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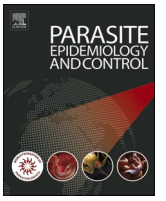

Understanding the research and practical needs required to control toxocariasis in Iran

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ABSTRACT

Human toxocariasis (HT) is a widespread zoonotic infection globally, notably prevalent in tropical areas. Enhancing our understanding of toxocariasis can lead to increased attention towards the socioeconomic impact and control of this neglected zoonosis. We conducted a comprehensive review of all available articles and official documents on toxocariasis in Iran to identify research gaps and critical needs for its control. This review highlights that despite numerous studies exploring various aspects of toxocariasis in definitive and paratenic hosts, as well as humans and environmental contamination, significant data deficiencies and gaps persist across different regions in the country. These gaps involve investigating the worm burden and reinfection rates in definitive hosts, developing more sensitive methods to detect and differentiate of *Toxocara* species, and understanding the behavior of definitive host animals. Additionally, identifying potential paratenic hosts for HT and exploring the organ-specific affinity and survival duration of *Toxocara* larvae within these hosts are essential areas for exploration. It's also imperative to comprehend the sylvatic and domestic cycles of the parasite in paratenic hosts. Furthermore, assessing egg density in the environment, exploring potential new sources such as water, and identifying regions with optimal climatic conditions for the survival and development of *Toxocara* eggs are crucial for the formulation of effective prevention and control strategies. Identifying at-risk groups, developing early diagnosis techniques, employing imaging methods, and identifying long-term complications in humans are also crucial. Community health organizations should prioritize health education for the public and professionals. Furthermore, accurately estimating definitive host populations, monitoring and preventing their movements in public places, implementing regular deworming practices for pets and stray hosts, and recognizing the infection's significance as a health priority are critical. This comprehensive understanding advocates for a holistic "one health" approach to control of HT.

1. Introduction

Human toxocariasis (HT), caused by the ascarid nematodes of the genus *Toxocara*, is a significant zoonotic parasitic infection

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worldwide, particularly prevalent in tropical regions (Chen et al., 2018). So far, a total of 26 species within the *Toxocara* genus are reported (Ziegler and Macpherson, 2019) however, *Toxocara canis* and *T. cati* are the only two species that are reported to be of public health significance. The species *T. canis* is regarded as being of more importance in humans worldwide, while the role of *T. cati* is still controversial (Maciag et al., 2022). Adult worms of *T. canis* and *T. cati* reside in the small intestine of definitive hosts (canids or felids, respectively). Excreted unembryonated eggs in the feces contaminate the environment and under appropriate conditions can develop to infectivity. In spite of frequent reporting of *Toxocara* species in different hosts and environmental samples, distinguishing between *T. can* is and *T. cati* eggs poses a challenge due to their alike morphologies and sizes (Chen et al., 2012). Ingestion of infective eggs by a wide spectrum of paratenic hosts lead to formation of larvae in the viscera and skeletal muscles of these animals (Yoshida et al., 2022). Definitive hosts can become infected by ingesting embryonated eggs and the consumption of paratenic hosts such as small rodents and birds harboring *Toxocara* larvae in their viscera and skeletal muscles. Puppies can also be infected via the transplacental and/or transmammary routes and kittens only via the transmammary route (Overgaauw, 1997; Yoshida et al., 2022). As an accidental host, humans become infected by swallowing embryonated eggs and consumption of raw or undercooked meat of paratenic hosts for example bovine liver (Yoshikawa et al., 2008a) as well as other potential domestic paratenic animals.

Though many individuals infected with *Toxocara* spp. may not display noticeable symptoms, the migration of *Toxocara* larvae throughout the body can result in varied symptoms depending on the affected organ. These symptoms are commonly categorized as visceral larva migrans (VLM), ocular larva migrans (OLM), neurotoxocariasis (NT), and covert/common toxocariasis (CT) (Ma et al., 2020a; Mohammadzadeh et al., 2018). VLM typically presents with inflamed and enlarged peripheral lymph nodes, liver, and spleen; as well as in rare cases it is associated with cardiac disorders (Kuenzli et al., 2016; Mazur-Melewska et al., 2020). OLM represents a localized eye infection leading to progressive ocular damage. NT, often asymptomatic, may exhibit clinical symptoms ranging from eosinophilic meningoencephalitis to mild neurological impairments. Studies have suggested associations between NT and conditions such as epilepsy, multiple sclerosis, schizophrenia, and cognitive disorders (Alizadeh Khatir et al., 2021; Kruszon-Moran et al., 2023; Taghipour et al., 2021; Taghipour et al., 2020). he covert form typically manifests nonspecifically, with symptoms including lymphadenopathy, allergic skin disorders (commonly urticaria), arthralgia, and asthma (Aghaei et al., 2018; Mazur-Melewska et al., 2020; Mohammadzadeh et al., 2018).

Recent estimates indicate that approximately 1.4 billion individuals globally, especially in tropical and subtropical regions, are infected with, or exposed to *Toxocara* species (Rostami et al., 2019b). Despite the significant public health and clinical importance of this infection, particularly in underprivileged communities, substantial knowledge gaps hamper the prevention and control programs of this disease across the globe (Rostami et al., 2019a). Addressing zoonotic diseases in both human and animal populations necessitates a collaborative One Health initiative involving veterinary, medical, and environmental disciplines to achieve optimal health outcomes for animals, humans, and the environment (Ebrahimipour et al., 2020; Holland, 2017). Enhancing knowledge about toxocariasis is crucial to elevate awareness of its socioeconomic impact, prompting the necessity for national and international One Health strategies to control this zoonosis (Holland, 2017; Maciag et al., 2022).

