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Seroprevalence of Toxocara Canis In Asthmatic Children and its Relation to the Severity of Diseases

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ABSTRACT

Background: Toxocariasis is a common parasitic infection worldwide even in developed countries. Through this health problem, the immune system is triggered and the antibody is produced, leading to some hypersensitive situations like asthma. In the present study, we tried to show a correlation between Toxocara Canis (*T. canis*) seropositivity and asthma in Isfahan city. **Methods:** This research is a cross-sectional study involving 40 asthmatics and 46 non-asthmatic cases aged 2-18 years. In all cases, *T. canis* IgG level was measured using enzyme-linked immunosorbent assay (ELISA) and compared between two groups. **Results:** The seroprevalence of IgG anti-*T. canis* antibodies were 45% in the asthmatic patients and 21.7% in the controls ($P= 0.022$). The more severe asthmatic patients had significantly more risk for *T. canis* seropositivity ($P= 0.019$). In the asthmatic patients, there was a significant correlation between Toxocara seropositivity and going to park or playground ($P= 0.001$). **Conclusion:** In this study, we found a significantly positive serology of *T. canis* in asthmatic children especially in more severe disease. To verify the etiologic role of Toxocara in asthma, more advanced studies are needed.

Keywords: Toxocariasis, Pediatric Asthma, seroprevalence.

1. INTRODUCTION

Asthma is a serious global health problem and one of the most common chronic diseases. Over the past decades, asthma has increased worldwide, mainly due to the effect of a wide number of environmental and lifestyle risk factors. Accordingly, identification of risk factors for inducing and trigger of asthma is of great importance (1).

The probable role of parasitic infections in the development of asthma is not well understood. Toxocarasis has been suggested as a possible etiologic cause of asthma (2, 3). Toxocariasis is azoonotic parasitic infection caused by larvae of a roundworm *Toxocara Canis* or *Toxocaracatis* (4). Humans become infected by ingesting embryonated eggs from soil (geophagia, pica), dirty hands, raw vegetables, and larvae from undercooked giblets (5). *Toxocara* larvae penetrate the intestinal mucosa and migrate to liver, lungs, and other organ systems (e.g., skeletal muscle, heart, brain, and eyes) by mechanical means and protease digestion. Migrating larvae are attacked by host immune responses, resulting in local inflammation associated eosinophilia and specific cytokine production (6).

In Iran, epidemiological studies with anti-*Toxocara* antibodies showed a higher rate of infection in children aged from 6 to 13 years. Total prevalence of this infection was 25.6% with a higher rate in urban (30.15%) than rural (20.2%) residents and higher rate in males than females (7).

Most previous studies revealed no association between Toxocariasis and asthma but a positive correlation was proved by other studies (8, 9, 10). The aim of this study is to investigate the association between asthma and *T. canis* IgG seroprevalence and relation to the severity of asthma..

2. MATERIAL AND METHODS

This research is a case-control study conducted on 86 patients aged 2-18 years who referred to Imam-Hussein clinics of Isfahan. A questionnaire was designed for the risk factors of *T. Canis* infection such as age, sex, keeping of dogs, and history of playing in sand or soil in play grounds and sand boxes. We used Enzyme-linked Immunosorbent Assay (ELISA) for detecting IgG antibodies for *Toxocara*. Written informed consent was obtained from all of the volunteer participants fol-

