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Original article

The global prevalence of *Toxocara* spp. in pediatrics: a systematic review and meta-analysis

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Background: Toxocariasis is a zoonotic parasitic disease caused by *Toxocara canis* and *Toxocara cati* in humans. Various types of T. canis are important.

Purpose: The current study aimed to investigate the prevalence of *Toxocara* spp. in pediatrics in the context of a systematic review and meta-analysis.

Methods: The MEDLINE (PubMed), Web of Sciences, Embase, Google Scholar, Scopus, and Cumulative Index of Nursing and Allied Health databases were searched to identify peer-reviewed studies published between January 2000 and December 2019 that report the prevalence of Toxocara spp. in pediatrics. The evaluation of articles based on the inclusion and exclusion criteria was performed by 2 researchers individually.

Results: The results of 31 relevant studies indicated that the prevalence of *Toxocara* spp. was 3%–79% in 10,676 cases. The pooled estimate of global prevalence of *Toxocara* spp. in pediatrics was 30 (95% confidence interval, 22%–37%; I^2=99.11%; P=0.00). The prevalence was higher in Asian populations than in European, American, and African populations.

Conclusion: Health policymakers should be more attentive to future research and approaches to *Toxocara* spp. and other zoonotic diseases to improve culture and identify socioeconomically important factors.

Key words: Learning disability, Neurobiology, Reading disability (dyslexia)

Key message

Is the global prevalence of toxocariasis high among children? The prevalence of toxocariasis is high in pediatric patients. Asian children are more susceptible to the disease than other children. Its virulence varies among different socioeconomic classes in various countries. Hand washing after soil contact, routine pet deworming, and appropriate disposal of pet feces in households with Asian pediatrics are needed to prevent toxocariasis.

Introduction

Toxocariasis or visceral migraine laryngeal syndrome is a zoonotic parasitic disease caused by T*oxocara canis* and *Toxocara cati* in humans. Various types of T. canis in particular can be important.[1,2] Each adult worm in the intestines of infected dogs and cats can release a large number of eggs daily through defecation. Toxocariasis is mostly transmitted to humans via water, food, and soil contaminated with eggs.[2,3] The eggs of this parasite are opened after entering the human digestive system. The larvae then pass through the intestinal mucosa to the bloodstream and diffuse into organs such as the liver, brain, and eye. Although the larva will be recognized and limited by the immune system forming granuloma, they can survive and persist in this form for up to 11 years.[4]

The visceral larva migrans (VLM), ocular larvae (OLM), and overt toxocariasis are the most common types of larvae. The clinical symptoms of infection are nonspecific but can include neurological, ocular, pulmonary (asthmatic), dermatological, and rheumatoid arthritis.[5] The pathology of this parasite is variable, but it can induce peripheral eosinophilia (20%–40%) and fever of unknown origin. The prevalence of parasites varies among geographic regions at rates of 2%–90%.[6-8]

Pediatrics are more susceptible to *Toxocara* infection since they are more likely to place a contaminated hand or even an egg into their mouth.[9] Seroepidemiological evaluations in different countries indicated a global distribution of toxocariasis. Considering the importance of the prevalence of this parasite in the population, this study aimed to evaluate the prevalence of

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toxocariasis in pediatric patients younger than 20 years of age based on a systematic review and meta-analysis of published studies.

Methods

This study was performed according to the MOOSE (Meta-Analyses of Observational Studies in Epidemiology) and the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses).[10-12]

1. Search strategy

In this systematic review, we assessed all original research studies that were relevant to the topic by searching the MEDLINE (PubMed), Web of Sciences, Embase, Google Scholar, Scopus, and Cumulative Index of Nursing and Allied Health databases using keywords such as toxocariasis, *Toxocara*, *Toxocara*-antibodies, Pediatrics, *Toxocara canis*, and *Toxocara cati*. The search was limited to articles published between January 2000 and December 2019. The researchers searched these databases and manually searched the reference lists and gray literature. Duplicate entries were reviewed by considering the title of published papers, authors, year of publication, and specifications of the source types. In questionable records, the texts were compared. After abstract and title review, some of the articles were eliminated. The retrieved papers were evaluated by 2 researchers (YM, BA) based on the inclusion and exclusion criteria.