Iran, a middle-income country situated in the WHO's Eastern Mediterranean region, exhibits diverse geo-climatic conditions and is as an endemic area for many parasitic diseases, including HT. The prevalence of *Toxocara* spp. eggs in public places of the country ranges from approximately 16% to 20% (Abbaszadeh Afshar et al., 2020; Fakhri et al., 2018; Maleki et al., 2018a). The prevalence of *Toxocara* infection among dogs and cats is 15.7% and 26.0%, respectively (Abbaszadeh Afshar et al., 2020; Eslahi et al., 2020). This high toxocariasis prevalence among definitive hosts, coupled with substantial environmental contamination by *Toxocara* eggs, significantly escalates the risk of human exposure. National HT seroprevalence is estimated to range from 6% to 11% (Abbaszadeh Afshar et al., 2020; Eslahi et al., 2020; Rostami et al., 2019b), displaying variations among provinces. Similar to many affected nations (Abbaszadeh Afshar et al., 2020; Eslahi et al., 2020; Zibaei and Sadjjadi, 2017), toxocariasis control is not a primary focus in Iran, where several aspects of the disease remain poorly understood. This study aims to pinpoint essential research and practical measures required to understand and control toxocariasis in Iran. With its diverse geographic, climatic, and socio-economic landscapes, the country presents a unique microcosm for studying the multifaceted aspects of toxocariasis. The country's position at the crossroads of several continents makes it a crucial focal point for investigating the biology, epidemiology, and control of this parasitic infection. Varying environmental conditions and cultural practices influence the dynamics of toxocariasis transmission, offering insights into the interplay of host-parasite relationships within a global context. Furthermore, the diverse population and the interaction between urbanization and rural areas provide a rich ground for studying the intricate pathways of transmission and the impact of changing demographics on the prevalence and spread of toxocariasis. By elucidating the complexities within Iran's toxocariasis landscape, we can glean invaluable insights that resonate and contribute significantly to the broader understanding and management of this global public health concern.

2. Definitive hosts of *Toxocara* spp.: knowledge and research needs

Domestic and wild carnivores like canids and felids, acting as definitive hosts, harbor adult *Toxocara* spp. in their intestines. Their role in excreting *Toxocara* eggs into the environment is indispensable in transmitting these infections to human populations (Merigueti et al., 2022; Zibaei, 2022). Domestic dogs and cats, whether stray or pets, have a more significant role in transmitting *Toxocara* infections to humans compared to wild carnivores (Rostami et al., 2020a; Rostami et al., 2020b). The prevalence of *T. canis* and *T. cati* in the country's dogs and cats exceeds global rates. Specifically, reported prevalence rates stand at 15.7% for *T. canis* in dogs and 26.0% for *T. cati* in cats, compared to global rates of 11.1% and 17.0% for these parasites, respectively (Abbaszadeh Afshar et al., 2020; Eslahi et al., 2020). Despite the absence of definitive data on dog and cat population, the Iran Veterinary Society estimates the total number of pets, including both species, to range between 6 and 8 million nationwide (https://www.hamshahrionline.ir/news/688182). In recent

years, there's been a notable surge in Iranians becoming pet owners, with an estimated one in ten individuals owning a pet (https://iranopendata.org). Moreover, estimates suggest a stray dog population of up to 3.6 million and approximately 2.1 million stray cats across the country (https://www.sharghdaily.com/100/298570). This number of stray dogs and cats is much more than reports from neighboring countries such as Turkey and Iraq (https://www.sharghdaily.com/100/298570). In addition, with the unscientific and indiscriminate support of stray dogs and cats by some people and non-governmental organizations, the number of these animals is increasing. This poses significant risk for many zoonotic diseases, including HT, as rate of *Toxocara* infection in stary dogs and cats was more than two-fold compared to pets (Rostami et al., 2020a; Rostami et al., 2020b). There is also reported considerable differences in prevalence of *Toxocara* infection in stary and pet dogs (1.8–50% vs. 1.9–41.8%) as well as in stary and pet cats (8.0–86% vs. 8.0–20.0%) (Table 1).

Some studies in other countries indicates that direct contact with dogs, mostly thorough by petting their hairs, may be a potential risk factor for human exposure *Toxocara* eggs (Aydenizöz-Özkayhan et al., 2008; Roddie et al., 2008a; Wael et al., 2011). This potential risk was also evaluated in Iran by four studies (Bakhshani et al., 2019; Karimi and Rezaei, 2022; Sasannejad et al., 2020; Tavassoli et al., 2012), three studies on dogs and one study in stray cats. Studies on dogs showed prevalence ranges of 7–31% in pets, 54–57% for shepherd dogs and stray dogs. Moreover, puppies were significantly more infected than adult dugs. One study on 168 stray cats on Northeast of the country indicated that 18 (10.8%) of them were positive to *T. cati* eggs in their hair. In three studies on the hair of dogs, there was no detected embryonated egg of *Toxocara*, while in the evaluated hair of cats 22.2% of detected eggs were embryonating and 2.3% were embryonated (Bakhshani et al., 2019). Embryonated eggs were detected just in kittens. These findings suggest that the petting of puppies and kitten hair may be as a neglected route of transmission toxocariasis to human, although the existence of embryonated eggs on the hair of definitive host and its risk for human is debatable (Keegan and Holland, 2010; Roddie et al., 2008b).

