Sistan and Baluchestan	ELISA	364	14
21	Beiromvand et al.[46]	2018	Khuzestan	ELISA	410	8
22	Mahmoudvand et al.[47]	2018	Lorestan	ELISA	316	14
23	Raissi et al.[48]	2018	Ilam	ELISA	296	49
24	Sarkari et al.[49]	2018	Fars	ELISA	617	39
25	Shokouhi et al.[50]	2018	Ilam	ELISA	383	84
26	Momen et al.[51]	2018	Isfahan	ELISA	46	10
27	Aghamolaie et al.[52]	2018	Mazandaran	ELISA	630	148

ELISA, enzyme-linked immunosorbent assay.

importance and probably reflects a past *Toxocara* infection rather than a recent one. Besides, seropositivity does not provide evidence for either active systemic toxocariasis or for CNS toxocariasis.[6] In addition, in the most carefully analysed studies, the seroprevalence rate of *Toxocara* infection was higher among case groups compared to control ones.

It has been demonstrated that *Toxocara* ova have high resistance to various environmental conditions and embryonation of the eggs can regularly take place throughout warm seasons. Moreover, appropriate humidity and oxygen, the type of soil, pH and vegetation density are other major factors that affect not only the development of second-stage larvae (L_2) within eggs, but also the durability and longevity of *Toxocara* ova.[19–21] According to the published data, East Azerbaijan, Mazandaran and Fars provinces showed the highest rates of seroprevalence.[22–24,52] These provinces have the most favourable climatic conditions for the survival of the *Toxocara* egg and the life cycle of the parasite, having a higher humidity and temperature.[25]

In addition, in East Azerbaijan and Fars provinces where high incidences were found, toxocariasis was found in 78.8% and 52.78% of stray cats, respectively.[26,27] Further, toxocariasis was, at 27%, the most prevalent helminthic infection in examined domestic dogs in Mazandaran province.[28]

Although our data were limited to only 15 of the 31 provinces in Iran, we doubt whether the prevalence in unstudied areas differs greatly. Nonetheless, further studies are highly recommended to complete the mapping of the country.

Most studies were carried out on children. This represents the most frequently infected group and therefore not representative of the whole population.[28]

Nevertheless, the high seroprevalence of human toxocariasis in our study must alert the authorities

