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Seroprevalence of Toxocariasis Among Hypereosinophilic Children: A Single Center Study, Tehran, Iran

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Abstract

Background: Toxocariasis is a parasitic disease causing hypereosinophilia. This study aimed to investigate the serological prevalence of toxocariasis among hypereosinophilic children in Children's Medical Center, Tehran, Iran, as well as to explore its relationship with epidemiological variables and some blood indices.

Methods: This descriptive cross-sectional study was performed in 2020 on children referred to referral children hospital for routine tests. A total of 282 children diagnosed with hypereosinophilia were selected and included in the study, and then, their serum was collected. After obtaining informed consent from their parents, the parents were asked to fill out a questionnaire. The serological ELISA test was used to assess the anti-*Toxocara* IgG antibody. Data were analyzed using SPSS software 18.

Results: Out of 282 hypereosinophilic children, 17 (6%) had serological results positive for anti-*Toxocara* antibody. The mean age of children with toxocariasis was higher than that of children without toxocariasis ($P = 0.312$). Furthermore, ESR and CRP variables were significantly higher in infected children than those in non-infected children ($P < 0.05$).

Conclusions: The results of the present study confirmed the relationship between toxocariasis and hypereosinophilia. Since the symptoms of toxocariasis are non-specific and may go undiagnosed, it was found necessary to examine toxocariasis in cases of hypereosinophilic individuals.

Keywords: Eosinophilia, Iranian Children, Toxocariasis, Visceral Larva Migrants

1. Background

Toxocariasis is a common zoonosis disease caused by *Toxocara canis* and *T. cati*, which are nematodes of dogs and cats, respectively. This disease is more common in tropical areas with low socioeconomic status, and children may be more susceptible to this disease due to their greater contact with the soil (1). The results of two systematic review studies have estimated the global prevalence of anti-*Toxocara* antibodies in humans at 19%. In Iran, the prevalence has been estimated to be between 1 and 29% (mean 11%) (2, 3). Moreover, the prevalence of anti-*Toxocara* antibodies are 24.2% in dogs and 32.6% in cats in Iran, with a significantly higher prevalence (69.4%) in red foxes. This can raise the risk of transmission to humans (4).

Humans, as an abnormal or paratenic host of the parasite, become infected through the ingestion of food or vegetables contaminated with the feces of dogs or cats, or through the ingestion of contaminated raw and undercooked meat of animals such as lambs or birds (5).

In humans, nematodes are not capable of completing their life cycle and maturing (6). As a result, human infections are induced by the migration of larvae of parasites to different parts of the body. In most cases, there are no specific clinical signs, but a wide range of clinical infections may appear in body organs (7). The disease appears in four main forms including the syndrome visceral larval migrants (VLM), ocular larval migrants (OLM), neurological complication (NLM), or covert forms (5, 8). VLM syndrome has a variety of clinical sign that may range from asymptomatic with mild eosinophilia to more severe and lethal forms including fever and pulmonary involvement, gastrointestinal manifestations, hypereosinophilia, and liver damage (e.g., hepatomegaly). In severe cases, pe-

ripheral blood leukocytes rise to 100,000 per microliter, with eosinophilic cells accounting for 80 - 90% (9). The term eosinophilia is defined as an increase in peripheral blood eosinophils to more than 600 cells per microliter (Cell/μL) of blood. Hypereosinophilia has generally been defined as a peripheral blood eosinophil count greater than 1500 Cell/μL (10). As noted earlier, it is challenging to diagnose toxocariasis due to different and non-specific clinical symptoms in humans. The statistics about the number of infections with this parasite and its connection with epidemiological variables in children with hypereosinophilia in Iran are undesirable. Also, most cases of eosinophilia are misdiagnosed as hypereosinophilia syndrome, which may lead to improper treatment if the serological tests for *Toxocara* spp. are not conducted.

2. Objectives

This descriptive cross-sectional study, therefore, aimed to determine the prevalence of toxocariasis in children with hypereosinophilia referred to Children's Hospital Medical Center in Tehran in 2018, as well as to explore its association with some epidemiological variables and blood indices.

3. Methods

This descriptive cross-sectional study was conducted on children with hypereosinophilia in the Children's Hospital Medical Center in 2018. The study was approved by the local ethics committee of Zoonosis Research Center, Tehran University of Medical Sciences, Tehran, Iran (IR.TUMS.VCR.REC.1397.334).