In addition to domestic dogs and cats, wild carnivorous could also play an important role in life cycle and transmission of *Toxocara* spp. There are a number of studies on sylvatic cycle of toxocariasis. For example, studies on golden jackal [48–53], red fox [49, 51, 53, 54], wolves [32], Persian leopard [33, 34], and wild cats [55] are among these studies (Table 1). The related prevalence in golden jackal and red fox has been reported 23.3% and 69.4%, respectively (Eslahi et al., 2020). In another study, fecal samples from 19 wolves were evaluated, revealing that 10 (52.6%) fecal samples tested positive for *Toxocara* spp. eggs; however, the species were not specified (Siyadatpanah et al., 2020). Moreover, the intestine of three unwanted or road-killed Persian leopards was evaluated and the parasite *Toxocara* detected from all of them 100% (3/3) and a total of 27 adult worms were isolated (Esfandiari et al., 2010; Ghaemi and Sadr-Shirazi, 2011).

Despite the fact that at least 60 studies on *Toxocara* spp. in definitive hosts have been performed, data from eight provinces is lacking (Fig. 1). Almost all previous studies focused solely on the detection of the parasite (egg and/or adult) in these animals, with several knowledge gaps remaining unaddressed. First, the parasite burden in the intestines of canids and felids hosts and their reinfection were not considered in previous studies. Parasite abundance is a key epidemiological measure in our understanding of the extent of infection in different definitive hosts. Furthermore, data on the prevalence and abundance of *T. canis* and *T. cati* in puppies and kittens in comparison with adult animals could be advantageous for control strategies. Unfortunately, the data pertaining to this aspect is currently unavailable, highlighting the need for future studies to place greater emphasis on this aspect. Furthermore, the role of feral hosts in the epidemiology of toxocariasis is not well understood, and more extensive and in-depth studies are required to evaluate the dispersal pattern of toxocariasis in sylvatic cycles, contribution of such hosts to the transmission of *Toxocara* spp., and susceptibility of different feral species of canids and felids to toxocariasis throughout the country.

The behavior of humans and definitive hosts, such as dogs and cats, significantly influences the spread and prevalence of toxocariasis within communities. Human activities, including improper disposal of pet waste, inadequate hygiene practices for pets, and lack of awareness about the risks associated with contaminated environments, contribute to the transmission of toxocariasis (Macpherson, 2005). Similarly, the behavior of definitive hosts, particularly their access to public spaces and the presence of stray animals, can increase the contamination of environments with *Toxocara* eggs, heightening the risk of infection for humans (Macpherson, 2013).

Table 1
Prevalence range of toxocariasis among studied definitive and paratenic hosts in Iran.

Animal	Number of studies	Total number of samples	No. of positive samples	Prevalence range%	*Toxocara* species
Definitive host					
Stray dogs	20	3470	413	1.8–50	*T. canis*
Household/pet dogs	9	1169	175	1.9–41.8	*T. canis*
Golden jackals (*Canis aureus)*	5	58	13	7.7–43.2	*T. canis*
Red foxes (*Vulpes vulpes*)	2	111	76	60.3–77.8	*T. canis*
Wolves (*Canis lupus)*	1	19	10	52.6	Unknown
Stray Cats	17	1560	534	8.0–86.3	*T. cati*
Household /pet cats	4	233	26	8.0–20.0	*T. cati*
Wild cat	1	8	5	62.5	*T. cati*
Persian leopard (*Panthera pardus saxicolor*)	2	3	3	100	*T. cati*
Dog /cat hair	4	606	178	10.8–44.3	*T. canis, T. cati*
Paratenic host					
Chicken	2	233	26	10.5–15.2	*T. canis, T. cati*
Partridge	1	106	0	0.0	–
Earthworms (*Lumbricus terrestris)*	1	240	4	1.7	*T. canis*