2. Eligibility criteria

For the current study, the inclusion criteria were publication in the English language and publication between January 2000 and December 2019. The study design and methodologies were cross-sectional. All other studies, such as reviews or meta-analyses, were excluded from the screening. Articles that were conducted on animals were also excluded.

We included all English observational studies published between January 2000 to December 2019 that assessed the prevalence of toxocariasis, therapeutic management, signs, and symptoms in pediatric patients with toxocariasis. Cross-sectional studies were also included. We excluded duplicate non–peer-reviewed, review, or meta-analysis articles and papers for which the abstracts and full texts were not available.

3. Data extraction

All of the included studies were listed by EndNote software (EndNote X7, Thomson Reuters, Toronto, ON, Canada) and subjected to review and data extraction by 3 independent authors. Two reviewers independently (BA and RGH) extracted the required data from the data contained in the identified articles using a uniform Excel sheet. Discrepancies in the extracted data were resolved through consensus. If agreement could not be reached, it was resolved by referral to a third investigator (YM). For the current study, the data extraction section contained the first author's name, year of publication, study location, study type, sample size, age, positive population prevalence, and method of detecting the infection.

4. Risk of bias

The quality of all studies was assessed by 2 independent authors using the Modified Newcastle-Ottawa Scale for cross-sectional studies.[13]

5. Statistical analysis

We used a random-effects model to generate a pooled prevalence presented as percentage and 95% confidence interval (CI) with Metaprop order. Interstudy heterogeneity was assessed using the I^2 heterogeneity statistic reported as a percentage (%) to determine the extent of interstudy variation. A forest plot was used to present the meta-analysis results schematically. Egger test and a funnel plot were applied to evaluate the presence of

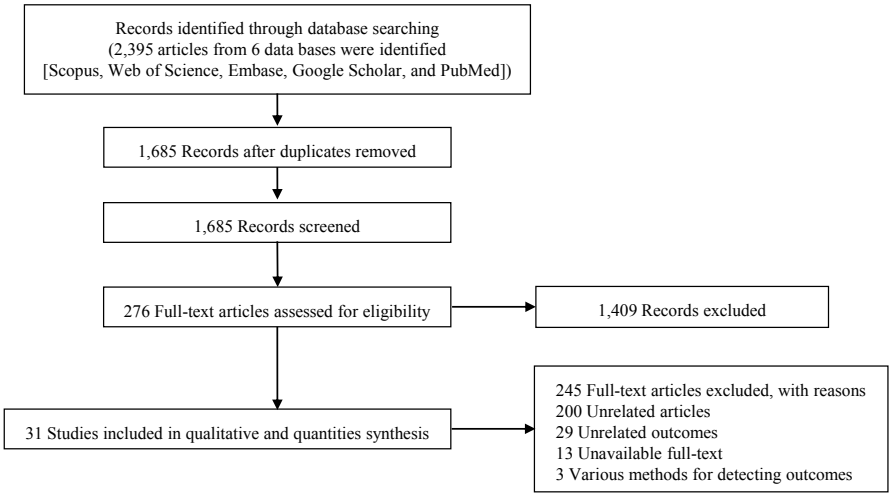

Fig. 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses diagram and search strategy results.

publication bias. In addition, a subgroup analysis was performed to identify different sources of heterogeneity. The statistical analysis was performed using STATA 15.0 (Stata Corp., College Station, TX, USA), and statistical significance was set at $P<0.05$.

Results

The conducted search retrieved 2,395 studies. After duplicate removal and title and abstract screening, 276 relevant studies remained. The search and screening results are illustrated in Fig. 1. The assessment of 31 studies revealed that the prevalence of *Toxocara* was 3%–79% in 10,676 cases. Of the total number of children (10,676), 3,525 had *Toxocara* infection (Table 1). In addition, most of the conducted studies used enzyme-linked immunosorbent assay (ELISA) to diagnose the infection. Furthermore, in most of the mentioned studies, the patients were younger than 12 years of age. The results from the different included studies are listed in Table 1.

The results demonstrated that the pooled prevalence of Toxocara in pediatric patients worldwide was 30 (95% CI, 22%–37%; $I^2=99.11\%$; $P=0.00$) (Fig. 2), but since the CI of Egger test did not include zero, a significant bias occurred in the publication of the results (coefficient=11.58; T=4.39; $P=0.001$; 95% CI, 6.23–16.93). The funnel plot is shown in Fig. 3.