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	Total n=86 (100%)	Case \$ n=40 (46.5%)	Control † n=46 (53.5%)	p#
Child's sex				
Girls	30 (34.9)	12 (30.0)	18 (39.1)	0.376 ^a
Boys	56 (65.1)	28 (70.0)	28 (60.9)	
Age category (years)				
	11 (12.8)	4 (10.0)	7 (15.2)	0.319 ^a
6-9	29 (33.7)	11 (27.5)	18 (39.1)	
10-13	32 (37.2)	19 (47.5)	13 (28.3)	
	14 (16.3)	6 (15.0)	8 (17.4)	
Age: mean (SD)	9.42 (3.66)	9.83 (3.46)	9.07 (3.82)	0.340 ^b
Presence of dogs at home				
Yes	2 (2.3)	2 (5.0)	0 (0.0)	0.125 ^a
No	84 (97.7)	38 (95.0)	46 (100)	
Going to the park/ garden				
Yes	32 (37.2)	16 (40.0)	16 (34.8)	0.618 ^a
No	54 (62.8)	24 (60.0)	30 (65.2)	
Toxocara-canis				
Positive	28 (32.6)	18 (45.0)	10 (21.7)	0.022a*
Negative	58 (67.4)	22(55.0)	36 (78.3)	

Numbers are presented as prevalence and percentage (%). a Using Pearson chi-square. bUsing student's t-test. \$ Case: Children with Asthma.† Control: Healthy children. *Significant at level of 5%.

Table 1. Demographic and prevalence of *Toxocara-canis* in children stratified by groups of study (case, control), in Iran, Isfahan, 2015-16, (n=86).

lowing a thorough explanation of the nature of the study. This study was approved by ethical committee of Isfahan University of Medical Sciences. Eliza Test for detecting T. CANIS IgG.

In this study, 4 mL of patients' venous blood was drawn under aseptic conditions from each patient. Serum was separated and stored at -20°C until studied. Specific anti-*Toxocara* IgG or M antibodies were determined by ELISA (enzyme-linked immunosorbent assay; Novum Diagnostica, Germany) according to manufacturer's instructions. The seroprevalence of *T. canis* was compared in both groups and in asthmatic patients the seroprevalence of *Toxocara* was compared according to the severity of asthma, being in a playground, the presence of other allergic diseases(allergic rhinitis and eczema), and disease duration.

Statistical Analysis

Statistical analysis was performed on SPSS version 22 statistics software. Data were expressed as a mean value (standard deviation) or frequency (percentage). For categorical variables, the difference between groups was tested by Pearson chi-square test or Fisher's exact test. For continuous variables, the difference between the mean of independent groups was tested by student's t-test or one-way ANOVA. The logistic regression analysis was performed and the results were expressed as odds ratios (OR), 95% confidence intervals (CI), and p-values. Two age

Toxo-cara-canis	Group of study		Model 1 \$			Model 2†		
	Case	Control	OR	95% CI	p	OR	95% CI	p
Total	40 (100)	46 (100)	-	-	-	-	-	-
Positive	18(45.0)	10(21.7)	Ref.	-	-	Ref.	-	-
Negative	22(55.0)	36(78.3)	2.95	(1.15, 7.52)	0.024*	6.66	(1.31, 34.00)	0.023*

Numbers are presented as prevalence and percentage (%). OR: odd ratio; 95% CI: 95% confidence interval; p: p-value; Ref.: Referenced variable in the logistic regression model. \$ Model 1: using logistic regression analysis with adjustment for potential variables; † Model 2: Using multivariate logistic regression analysis after adjustment for confounders such as, age category, sex, going to the park/ garden, and presence of dogs at home. *Significant at level of 5%.

Table 2. The prevalence of presence of *Toxocara-canis* stratified by groups of study (case vs. control), in Iran, Isfahan, 2015-16, (n=86).

categories of 1-10 and 11-18 years were considered. The OR for the presence of *T. canis* for various independent variables was estimated. Also, the relationship between the prevalence of severity of asthma/allergic rhinitis/eczema and sex/age groups was examined for the studied groups. All statistical tests performed in this study were two-tailed and p-values less than 0.05 were considered to be statistically significant.

3. RESULTS

In this work, 40 asthmatic patients (12 females and 28 males) with a mean age of 9.83 ±3.46 and 46 non-asthmatic children (18 females and 28 males) with a mean age of 9.07 ±3.82 were recruited. Both groups of asthma and controls were age and sex matched. Only 2 patients in the case group and none of the patients in control group had dogs in their home (Table 1).