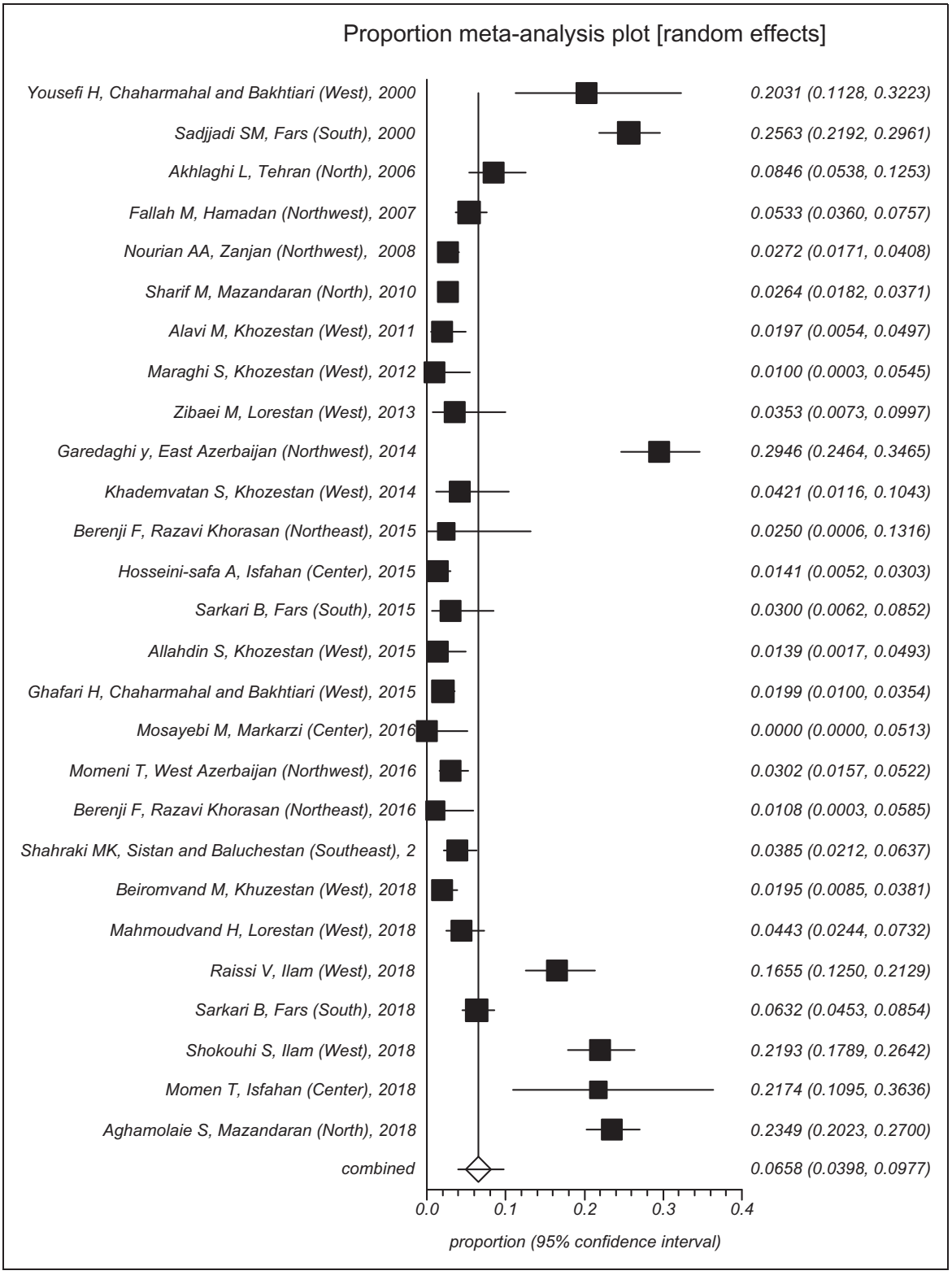

Figure 1. Forest plot of the current systematic review.

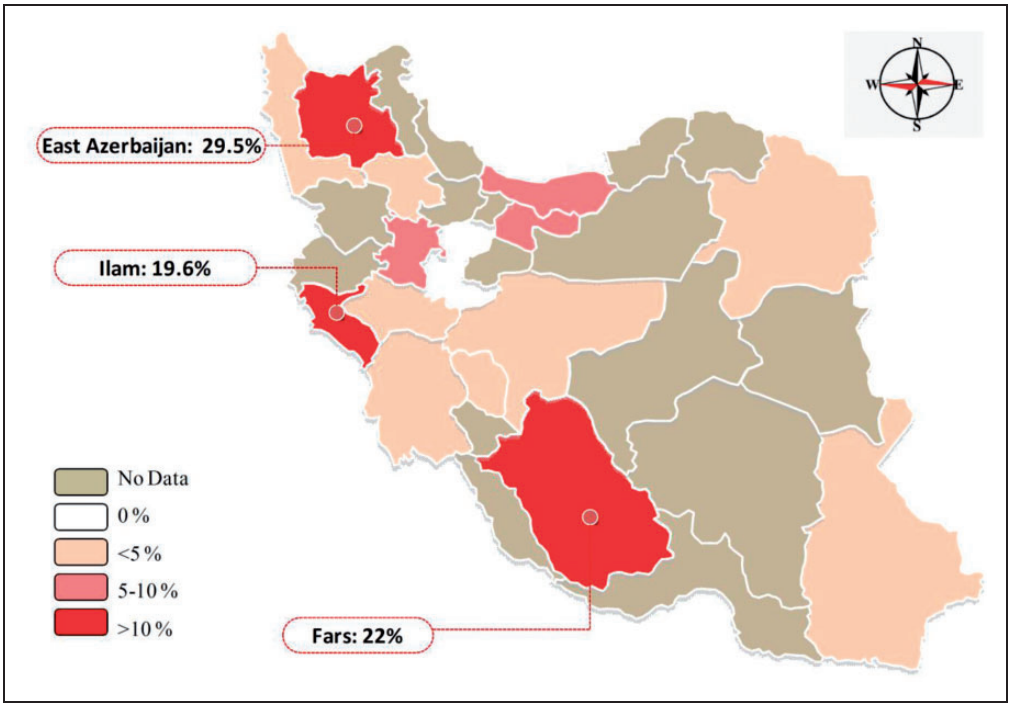

Figure 2. The average seroprevalence of human toxocariasis in different provinces of Iran.