Inclusion criteria were children referring to the Children's Hospital Medical Center for blood testing. CBC test was used to count peripheral blood cells and eosinophils. The children whose eosinophil count exceeded 1000 per mL of blood were included in the present study, and their blood serum was separated and placed in a freezer at -20 degrees. Children with eosinophil count of less than 1000 per microliter of blood were excluded. Then, a questionnaire consisting of demographic information, place of residence, contact with dogs and cats, or soil, as well as symptoms such as fever, were filled out by the parents of the children. Some blood factors such as ESR, CRP, SGOT, SGPT, and ALK were measured and entered into a questionnaire.

ELISA test was administered by NOVATEC's anti-*Toxocara* IgG antibody ELISA kit (catalog number: TOCG0450) on isolated sera. The absorbance of the samples at wavelengths of 450 and 620 nm was measured by ELISA reader. The results of ELISA test and other variables were inputted into SPSS-23 software, and descriptive and chi-square tests were used to analyze the data.

4. Results

The present study was conducted on 282 children with hypereosinophilia with a mean age of 3.0 ± 4.1 years. The mean eosinophilia count was 1.2 ± 1.3 per mL of blood. Of the total children studied, 185 (65.6%) were males, and the rest were females 97 (34.4%).

Of all children in the study, the serology test results were positive for *Toxocara* spp. in 17 (6.02%) children (95% CI: 3.2 - 8.8%). Among infected children, 8 (47.1%) were males, and 9 (52.9%) were females. No significant relationship was observed between sex and the prevalence of *Toxocara* infection (P = 0.097).

The mean age of children with toxocariasis was 4.4 ± 5.7 years, which was higher than that of children without toxocariasis, with a mean age of 2.9 ± 3.9 years (P = 0.312).

The mean eosinophil count was 1.4 ± 2.3 per mL in children with positive serology and 1.2 ± 1.2 per mL in children with negative serology, and no significant relationship was observed. Among other blood factors in Table 1, ESR and CRP variables in children with toxocariasis were significantly higher (P < 0.03). The correlation coefficient between ESR and CRP was equal to 0.672 (P < 0.001).

Other data such as keeping of animals, contact with dogs and cats, contact with soil, place of residence, and ingestion of foods suspected of contaminants such as unpasteurized milk, raw meat, and eggs were collected from 16 children with toxocariasis and 60 non-toxocariasis children. In short, none of the children had a history of keeping animals or digesting foods suspected of contaminants. There was no significant difference between seropositivity rate and residential area (rural vs. urban) (P = 0.634). The factors such as soil contact, dog and cat contact, marginalization, and fever were higher in children with toxocariasis (93.8%, 81.3%, 87.5%, and 37.5%, respectively). Although these differences were not significant, they were reported as a risk factor in hyperosinophilic children with toxocariasis (OR > 1.0) (Table 2). There was no significant association between SGOT, SGPT, and ALKP values with toxocariasis seropositivity in our study (P > 0.05).

5. Discussion

According to our results, the prevalence of toxocariasis in hyperosinophilic children referred to Children's Hospital Medical Center was 6%. The prevalence rate reported by most studies worldwide was higher than that of the present study. In a 2004 study in Ahvaz, 50% of children aged 6 - 12 years with hypereosinophilia had a titer positive for anti-*Toxocara* antibody (11). In two studies conducted by Maraghi et al., however, a lower prevalence was reported in Ahvaz (19%) and Abadan (11.1%) cities (12, 13). In studies in Mashhad, Shiraz, Babol, and Arak cities, the prevalence

Table 1. Laboratory Characteristics of Children with Hypereosinophilia Who Visited the Children's Hospital Medical Center for Blood Testing as an Outpatient