The number of *T.canis*-seropositive patients in case group was 18 (45%) and in the healthy control group was 10 (21.7%), suggesting a statistically significant difference (P= 0.022) (Table 2). Table 3 presents the association of

	Total	Toxocara-canis		OR	95% CI	P-value	
		Positive	Negative				
Child's sex	Girl	12 30.0%	4 22.2%	8 36.4%	1	-	-
	Boy	28 70.0%	14 77.8%	14 63.6%	1.50	(0.43 5.19)	0.33 ^a
Presence dog at home	No	38 95.0%	16 88.9%	22 100.0%	1	-	-
	Yes	2 5.0%	2 11.1%	0 0.0%	2.25	(0.63 7.79)	0.20 ^a
Going to the park/ garden	No	24 60.0%	2 11.1%	22 100.0%	1	-	-
	Yes	16 40.0%	16 88.9%	0 0.0%	12.01	(3.18 45.45)	0.001 ^a
Age (year) Mean ± SD	9.82± 3.48	9.59 ± 3.92	10.11 ± 2.95				0.64 ^b

a: P-value are resulted from Pearson chi-square – b: P-value are resulted from t-test , *Significant at level of 5%.

Table 3. Association of demographic characteristics with *Toxocara-canis* serology in children with asthma (case group), in Iran, Isfahan, 2015-16.

	Total	Toxocara-canis		Model1		Model2		
		Positive	Negative	OR(95%CI)	P-value	OR(95%CI)	P-value	
Allergic Rhinitis	Negative	15 37.5%	5 27.8%	10 45.5%	1	-	1	-
	Positive	25 62.5%	13 72.2%	12 54.5%	1.83 (0.55 6.4)	0.34	1.83 (0.55 6.4)	0.76
Eczema	Negative	34 85.0%	15 83.3%	19 86.4%	1	-	1	-
	Positive	6 15.0%	3 16.7%	3 13.6%	1.49 (0.43 5.2)	0.53	1.93 (0.09 39.4)	0.67
The severity of Asthma	Mild	15 37.5%	1 5.6%	14 63.6%	0.04 (0.004 0.37)	0.005*	0.03 (0.002 0.39)	0.01*
	Moderate	8 20.0%	6 33.3%	2 9.1%	1.64 (0.25 10.8)	0.61	1.63 (0.22 12.1)	0.63
	Severe	17 42.5%	11 61.1%	6 27.3%	1	-	1	-
dx-duration (years) (Mean ± SD)	5.2 ± 3.6	3.3 ± 2.85	7.5 ± 3.01					<0.001*

Table 4. Association of severity of asthma, allergic rhinitis, eczema, and dx-duration with *Toxocara-canis* in serology in children with asthma, Iran, Isfahan, 2015-16.

demographic characteristics with the prevalence of *T. canis* in children with asthma using logistic model and t-test. In the case group, 16 patients (40%) had a positive history of playing in the park and playground. The results showed that patient going to the park/garden had a significantly higher risk for positive *T. canis* (P= 0.001). There was not any association between positive seroprevalence of *T. canis* with age, sex, and keeping dogs at home (P=0.64, 0.33, 0.2, respectively).

In the case group, 15 patients (37.5%) had mild, 8(20%) moderate, and 17(42.5%) had severe asthma. The results showed that patients with mild severity of asthma had a significantly lower risk for *T. canis*-seropositivity than patients with severe asthma (P=0.01). Mean duration of disease in asthmatic patients was 5.2 ± 3.6. Disease duration in patients with positive *T. canis* was significantly higher than that in negative serology (P< 0.001). In this work, 25 (62.5%) of asthmatic patients had allergic rhinitis and 6 cases (15%) had Eczema. There was no significant correlation between the frequency of antibodies against *T. canis* and presence of allergic rhinitis and eczema (P= 0.76 and 0.67, respectively) (Table4).