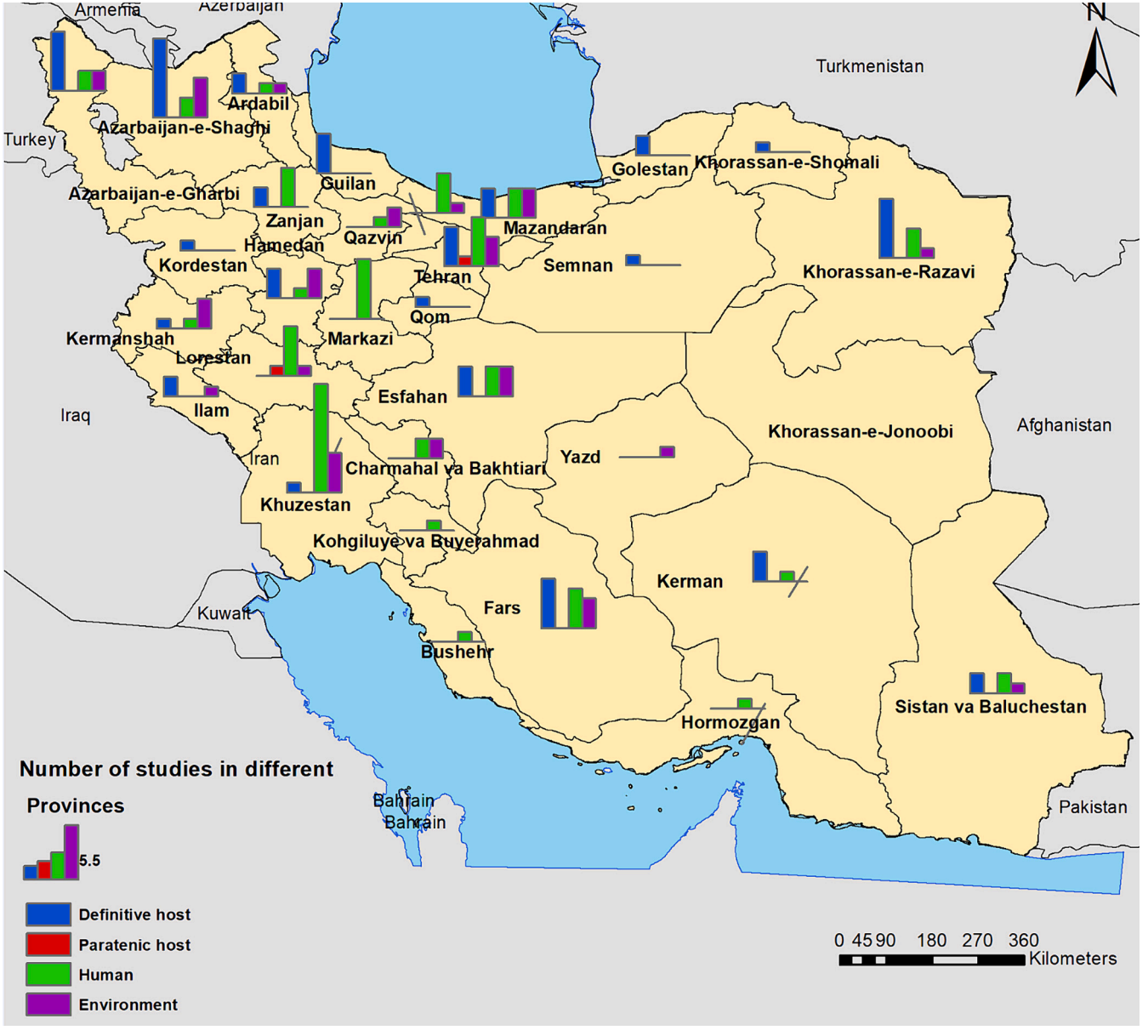

Fig. 1. Scattering of previous studies on toxocariasis on different definitive and paratenic hosts as well as environment samples in different provinces of Iran.

Therefore, understanding and modifying these behaviors are crucial in controlling and reducing the incidence of toxocariasis in populations. Currently, there is no study evaluating the impact of animal or human behavior on the transmission dynamics of the parasite in Iran. Therefore, further comprehensive studies are necessary to gain a better understanding of this aspect.

Most studies in Iran utilized morphology to identify the adult worms and/or eggs in the feces microscopically (direct smear and/or concentration method). Formalin-ether/ethyl acetate sedimentation, flotation using sucrose, zinc sulfate, sodium chloride as well as intestinal scraping were also used to diagnose *Toxocara* spp. in definitive hosts (Abbaszadeh Afshar et al., 2020). There is also a little information regarding the differentiate of *Toxocara* species in definitive hosts (Karimi et al., 2022a; Khademvatan et al., 2013; Mikaeili et al., 2013; Pourshahbazi et al., 2023; Torkan et al., 2017). Five molecular studies (five examined cats feces and one examined dog feces) indicated host-specific distribution of *Toxocara* spp. More than 95% of isolated *Toxocara* worms from cats were *T. cati* and 100% isolated worms in dogs were *T. canis* (Karimi et al., 2022a; Khademvatan et al., 2013; Mikaeili et al., 2013; Pourshahbazi et al., 2023; Torkan et al., 2017). Detecting excretory and secretory antigens (ES-Ag) of *Toxocara* spp. in the feces of definitive hosts offers a valuable alternative to traditional concentration techniques. These coproantigens, found in infected cats and dogs, are detectable with heightened sensitivity through antigen capture immunological techniques, even post-treatment or in self-limited situations (Elsemore et al., 2017; Hauck et al., 2023). Previous studies did not utilize such methods; however, incorporating this technique could enhance the identification of infections in definitive hosts. It serves as an appropriate tool to assess the influence of host age on *Toxocara* egg and antigen results. Analyzing the patterns of egg and/or antigen positivity in the results can help differentiate spurious eggs in hosts, particularly when both eggs and antigens are present (Elsemore, 2020).

3. Key gaps on potential paratenic hosts of toxocariasis

Paratenic hosts are crucial for the continuity of *Toxocara* spp.'s life cycle in the environment. Once paratenic hosts ingest embryonated eggs, the hatched larvae penetrate the intestinal wall, migrate through the liver and bloodstream to reach the lungs, subsequently spreading throughout the host's body (Holland and Hamilton, 2013). These third-stage larvae can persist in tissues until transmission to definitive hosts, or even humans. Various animals like rodents (mice, rats, gerbils, guinea pigs, and hamsters), lagomorphs (rabbits), avian species (chickens, quail, and pigeons), as well as mammals such as pigs and monkeys, have served as paratenic host models (Antolová et al., 2013; Strube et al., 2013). Additionally, animals like cattle, ducks, lambs, and ostriches have potential as natural paratenic hosts (Hoffmeister et al., 2007; Noh et al., 2012; Salem and Schantz, 1992; Yoshikawa et al., 2008a).