to the importance of widespread anti-helminthic treatment of dogs and cats, the most important final hosts, in prevalent areas. Assistance to animal owners and the enforcement of appropriate legislation is required.

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References

1. Otero D, Alho AM, Nijsse R, et al. Environmental contamination with *Toxocara* spp. eggs in public parks and playground sandpits of Greater Lisbon, Portugal. *J Infec Pub Health* 2018; 11: 94–98.
2. Espinoza YA, Huapaya PE, Roldán WH, et al. Seroprevalence of human toxocariasis in Andean communities from the Northeast of Lima, Peru. *Rev Ins Med Trop São Paulo* 2010; 52: 31–36.
3. Roldán WH, Espinoza YA, Huapaya PE, et al. Frequency of human toxocariasis in a rural population from Cajamarca, Peru determined by DOT-ELISA test. *Rev Inst Med Trop São Paulo* 2009; 51: 67–71.
4. Rokni M, Massoud J and Mowlavi G. Report of 10 cases of Visceral larva migrans in Iran. *Iranian Journal of Public Health* 2000; 29: 61–66.
5. Zibaei M and Sadjjadi S. Trend of toxocariasis in Iran: a review on human and animal dimensions. *Iranian J Vet Res* 2017; 18: 233–242.
6. Fillaux J and Magnaval JF. Laboratory diagnosis of human toxocariasis. *Vet Parasitol* 2013; 193: 327–336.
7. Sarvi S, Daryani A, Sharif M, et al. Zoonotic intestinal parasites of carnivores: A systematic review in Iran. *Vet World* 2018; 11: 58–64.
8. Glickman LT and Schantz PM. Epidemiology and pathogenesis of zoonotic toxocariasis. *Epidemiol Rev* 1981; 3: 230–250.
9. Roldán WH, Cavero YA, Espinoza YA, et al. Human toxocariasis: a seroepidemiological survey in the Amazonian city of Yurimaguas, Peru. *Rev Inst Med Trop Paulo* 2010; 52: 37–42.
10. Maleki B, Khorshidi A, Gorgipour M, et al. Prevalence of *Toxocara* spp. eggs in soil of public areas in Iran: a systematic review and meta-analysis. *Alexandria J Med* 2018; 54: 97–101.
11. Portus M, Riera C and Prats G. A serological survey of toxocariasis in patients and healthy donors in Barcelona (Spain). *Eur J Epidemiol* 1989; 5: 224–227.
12. Alderete J, Jacob C, Pastorino AC, et al. Prevalence of *Toxocara* infection in schoolchildren from the Butantã