	Total		Positive Toxocariasis		Negative Toxocariasis		P-Value
	Mean ± SD	Median (The First Quartile-Third Quartile)	Mean ± SD	Median (The First Quartile-Third Quartile)	Mean ± SD	Median (The First Quartile-Third Quartile)	
WBC	15.2 ± 52.9	10.6 (8.4 - 13.7)	14 ± 7.9	11.5 (10.1 - 14.3)	15.3 ± 54.5	10.6 (8.4 - 13.7)	0.201
ESR	20.5 ± 16.9	15.0 (10.0 - 26.0)	13.1 ± 12.2	12.0 (4.5 - 15.0)	21 ± 17.0	15.0 (10.0 - 26.0)	0.019
EOS#	1.2 ± 1.3	0.85 (0.70 - 1.2)	1.4 ± 2.3	0.76 (0.65 - 1.1)	1.2 ± 1.2.1	0.86 (0.71 - 1.2)	0.327
EOS	4.4 ± 9.1	8.2 (6.3 - 11.2)	8.8 ± 6.5	7.1 (4.9 - 11.0)	9.2 ± 4.3	8.4 (6.3 - 11.2)	0.160
SGOT	64.5 ± 44.8	32.0 (22.2 - 47.0)	38.8 ± 31.2	34.0 (14.5 - 42.5)	45.2 ± 66.1	32.0 (22.0 - 48.0)	0.668
SGPT	69.3 ± 41.6	26.0 (16.0 - 48.5)	40.8 ± 33.5	26.0 (19.5 - 55.5)	41.6 ± 71.1	26.0 (16.0 - 48.0)	0.572
ALK	346.5 ± 487.5	390.0 (270.0 - 586.5)	617.8 ± 528.1	418.0 (306.5 - 877.5)	479.1 ± 331.2	380.0 (294.0 - 564.7)	0.437
CRP	6.5 ± 15.0	1.0 (1.0 - 5.0)	11.1 ± 4.4	1.0 (1.0 - 3.0)	6.6 ± 15.2	0.2 (1.0 - 5.0)	0.033

Table 2. Investigated Exposures of Children with Hypereosinophilia Who Visited the Children's Hospital Medical Center for Blood Testing as an Outpatient

	Total of Examined, No. (%)	Positive Toxocariasis, No. (%)	Negative Toxocariasis, No. (%)	OR (95% CI)	P-Value
History of contact with soil				1.3 (0.12, 13.1)	1.0
No	4 (5.3)	1(6.3)	3 (5.0)		
Yes	72 (94.7)	15 (93.8)	57 (95.0)		
History of contact with animals				1.7 (0.40, 7.7)	0.431
No	10 (13.2)	3 (18.8)	7 (11.7)		
Yes	66 (86.8)	13 (81.3)	53 (88.3)		
Residential place				1.6 (0.28, 9.0)	0.634
Urban	7 (9.2)	2 (12.5)	5 (8.3)		
Rural	69 (90.8)	14 (87.5)	55 (91.7)		
Fever				2.7 (0.80, 8.9)	0.173
No	17 (22.4)	10 (62.5)	49 (81.7)		

of anti-*Toxocara* antibodies in hypereosinophilia were reported to be 22.5%, 2%, 23.5%, and 16%, respectively (14-17).

Out of 103 patients with eosinophilia of an unknown origin in Korea in 2006, 83.5% had a titer positive for anti-*Toxocara* antibody, of whom 68% were diagnosed with toxocariasis (18). In another study by Kim et al. in 2017, out of 69 patients with eosinophilia of an unknown origin, 65.2% had positive serological results for anti-*Toxocara* antibodies, and treatment with the anti-parasitic medication was highly effective in alleviating patients' eosinophilia (19).

In another Korean study, 50.5% of the subjects with eosinophilia had serology results positive for anti-*Toxocara* antibodies and 45.5% had toxocariasis (20). In a recent study, a high prevalence of this infection (22.2%) was reported in patients with eosinophilia (21). In Turkey, 32.6% of patients with eosinophilia tested positive for anti-*Toxocara* antibodies (22). Due to the fact that the prevalence of toxocariasis varies in diverse climates and the survival of parasite eggs, including *Toxocara* eggs, is higher in humid climates, the higher prevalence of toxocariasis in Korea and Turkey can be attributed to the high humidity of these regions compared to areas like Iran (23). Divergent prevalence of this parasite in different studies may be due to disparity of age groups. Since the majority of studies have been performed on adults (e.g., housewives who are more exposed to products such as vegetables or farmers and ranchers due to their greater exposure to soil or animals), they have reported a higher prevalence. As noted in the present study, there was a significant association between the prevalence of toxocariasis and age (P-value < 0.001). The average age of infected and non-infected children was 10 and 3 years, respectively, suggesting that the

increased age is associated with a higher risk of developing this infection. This may have been due to the fact that children at the age of 10 are more likely to spend time outdoors and come in contact with dirt and animals (e.g., dogs and cats) than younger children.