In Iran, *Toxocara* larvae have been discovered in naturally infected broiler chickens (Shokri et al., 2022; Zibaei et al., 2017), swallows (*Hirundo rustica*) (Fakhar et al., 2018), and earthworms (*Lumbricus terrestris*) (Table 1) (Rasouli et al., 2020). Studies focusing on chickens have revealed a prevalence of *Toxocara* infection ranging from 10% to 15%. Molecular evaluations have indicated that chickens can be susceptible to infections by both *T. canis* and *T. cati*. Notably, while earthworms were identified as carrying *T. canis*, the specific *Toxocara* species in infected swallows was not determined. Furthermore, certain experimental studies utilized Mongolian gerbils, Wistar rats, and chickens as paratenic host models infected with *T. cati* embryonated eggs. These investigations aimed to assess *Toxocara* larvae's migrating patterns and resulting pathological changes (Oryan et al., 2010; Zibaei et al., 2010). Findings from these studies indicated the survival of *T. cati* larvae for at least 240 days in chicken tissues and 90 days in Mongolian gerbils and Wistar rats. This suggests the potential role of these animals as paratenic hosts for *Toxocara* spp. in the country (Oryan et al., 2010; Zibaei et al., 2010). Despite the aforementioned evidence, the understanding of paratenic hosts' significance in the sylvatic cycles of toxocariasis remains very incomplete. Future investigations could expand this knowledge by exploring other potential paratenic hosts, including various terrestrial worms, cockroaches, poultry, crows, birds of prey, among others (Fellrath and Magnaval, 2014; González-García et al., 2017).

Although rare, consuming undercooked meat or organs from paratenic hosts, particularly bovines, poses a potential risk for HT (Choi et al., 2012; Karaca et al., 2018; Yoshikawa et al., 2008b). Despite this, limited worldwide studies have evaluated the prevalence of toxocariasis in domestic herbivores, revealing varied *Toxocara* seroprevalence rates: 10.1% in goats (Kantzoura et al., 2013), 38.5% in bovines (Giudice et al., 2021), 44.6% in horses (Heredia et al., 2018), 13.0–51.0% in sheep (Kantzoura et al., 2013; Lloyd, 2006; Rassier et al., 2013; Santarém et al., 2011), and ranging from 58.5% to 89.0% in chickens (Campos-da-Silva et al., 2015; Oliveira et al., 2018; Von Söhsten et al., 2017). Iran, like most of affected countries, lacks a clear understanding of the role of domestic herbivores in transmitting toxocariasis to humans and definitive hosts, necessitating further research. Moreover, human dietary habits and the methods of consuming and cooking meat from paratenic animals can contribute significantly to disease transmission, although there is also a lack of research in this area. Feedlot systems appear to act protectively against *Toxocara* infection in domestic herbivores, likely due to reduced contact with dogs and cats and the use of elevated feeding troughs to prevent soil or grass contamination (Giudice et al., 2021). The limited research on paratenic hosts (Zibaei and Sadjjadi, 2017) emphasizes the necessity for more extensive investigations to comprehensively assess their role in the entire country's toxocariasis epidemiology (Fig. 1). Furthermore, these studies should explore histopathological changes, assess organ-specific affinity, and examine larvae survival times in different paratenic host species.

4. Information on human toxocariasis and research gaps in Iran

HT can occur in all ages through consuming embryonated eggs in contaminated food, water, utensils, or raw/undercooked meat from paratenic hosts carrying third-stage larvae of *Toxocara* spp. Children and those in close contact with dogs or cats are at higher risk of toxocariasis (Ma et al., 2018). The first documented human toxocariasis case occurred over half a century ago when *Toxocara* larvae were detected in the eyes of children suspected to have retinoblastoma (Wilder, 1950). Many cases of HT show no or mild self-limiting symptoms. However, in some individuals, toxocariasis can be linked to internal, allergic, ocular, and neurological disorders (Auer and

Walochnik, 2020; Yoshida et al., 2022).

The prevalence of HT is depended to socio-economic indicators, geo-climatic factors, environmental contamination, and the presence of dogs and cats (Ma et al., 2020b; Rostami et al., 2019a). Estimated prevalence rates of HT stand at 38% in Africa, 34% in Southeast Asia, 28% in Latin America, 24% in the Western Pacific region, 13% in North America, 11% in Europe, and 8% in the Eastern Mediterranean region. It is estimated that approximately 1.4 billion people are infected or exposed to *Toxocara* spp. (Rostami et al., 2019b). In Iran, 29 studies evaluated the seroprevalence of HT, with meta-analyses indicating a pooled prevalence of 6–11%, varying across different provinces (Abbaszadeh Afshar et al., 2020; Eslahi et al., 2020; Rostami et al., 2019b). The highest prevalence rates among the general population were observed in East Azerbaijan, Mazandaran, and Fars provinces (Abbaszadeh Afshar et al., 2020). East Azerbaijan and Fars have high numbers of both shepherd and stray dogs, and possibly cats. Meanwhile, the high seroprevalence rates in Mazandaran province could be attributed to a substantial population of stray, shepherd, and pet dogs and cats, along with favorable climatic conditions such as moderate temperature, high relative humidity, and significant rainfall (Aghamolaie et al., 2019; Rostami et al., 2019b). Corroborating this evidence, a recent global study revealed a significant increase in HT seroprevalence with rising relative humidity, mean temperature, and precipitation rates (Rostami et al., 2019b). Unfortunately, apart from Turkey (with 7 studies) and Iraq (with 2 studies), there is a lack of studies on HT in neighboring countries. The pooled seroprevalence rates in Turkey and Iraq were 6.7% and 8% (Al-Asady and Al-Nasiri, 2020), respectively, slightly lower than the seroprevalence rates in Iran (Aghamolaie et al., 2019). However, the number of studies conducted in these countries is very limited for comparison. Lower seroprevalence rates could potentially be due to the smaller number of stray dogs in Turkey and Iraq, which are approximately one-eighth of the number found in Iran. The most of previous studies in the country were focused on children and those with allergic disorders, and only five studies were performed on general population. Moreover, few number of studies assessed *Toxocara* exposure in cancer (Kazemi et al., 2023; Raissi et al., 2021), uveitis (Einipour et al., 2016; Fata et al., 2021), myositis (Saki et al., 2021), and HIV positive patients (Zibaei et al., 2023) as well as pregnant women (Raissi et al., 2022; Raissi et al., 2020b), municipal workers (Asadi et al., 2020; Erfani et al., 2020), and cat and dog owners (Karimi et al., 2022b; Nijsse et al., 2016; Zibaei et al., 2022).