region, São Paulo, Brazil. *Mem Inst Oswaldo Cruz* 2003; 98: 593–597.
13. Demirci M, Kaya S, Çetin E, et al. Seroepidemiological investigation of toxocariasis in the Isparta region of Turkey. *Iranian J Parasitol* 2010; 5: 52.
14. Hadi A. Serodiagnosis of Toxocariasis in Human in Baghdad /Iraq. *Online J Vet Res* 2017; 21: 45–50.
15. Alonso J, Stein M, Chamorro M, et al. Contamination of soils with eggs of *Toxocara* in a subtropical city in Argentina. *J Helminthol* 2001; 75: 165–168.
16. Rahimi MT, Ashrafi K, Koosha S, et al. Evaluation of Fast-ELISA versus standard-ELISA to diagnose human fasciolosis. *Arch Iranian Med* 2011; 14: 18–21.
17. Rakhshanpour A, Harandi MF, Moazezi SS, et al. Seroprevalence of human hydatidosis using ELISA method in Qom province, central Iran. *Iranian J Parasitol* 2012; 7: 10–17.
18. Roddie G, Stafford P, Holland C, et al. Contamination of dog hair with eggs of *Toxocaracanis*. *Vet Parasitol* 2008; 152: 85–93.
19. Shafiei R, Ghatee MA, Jafarzadeh F, et al. Genotyping and phylogenetic analysis of unusually located hydatid cysts isolated from humans in north-east Iran. *J Helminthol* 2020; 94: e64.
20. Gamboa M. Effects of temperature and humidity on the development of eggs of *Toxocaracanis* under laboratory conditions. *J Helminthol* 2005; 79: 327–331.
21. Ma G, Holland CV, Wang T, et al. Human toxocariasis. *Lancet Infect Dis* 2018; 18: e14–e24.
22. Sadjjadi S, Khosravi M, Mehrabani D, et al. Seroprevalence of *Toxocara* infection in school children in Shiraz, Southern Iran. *J Trop Ped* 2000; 46: 327–330.
23. Sharif M, Daryani A, Barzegar G, et al. Seroprevalence of toxocariasis in schoolchildren in Northern Iran. *Pakistan J Bio Sci* 2010; 13: 180–184.
24. Yagoob G. Seroepidemiology of Human Toxocariasis in Children in East-Azerbaijan Province, Iran. *Cukurova Med J* 2013; 38: 581–586.
25. Sarvi S, Daryani A, Sharif M, et al. Domestic dog as a human health hazard in north of Iran. *J Parasit Dis* 2016; 40: 930–934.
26. Mahmoud Sadjjadi S, Oryan A, Jalai AR, et al. Prevalence and intensity of infestation with *Toxocara cati* in stray cats in Shiraz, Iran. *Vet Arhiv* 2001; 7: 149–157.
27. Hajipour N, Baran AI, Yakhchali M, et al. A survey study on gastrointestinal parasites of stray cats in Azarshahr, (East Azerbaijan province, Iran). *J Parasit Dis* 2016; 40: 1255–1260.
28. Okulewicz A, Perec-Matysiak A, Buńkowska K, et al. *Toxocara canis, Toxocara cati* and *Toxascaris leonina* in wild and domestic carnivores. *Helminthologia* 2012; 49: 3–10.
29. Yousefi H, Avizhgan M, Taheri AG, et al. A survey about toxocariasis in Chaharmahal-va Bakhtiari province in first 6 month of 2000. *Iranian J Infect Dis Trop Med* 2001; 13: 16–20.
30. Akhlaghi L, Ourmazdi H, Sarafnia A, et al. An Investigation on the toxocariasis Seroprevalence in Children (2-12 Years Old) from Mahidasht Area of Kermanshah Province (2003–2004). *Razi J Med Sci* 2006; 13: 41–48.
31. Fallah M, Azimi A and Taherkhani H. Seroprevalence of toxocariasis in children aged 1-9 years in western Islamic Republic of Iran, 2003. *Eastern Medi Health J* 2007; 13: 1073–1077.
32. Nourian A, Amiri M, Ataeian A, et al. Seroepidemiological study for toxocariasis among children in Zanjan-northwest of Iran. *Pakistan J Bio Sci* 2008; 11: 1844.
33. Alavi S, Hosseini S, Rahdar M, et al. Determination of seroprevalence rate of *Toxocaracanis* in 6-15 years aged rural and urban school children in Ahvaz, Iran. *Jundishapur Sci Med J* 2011; 72: 240–248.
34. Maraghi S, Rafiei A, Hajihossein R, et al. Seroprevalence of toxocariasis in hypereosinophilic individuals in Ahwaz, south-western Iran. *J Helminthol* 2012; 86: 241–244.
35. Zibaei M, Firoozeh F, Bahrami P, et al. Investigation of anti-*Toxocara* antibodies in epileptic patients and comparison of two methods: ELISA and Western blotting. *Epilepsy Res Treat* 2013; 2013: 156815.
36. Khademvatan S, Khajeddin N, Izadi S, et al. Investigation of anti-*Toxocara* and anti-Toxoplasma antibodies in patients with schizophrenia disorder. *Schizophrenia Res Treat* 2014; 2014: 230349.
37. Berenji FHM, Fata A, Mahmoudi M, et al. Serological study of toxocariasis in patients with hypereosinophilia referred to educational hospitals of Mashhad University of Medical Sciences. *MedJ Mashhad Uni Med Sci* 2015; 58: 26–31.
38. Hosseini-Safa A, Mousavi SM, Badorani MBB, et al. Seroepidemiology of Toxocariasis in Children (5–15 yr Old) Referred to the Pediatric Clinic of Imam Hossein Hospital, Isfahan, Iran. *Iranian J Parasitol* 2015; 10: 632–636.
39. Sarkari B, Lari M, Shafiei R, et al. A Comparative Seroprevalence study of toxocariasis in hypereosinophilic and apparently healthy individuals. *Archives Ped Infect Dis* 2015; 3: e17911.
40. Allahdin S, Khademvatan S, Rafiei A, et al. Frequency of *Toxoplasma* and *Toxocara* Sp. Antibodies in Epileptic Patients, in South Western Iran. *Iranian J Child Neuro* 2015; 9: 32–37.
41. Ghaffar Naqnehi H, Khalili B and Kheiri S. Seroepidemiology of *Toxocaracanis* Infection in 2-14 years old Children Referred to Health Care Centers of Chaharmahal and Bakhtiari Province by ELISA Method in 2014. *J Shahrekord Uun Med Sci* 2016; 17–23.
42. Mosayebi M, Moini L, Hajihossein R, et al. Detection of Specific Antibody Reactivity to *Toxocara* Larval Excretory-secretory Antigens in Asthmatic Patients (5-15 Years). *Open Microb J* 2016; 10: 162–167.
43. Momeni T, Mahami-Oskouei M, Fallah E, et al. Latent and asymptomatic *Toxocara* infection among young population in Northwest Iran: The necessity of informing people as a potential health risk. *Scientifica (Cairo)* 2016; 2016: 3562056.
44. Berenji F, Pouryousef A, Abdolmajid F, et al. Seroepidemiological study of toxocariasis in the owners