The subgroup analysis by continent showed that the pooled prevalence of *Toxocara* in pediatric patients in Asia, America, Africa, and Europe was 35% (95% CI, 3%–67%; $I^2=99.43\%$; $P=0.00$), 31% (95% CI, 22%–40%; $I^2=99.01\%$; $P=0.00$), 21% (95% CI, 1%–52%; $I^2=98.75\%$; $P=0.00$), and 26% (95% CI, 19%–34%; $I^2=85.94\%$; $P=0.00$), respectively (Table 2 and Fig. 4).

1. Meta-regression analysis

We used a meta-regression analysis to assess the effect of suspected variables such as year of study and sample size on heterogeneity. The results of the meta-regression analysis shown in Table 2 did not show any significant association between this variable and the prevalence of *Toxocara* spp. in pediatric patients (Table 3 and Fig. 5).

Table 1. Studies examining the prevalence of *Toxocara* spp. in pediatric patients

Study	Country	Year	Sample size (n)	Age range (yr)	Specimen	Study design	Prevalence (%)	Methods	NOS score
Sadjjadi et al.[21]	Iran	2000	519	6–13	Serum	CS	51.30	ELISA	6
Alonso et al.[33]	Brazil	2000	206	1–14	Serum	CS	37.9	SLISA	7
Aguiar-Santos et al.[34]	Brazil	2004	386	0–18	Serum	CS	39.4	ELISA	7
Muradian et al.[35]	Brazil	2005	338	1–15	Serum	CS	79.40	ELISA	7
Paludo et al.[36]	Brazil	2007	450	1–12	Serum	CS	28.8	ELISA	7
Nourian et al.[37]	Iran	2008	810	1–2	Serum	CS	2.7	ELISA	6
Espinoza et al.[38]	Peru	2008	182	6–12	Serum	CS	32.5	ELISA	6
Zarnowska et al.[39]	Poland	2008	343	-	Serum	CS	24.70	ELISA	6
Dar et al.[40]	India	2008	110	5–16	Serum	CS	32.7	ELISA	6
Antonios et al.[41]	Egypt	2008	128	1–12	Serum	CS	6	ELISA	6
Alavi et al.[42]	Iran	2008	29	6–15	Serum	CS	55	ELISA	7
Sviben et al.[43]	Croatia	2009	142	3–18	Serum	CS	43	ELISA	7
Yazar et al.[44]	Turkey	2010	112	-	Stool	CS	21.4	ELISA	6
Santar m et al.[45]	Brazil	2011	252	1–15	Serum	CS	11.10	ELISA	6
Mattia et al.[46]	Brazil	2012	353	0–12	Serum	CS	36.8	ELISA	8
Manini et al.[9]	Brazil	2012	90	1–12	Serum	CS	17.80	ELISA	7
Sariego et al.[47]	Cuban	2012	1,011	5–14	Serum	CS	38.80	ELISA	6
Schoenardie et al.[48]	Brazil	2013	427	1–12	Serum	CS	50.60	ELISA	6
Kanobana et al.[49]	Cuban	2013	958	5–14	Serum	CS	40	ELISA	6
Guilherme et al.[50]	Brazil	2013	167	0–15	Serum	CS	4.2	ELISA	7
Pautova et al.[51]	Russia	2013	144	1–17	Serum	CS	18.8	ELISA	8
Mendon a et al.[52]	Brazil	2013	1,309	4–11	Serum	CS	48.4	ELISA	7
Oliart-Guzm n et al.[53]	Brazil	2014	539	6 m–69 m	Serum	CS	23-28	ELISA	7
Archelli et al.[54]	Spain	2014	120	0–3	Serum	CS	38.3	ELISA	7
Marchioro et al.[55]	Brazil	2015	554	1–12	Serum	CS	7.4	ELISA	7
Mart nez et al.[56]	Venezuela	2015	224	1–6	Serum	CS	29	ELISA	7
Cort s et al.[57]	Mexico	2015	183	3–16	Serum	CS	12	ELISA	7
Mazur-Melewska et al.[23]	Poland	2016	42	1–18	Serum	CS	30.3	ELISA	6
Gabrielli et al.[57]	Serbia	2017	40	2–14	Serum	CS	10	ELISA/WB	7
Sowemimo et al.[58]	Nigeria	2017	308	0–5	Serum	CS	37	WB	7
Fialho et al.[59]	Brazil	2017	200	1–12	Serum	CS	16	ELISA	7

NOS, Newcastle-Ottawa scale; CS, cross-sectional; ELISA, enzyme-linked immunosorbent assay; CE, cryptogenic epilepsy; WB, Western blot.