In the present study, no significant relationship was observed between the sex of infected and non-infected children. The results were consistent with the study findings of Alavi et al. in Ahvaz (11). However, infection was found to be significantly higher in boys, which was probably due to the specific behaviors of boys and the type of games they play outdoors.

As discussed earlier, toxocariasis is transmitted to humans through the ingestion of contaminated food or close contact with animals or soil contaminated with dog and cat feces. These factors can contribute to the spread of the disease. In the present study, no significant relationship was observed between the prevalence of toxocariasis and factors such as children's contact with soil and animals, ingestion of undercooked and raw food, place of residence, and symptoms such as fever; however, these factors were reported as risk factors for toxocariasis (OR > 1.0). A number of authors, such as Berenji et al. have reported a significant relationship between the prevalence of toxocariasis and contact with animals such as dogs and cats ($P < 0.05$) (23), while in the present study, similar to the study of EbrahimiFard et al., no significant relationship was found in this regard (16). However, the role of animals such as dogs and cats was considered in the present study as a risk factor for toxocariasis. In general, religious and racial differences can be linked to the prevalence of toxocariasis. For example, in Muslim countries like Iran, close contact with animals such as dogs is prohibited, which may explain the lower prevalence of the disease in Iran than in other countries.

In the study of Kwon et al., the prevalence of toxocariasis was higher in patients with hypereosinophilia who had ingested undercooked or raw meat (OR: 7.8; CI: 2.0 - 29.9), which was in line with our study result (18). In the study of Song et al., ingestion of raw meat was considered as a risk factor (OR: 5.8; CI: 1.7 - 19.1) in eosinophilic patients with toxocariasis (21). In EbrahimiFard et al.'s study, there was a significant relationship between the place of residence (a higher rate in rural areas) and the prevalence of toxocariasis ($P = 0.001$) (16); nonetheless, Mosibati et al. found no significant relationship between these two variables, which was consistent with our study result (17). Other relevant factors such as eosophilia, raw meat consumption, and pica behavior have been discovered to be associated with higher seropositively of *T. canis* (24). Toxocariasis should always be considered in any child with hypereosinophilia and compatible clinical signs and symptoms, even in low endemic regions. Another finding of this study was the significant relationship detected between ESR and CRP blood factors in infected children compared to non-infected children. CRP is a non-specific reactive protein, the level of which spikes in the blood in the event of inflammation or infection. A positive result indicates an infection, but this test does not determine the cause of the disease. ESR is another factor used for diagnosing the inflammation, but like CRP, it is non-specific and unable to specify the cause of the inflammatory disease (25). In the present study, the two factors increased significantly ($P < 0.03$) in hypereosinophilic children with toxocariasis. As a result, it can be argued that ESR and CRP are factors that rise dramatically in the blood in the wake of toxocariasis and, therefore, should be considered in the diagnosis of toxocariasis. SGOT (AST) and SGPT (ALT) are hepatic transaminases measured to evaluate liver function. These factors increase as a result of liver damage in the peripheral blood. ALK, along with the above two factors, is often requested to evaluate liver damage (26). In our study, there was no significant association between toxocariasis seropositivity and liver function tests.

Inherited to the restrictions in most of the cross-sectional seroprevalence study, our study is not an exception and has some limitations. The sample size of the current study was not large enough, and unable to follow up the infected children. Moreover, cross-reactive antibodies elicited by the exposure to other helminths may have reduced the specificity of ELISA method for diagnosing toxocariasis.

5.1. Conclusions

The results of the present study confirmed the relationship between toxocariasis and hypereosinophilia. Since the symptoms of toxocariasis are non-specific and may go undiagnosed, it was found necessary to examine the hyper-eosinophilic individuals for toxocariasis. This evaluation may have prevented the misdiagnosis of idiopathic eosinophilia.

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Footnotes

Authors' Contribution: M.S. provided project administration and wrote the manuscript. B.N. collected the strain, worked on concept and design of the study, and critically revised the paper. S.S. and M.s. analyzed and interpreted the data. B.N., M.Z., and M.Z. critically revised the

paper. All authors read and approved the final version of the manuscript, as well as the authorship list.

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