of domestic cats and dogs in Mashhad, Northeastern Iran. *Iranian J Parasitol* 2016; 11: 265.
45. Shahraki MK, Dabirzadeh M, Afshari M, et al. Epidemiological Study of *Toxocarcanis* in Children under 14-Years-Old and Dogs in Zabol and Chabahar Districts, Southeast of Iran. *Iranian J Parasitol* 2017; 12: 101–107.
46. Beiromvand M, Rafiei A, Mirzavand S, et al. Screening of cystic echinococcosis and toxocariasis in rural inhabitants of Khuzestan Province, southwest Iran. *Trop Biomed* 2018; 35: 32–40.
47. Mahmoudvand H, Taee N, Ebrahimzadeh F, et al. Seroprevalence and risk factors of *Toxocara canis* infection in children (2–15 years old) referred to Health Centers of Lorestan Province, Iran. *J Ped Infect Dis* 2018; 13: 20–24.
48. Raissi V, Sohrabi Z, Getso M, et al. Risk factors and prevalence of toxocariasis in pregnant women and diabetic patients compared to healthy adults in Ilam province, western Iran. *EXCLI J* 2018; 17: 983.
49. Sarkari B, Alirezaei R, LayeghGigloo A, et al. Seroprevalence and risk factors for *Toxocara* infection among children in a rural community in Fars province, southern Iran. *Parasite Immunol* 2018; 40: e12582.
50. Shokouhi S and Abdi J. Seroprevalence of *Toxocara* in children from urban and rural areas of Ilam province, West Iran. *Osong Pub Health Res Perspec* 2018; 9: 101.
51. Momen T, Esmaeil N and Reisi M. Seroprevalence of *Toxocara canis* In Asthmatic Children and its Relation to the Severity of Diseases. *Med Arch* 2018; 72: 174.
52. Aghamolaie S, Seyyedtabaei SJ, Behniafar H, et al. Seroepidemiology, modifiable risk factors and clinical symptoms of *Toxocara* spp. infection in northern Iran. *Trans R Soc Trop Med Hyg* 2018; 113: 116–122.