Toxocara larvae, like in other paratenic hosts, do not mature into adults in humans. Therefore, stool examination to detect eggs is not applicable for laboratory diagnosis. The definitive diagnostic method remains the detection of larvae in tissues through histopathological examination. However, this test is limited due to difficulties in collecting biopsy specimens and its time-consuming nature (Smith and Noordin, 2006). The current most used mrthod for diagnosing HT is an indirect enzyme-linked immunosorbent assays (ELISAs) that employs excretory–secretory (ES) antigens from third-stage larvae of *T. canis* to detect specific antibodies in humans (Rubinsky-Elefant et al., 2010). In Iran, almost all diagnosed human cases have relied on ELISA, with only a few using the IFA or Western Blot tests (Eslahi et al., 2020). To date, there remains no effective serological method worldwide, that can differentiate between *Toxocara* species in humans. Monitoring the disease presents a challenge for clinicians because routine serological tests like ELISA cannot distinguish between chronic and recent infections. Further research will be essential to accurately differentiate active disease from chronic infection (Ma et al., 2020b).

Despite numerous studies conducted on HT in the country, there remain several critical information gaps in this field (Fig. 1). While several sero-surveys have been carried out in different regions of the country, many of these regional studies had limited sample sizes, which hindered comprehensive nationwide estimations. Additionally, prevalence data is absent for approximately 17 out of the 31 provinces. Unfortunately, most available studies only estimated seroprevalence and did not evaluate risk factors or clinical symptoms related to toxocariasis in humans. In a study in the north of Iran, Aghamolaie et al. (2019) reported that older age, eating improperly washed vegetables, and frequent contact with cats, dogs, or soil are significantly associated with an increased risk of human toxocariasis in Mazandaran province. Moreover, this study indicated that *Toxocara* seropositive individuals had higher odds of having asthma, skin allergic disorders, cough, and ophthalmic disorders. There is also a scarcity of data regarding dog and cat owners. Notably, a well-designed case-control study investigating potential risk factors for infection acquisition in high-risk groups, such as children and pet owners, is lacking. More comprehensive investigations are needed to pinpoint at-risk populations in both rural and urban areas and to understand the consequences of chronic infection and larvae localization in tissues and the central nervous system. It is imperative to focus on early diagnosis and the development of imaging techniques capable of tracking larvae in infected human organs. This step is crucial for effectively managing toxocariasis cases and warrants further investigation in Iran and other regions across the globe (Dietrich et al., 2020; Hernanz et al., 2021).

5. Environmental knowledge needs for toxocariasis

Female worms of *Toxocara* spp. can produce up to 200,000 eggs per day (Magnaval et al., 2005). On the other hand, dogs, cats, and other definitive hosts excrete millions of tons of droppings daily, resulting in the spread of millions of *Toxocara* eggs in the environment and public places (Mizgajska-Wiktor et al., 2017). Eggs passed in the feces are not infective and must be in the soil to become embryonated. The accidental ingestion of soil contaminated with infective *Toxocara* eggs is thought to be the main source of human toxocariasis, especially in children (Fakhri et al., 2018). The global prevalence of *Toxocara* eggs in soild of the public places was estimated to be 21% (16–27%). The mean estimated prevalence rates in the different WHO regions ranged were 35% in Western Pacific, 27% in Africa, 25% in South America, 21% in South-East Asia, 18% in Middle East, 18% in Europe, and 13% in North and Central Americas. Iran was the country with highest prevalence (20%) in the Middle East and North Africa region (Nijsse et al., 2020). Approximately 16% and 23% of public places in Turkey and Iraq, Western neighbors, were contaminated with *Toxocara* eggs, respectively. The environmental dimension of toxocariasis has been investigated in many studies and soil sampled from public parks, vegetables, and grasses (Rezaei et al., 2023; Saraei et al., 2012; Siyadatpanah et al., 2013) were among main studied sources of *Toxocara* ova (Choobineh et al., 2019; Mazhab-Jafari et al., 2019; Raissi et al., 2020a; Rezaiemanesh et al., 2021; Sazmand et al., 2020;

Shirvani et al., 2019). In a recent review, the mean prevalence of *Toxocara* spp. ova in samples of soil and raw vegetable were reported as 13–29% and 1–3%, respectively (Abbaszadeh Afshar et al., 2020; Fakhri et al., 2018). Some provinces such as Khuzestan, East-Azarbaayjan, Tehran, and Lorestan indicated most prevalence of *Toxocara* eggs in the environment, and also data was not available for about 18 provinces (Abbaszadeh Afshar et al., 2020).

Understanding the environmental aspect of *Toxocara* spp. requires standardized egg detection methods. Employing advanced techniques like molecular assays can effectively analyze environmental samples, aiding in precise species differentiation and evaluation of *Toxocara* eggs. It's crucial to identify parasite species in public areas and vegetable samples for better control strategies against HT. Previous research mostly relied on microscopic detection at the genus level, neglecting species differentiation (Maleki et al., 2018b). Further investigation into urban and rural areas is necessary. Evaluating parasite egg density across different geographic divisions, public spaces, food, and water sources (Dubna et al., 2007; Mizgajska-Wiktor and Jarosz, 2007), as well as determine the type of *Toxocara* species in these sources, can enhance our understanding of environmental contamination (Paller and de Chavez, 2014).