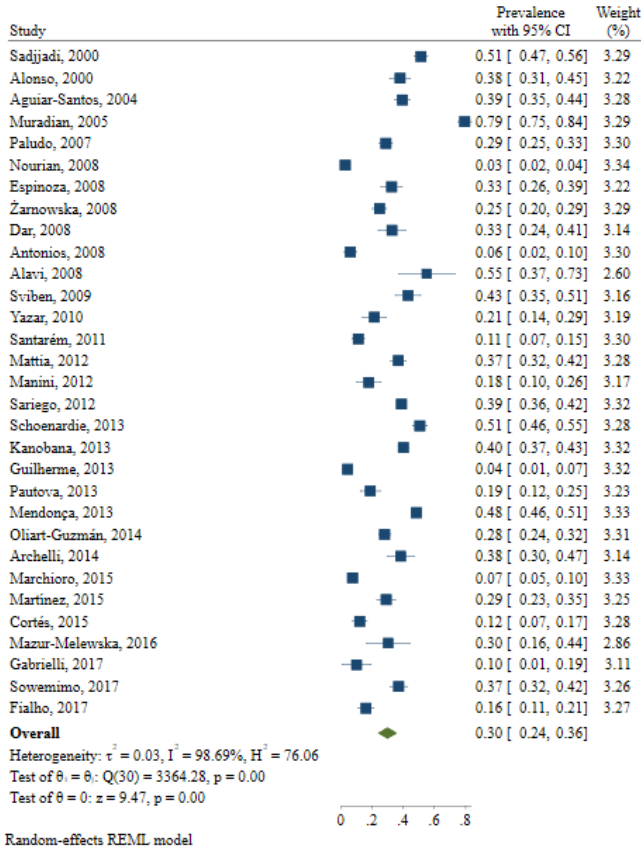

Fig. 2. Meta-analysis of the global prevalence of *Toxocara* spp. in pediatric patients.

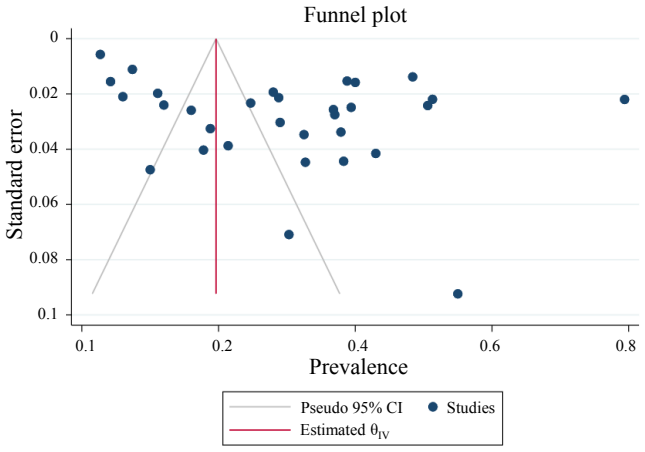

Fig. 3. Publication bias of the prevalence of *Toxocara* spp. in pediatric patients. CI, confidence interval.

Discussion

Toxocara is a worldwide worm and common intestinal parasite for cats and dogs that have the ability to infect humans.[14] *Toxocara* can be responsible for a variety of clinical manifestations.[14] The worm's eggs can pass through the feces of animals and preserve infectivity for a long time in the soil.[14] Soil contamination with Toxoplasma is more frequent in humans.[15]

Table 2. Pooled prevalence of Toxocara spp. in pediatric patients by continent

Continents	Prevalence (95% CI)	Between studies			Between subgroups	
		I^2	Q	Phetero-geneity	Q	Phetero-geneity
Africa	21% (1–52)	98.75%	80.25	0.001	1.01	0.80
American	31% (22–40)	98.83%	172.82	0.001		
Asian	35% (11–58)	98.95%	523.25	0.081		
European	21% (1–52)	88.45%	42.67	0.001		

CI, confidence interval.

It can be concluded that in some cases, closer contact with animals can increase the exposure risk for this parasite.[9,16] The current study aimed to systematically review the prevalence of *Toxocara* infection in pediatric patients. The results of 31 relevant studies indicated that the global prevalence of *Toxocara* in pediatric patients was 30 (95% CI, 22%–37%; I^2=99.11%; P=0.00). The prevalence may vary among sample populations and geographical regions.

Oliart-Guzmán et al.[17] investigated the seroprevalence of *Toxocara* in households with children in Western Brazilian Amazon over 7 years. They concluded that the prevalence of infection in pediatric patients less than 5 years of age was 28%, 23.3%, and 13.9% in 2003, 2010, and 2011, respectively. Oliart-Guzmán et al.[17] suggested that water quality and the treatment of infected animals can be an appropriate strategy for preventing infection in these patients. Roldan et al.[18] investigated eosinophilia and other risk factors of *Toxocara* infection. They used 2 groups of seropositive and seronegative pediatrics. Their results showed that a dry cough and eosinophilia are significantly associated with *Toxocara* infection.[17]

Serologic techniques are reliable methods that can detect larval antiantigens. The most commonly used serologic test is ELISA testing, which applies the secretion antigens of the parasite larvae.[2] Seroepidemiological evaluations in different countries have shown a global distribution of toxocariasis. The prevalence in American pediatrics is 4.6%–7.3% in the USA, 2.5% in Germany, and 19% in the Netherlands.[19] In Iran, the prevalence among school children was 25.6% in Shiraz and 31% in Ilam.[20,21] Musso et al.[22] reported the association of viral and bacterial central nervous system infections in pediatrics with *Toxocara* by evaluating the serum and cerebrospinal fluid of 381 patients. Toxocara immunoglobulin G (IgG) was present in 32% of meningitis and 34% of control group patients, a difference that was not statistically significant.

As mentioned above, *Toxocara* can have a variety of clinical manifestations.[14] Mazur-Melewska et al.[23] evaluated the pulmonary presentation of *Toxocara* in 119 positive patients who were 1–19 years of age. Their results suggested that high levels of eosinophilia and hyperimmunoglobulinemia E could be related to *Toxocara* infection. In addition, Pinelli et al.[24] assessed *Toxocara* infection in patients with suspected VLM and OLM from 1998 to 2009. Their results indicated a significantly

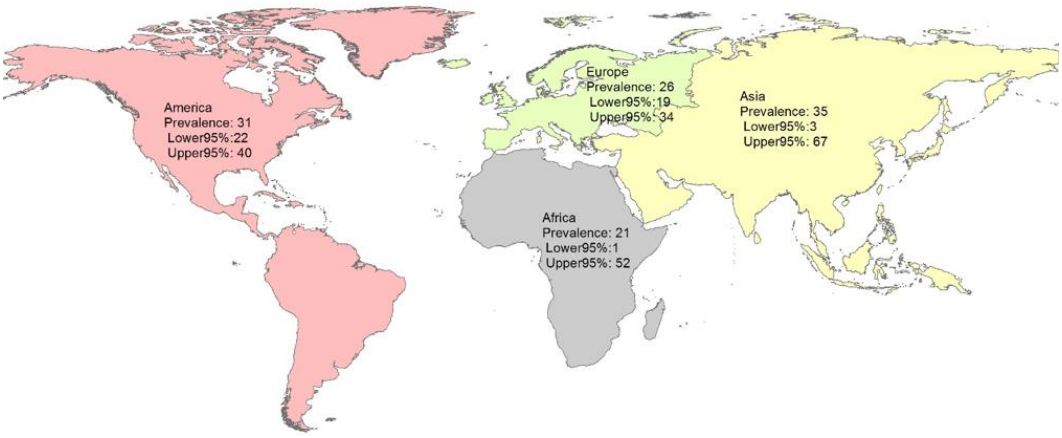

Fig. 4. Global prevalence (%) of *Toxocara* spp. in pediatric patients by continent.

Table 3. Meta-regression analysis to assess the effect of suspected variables on the pooled prevalence of Toxocara spp. in pediatric patients

Prevalence	Univariable model			Multivariable model		
	β	SE	*P* value (95% CI)	*β*	SE	*P* value (95% CI)
Toxocara spp. in the pediatrics						
Sample size	0.001	0.0003	0.388 (-0.001 to 0.003)	0.002	0.003	0.370 (-0.001 to 0.003)
Years of published	-0.013	0.008	0.084 (-0.001 to 0.003)	-0.014	0.008	0.094 (-0.300 to 0.002)

SE, standard error; CI, confidence interval.