Toxocara egg survival is influenced by climatic conditions (Azam et al., 2012). Therefore, studying survival rates in diverse regions of countries, including Iran, under different climates can provide valuable data for authorities to enhance the management of HT in endemic regions. Optimal climatic conditions for the development (embryonation) or survival of *Toxocara* eggs in soil are temperatures ranging from 23 to 35 °C, with a relative humidity exceeding 70% and soil moisture levels between 51 and 59% (Erofeeva and Vasenev, 2020; Fakhri et al., 2018). Studies have identified the soil mixture in lawns as the most favorable environment for egg survival, showing a survival rate of approximately 70% (Erofeeva and Vasenev, 2020). Further assessment is needed to understand the impact of climate factors on the prevalence of *Toxocara* infection. However, here, we provided a map showing prevalence of *Toxocara* infection in dogs, cats and human in different climatic zones (Fig. 2). As shown in Fig. 2, the highest prevalence rates as well as most available data are for cold to temperate region regions with moderate and high rainfalls. Given *Toxocara* eggs' persistence in the

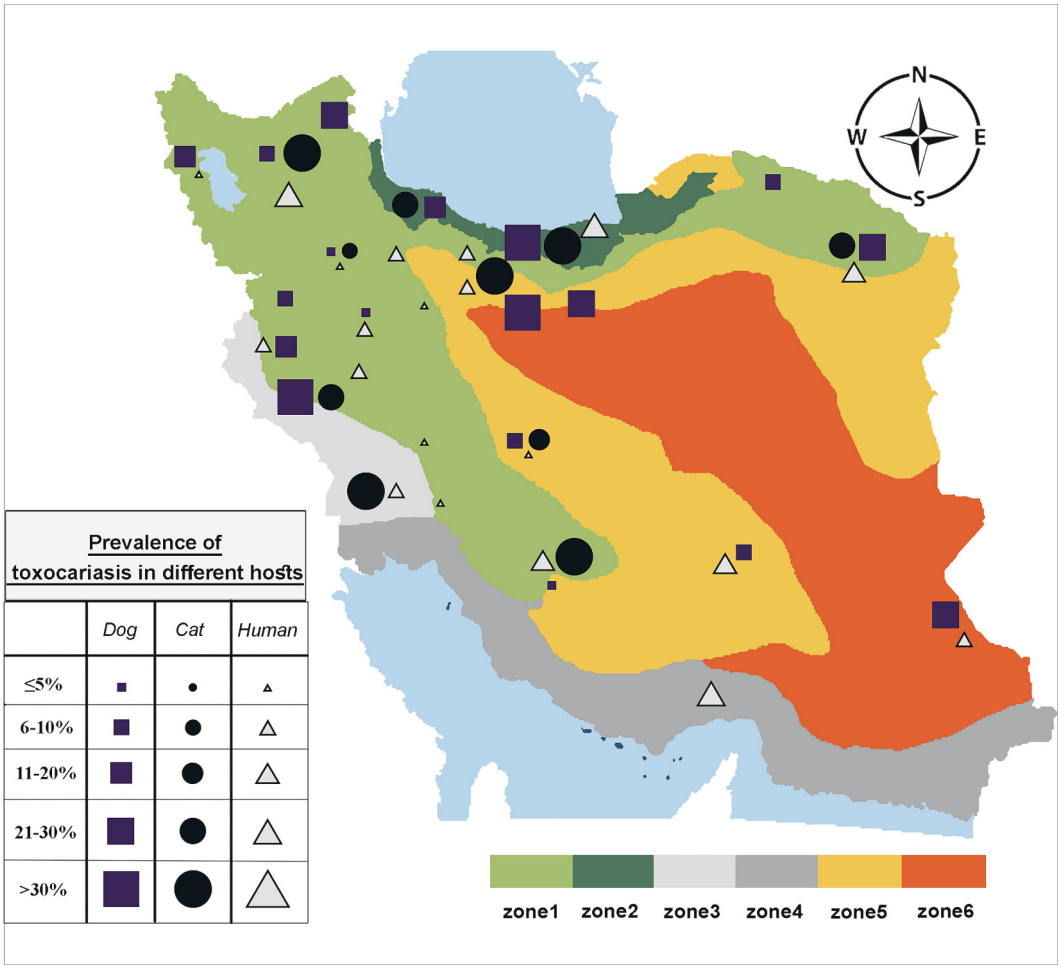

Fig. 2. Prevalence of *Toxocara* infection in dogs, cats and humans in different areas of Iran based on climatic zones. **Zone 1**: Cold to very cold with moderate rainfall; **Zone 2**: Temperate with lots of rainfall; **Zone 3**: Slightly Warm with moderate rainfall; **Zone 4**: Very warm with low rainfall; **Zone 5**: Hot with low rainfall; **Zone 6**: Very hot with very low rainfall.

environment, exploring other potential sources of infection for humans and paratenic hosts, particularly water sources, is crucial (Bowman, 2021). It is indicated that *Toxocara* spp. is among the significant water-borne parasites in Eastern-Mediterranean region (Abuseir, 2023). A seroprevalence indicated untreated water is related with a non-significant increased risk (odds ratio; 1.34, 95% CI, 0.91 to 1.96) of *Toxocara* seropositivity study in Mazandaran province, North of the country (Aghamolaie et al., 2019). However, the investigation of *Toxocara* egg contamination in drinking water remains unexplored and should be a focal point for future research. Understanding their role in *Toxocara* transmission necessitates assessing various water sources, including wells, springs, rivers, qanats, recreational areas, and tap water.