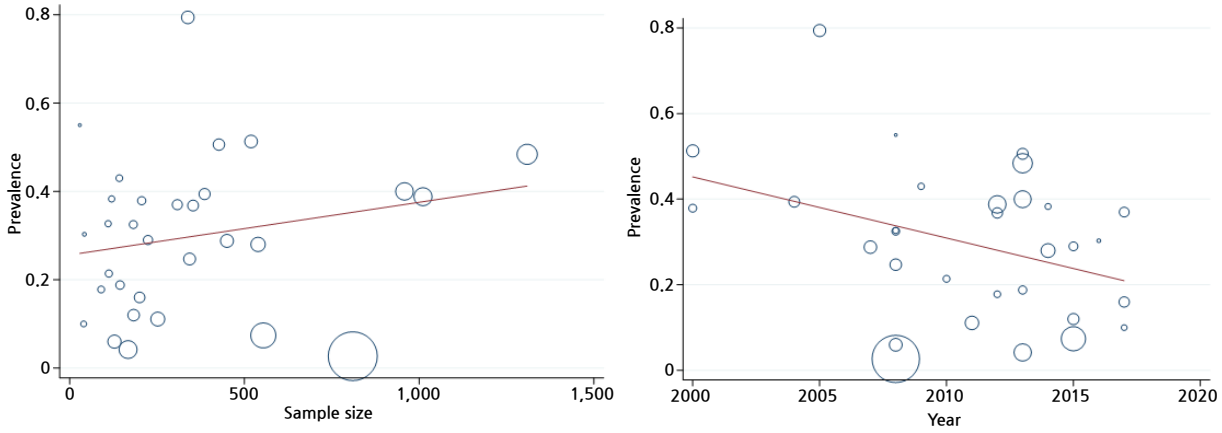

Fig. 5. Meta-regression graph of the prevalence of Toxocara spp. in pediatric patients by sample size and publication year.

decreased rate of infection in the Netherlands that has increased over time as the children grew up.

Epilepsy is a neurological disorder that leads to epileptic seizures.[25,26] Epilepsy can be idiopathic or due to trauma, hypoxia, or infection.[27,28] El-Tantawy et al.[29] assessed *Toxocara* infection in cryptogenic epilepsy patients. The etiology was unknown in these patients, but brain diseases are mostly suspected. Anti-*Toxocara* IgG was found in 48% of the cryptogenic epilepsy patients and 46 of the controls, but the difference was not statistically significant.[29,30]

Sharghi et al.[31] investigated *Toxocara* infection as a risk factor for asthma in 95 patients aged 2–15 years and 229 controls. The result showed no statistically significant association between *Toxocara* and asthma, but *Toxocara* prevalence showed a significantly higher rate in Hispanic children of Puerto Rican descent. It can be concluded that this race is more susceptible to the disease. In addition, Silva et al.[32] reported the prevalence of *Toxocara* as a risk factor for atopia and asthma. They reported that the prevalence in northern Brazil is 63% in 791 patients and there is an association between *Toxocara* infection and serum IgE causing cross-reaction and atopia.

These results show a 35% prevalence of *Toxocara* infection in Asian pediatrics, a rate that is higher than that in other continents. We assume that the factors responsible for this variation likely represent differences in public health and sanitation status, cultural and social conditions, environmental hygiene, and climate.[31,32] This was a comprehensive meta-analysis of 31 valid publications evaluating 10,676 pediatrics on this topic. Most of

the evaluated studies had an appropriate study population. The possibility that some patients were included in more than one report was low. The number of case reports in our assay was low, which leads to a lower risk of publication bias and increases the level of evidence of our findings. The limitations of this study are its high heterogeneity in the pooled estimate, differences in the diagnostic methods, and study population in primary studies.

According to this systematic review and meta-analysis, the global prevalence of *Toxocara* in pediatrics varies widely among geographical regions. The prevalence of *Toxocara* in Asian pediatrics was higher than those in other continents, which shows that in this country and in other continents, health policymakers should be more focused on future research and approaches related to *Toxocara* and other zoonotic diseases, improve the culture, and identify socioeconomically important factors.

Footnotes

Conflicts of interest: No potential conflict of interest relevant to this article was reported.

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