6. Administrative and organizational: practical measures need

Due to its omnipresence as a zoonotic disease, the control of toxocariasis encounters significant challenges, particularly in underdeveloped areas. The proximity of frequent definitive hosts near human communities, the presence of diverse paratenic hosts, and numerous poorly understood aspects of toxocariasis epidemiology, notably within the sylvatic cycle of *Toxocara*, contribute to various problems in disease control. Regrettably, toxocariasis is often not prioritized in health and veterinary agendas across many countries, resulting in insufficient financial resources and inadequate control strategies in endemic regions. In numerous endemic areas for toxocariasis, policymakers and decision-makers allocate little or no attention to managing and controlling this infection in both animals and humans.

Estimating the dog and cat populations in each province, including both pets and strays, and monitoring their movements in public areas and parks are vital for controlling zoonotic infections, especially toxocariasis (Smith et al., 2019). Iran faces challenges due to the increased population of dogs and cats, both domestic and stray, driven by greater pet ownership and the support of strays by certain individuals. Official national data on these definitive hosts for Toxocara is lacking, although some unofficial statistics are available. Another critical issue is the lack of routine deworming in these animals, which can reduce environmental contamination (Maciag et al., 2022; Nijsse et al., 2016). Educating the public and professionals about pet care principles and zoonotic risks is crucial but often overlooked. Public health education, particularly for children, who are more susceptible to toxocariasis, is essential. Conducting Knowledge, Attitude, and Practices (KAP) studies among medical staff, patients, and various age groups is necessary. Continuous

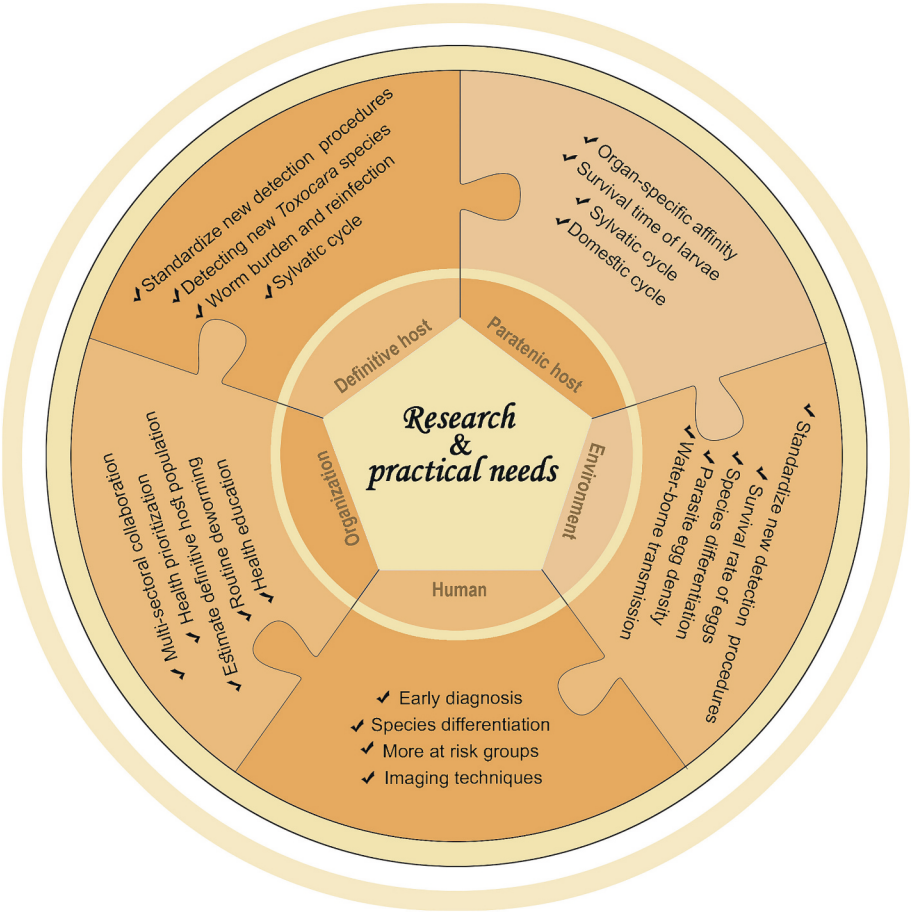

Fig. 3. Depiction of significant research and practical measures needs to implement control strategies for toxocariasis in endemic regions.

medical education (CME) for healthcare professionals and scientists is essential to improve toxocariasis detection and management. Unfortunately, CME focusing on toxocariasis is not a priority in the health system and should be given greater attention. Effectively controlling toxocariasis requires collaborative efforts among various sectors, including the Ministry of Health, the Veterinary Organization, universities, research centers, and related institutions. Fig. 3 descripted of significant research and practical measures needs to implement control strategies for toxocariasis in the country and other endemic regions across the world.

7. Conclusion

Unfortunately, the control of toxocariasis is not considered a top priority in most countries worldwide. Compared with neighboring countries, more studies have been performed on various aspects of Toxocariasis in Iran. Despite this, this comprehensive review revealed that previous studies conducted have failed to comprehensively address all aspects of toxocariasis in definitive and paratenic hosts, humans, and environmental contamination in different regions of Iran. In addition to further studies to fill the above-mentioned gaps, the following preventive measures are suggested to reduce the burden of infection in both humans and animals: pet owners should keep their pets away from stray animals, ensure daily bathing for pets, and administer anthelminthic treatment regularly. Measures to eliminate stray animals or prevent their entry into children's play areas or family picnic spots in parks should be ensured. Individuals or non-governmental organizations should be prevented from feeding stray dogs and cats, and shelters should be provided for these animals.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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