4. DISCUSSION

Prevalence of asthma is increasing during two past decades worldwide. The role of parasitic infections in the development of asthma is not well understood (8). The present study showed that *Toxocara Canis* positive results were significantly higher in those with asthma than in those without asthma (OR=6.66 and P= 0.022)

Some epidemiological and experimental studies suggest that infection with *T. canis* contributes to the development of allergic manifestations, including asthma,

so the role of toxocariasis as an important risk factor for asthma and other allergic diseases have been hypothesized (11). Although some studies suggest that parasitic infections protect against the development of asthma, others show that parasitic infections actually predispose an individual to asthma.

Toxocariasis is one of the most common helminthic infections in humans worldwide that is caused by the nematode of *T. canis* or *cati* belonging to the order of *Ascaris*. *Toxocara* infestation mainly occurs via accidental ingestion of contaminated soil, mainly in parks and gardens; so, it mostly affects children. They ingest infective eggs (geophagy and onychophagy) by putting their fingers in their mouths (12). Several studies have shown seroprevalence of toxocariasis ranging between 9.7 and 43% (13). Prevalence of *Toxocara* infection in Iran has been reported in children from 2.7% in Zanjan (9) to 25.6% in Shiraz (14,7).

In this study, the seroprevalence of *Toxocara Canis* in Isfahan was higher than the previous study in Iran. The explanation for this result could be the availability of a large number of parks and play spaces in Isfahan as a metropolis in Iran and contamination of them by the feces of dogs. The hygiene hypothesis proposes that infections with different pathogens including helminths can protect against allergies (15) However, *Toxocara* infections do not appear to protect against allergy. However, it may have a role in the development of this immunopathology (14). The induction of a Th2 type of immune response characterized by the production of high levels of IgE and Eosinophilia is a shared immunological pathway in allergic diseases and Toxocariasis (11, 16). Some epidemiological studies have suggested an association between *Toxocara* infections and allergic diseases including asthma. A study by Gonzalez-Quintela et al. on 134 subjects with *Toxocara* exposure showed evidence of an intriguing interaction between *Toxocara* exposure and allergic sensitization for both total serum IgE levels and blood eosinophil counts (17).

In a study in Arak City (Iran) in 2014, the seroprevalence of antibodies against *Toxocara* species was estimated at 1.8% in asthmatic children, though no antibodies against *T. canis* were detected in the control group (18). In comparison, the prevalence of seropositivity in both asthmatic and control groups in our study was higher than that in the above study. The explanation for this observation can be the difference in eating habits, personal hygiene, and more contamination of outdoor places.

In our study, just two people with asthma and nobody in control group keep the dog in their home. This result is because of religious beliefs in Iran, so the main source of contamination may be playgrounds, parks, and

gardens. The reported prevalence of soil contamination with *Toxocara* species eggs varies among studies from 6.6% to 87.1 % (19). The weighted overall prevalence of *Toxocara* spp. in soil samples in different cities of Iran was 16% (95% CI = 11–21%) (20). According to a study in Khorram Abad in Iran, public park contamination in an urban area was 42%(21). Keeping the dog in the house has been a risk factor for seropositivity in several studies (13). Nevertheless, some authors have found no association between a dog owner and frequency of *Toxocara* infection, which could be explained by appropriate hygiene measures taken by adults (22).

In a systematic review by Aghaeiet al., reviewing 17 studies, an increased risk for asthma was observed in children with *Toxocara* infection seropositivity (OR = 1.91) (23). In a meta-analysis by Lingling Li et al., among 10 studies included, a significant association was noted between *Toxocara* exposure and asthma (24).

In comparison, Sharghi et al. did not find any association between *Toxocara* seropositivity and asthma among 95 asthmatic and 229 non-asthmatic children probably due to the lower number of asthmatic cases in that study (8).

Our study showed a higher rate of positive TC serology in more severe asthma. In a study by López M et al. on 47 asthmatic children and 53 non-asthmatics, a total seropositivity of 55%, 57.4% of children with asthma and 52.8% in the control group was reported. However, among asthmatics with severe symptoms (grade II, III, and IV), there was a 67.7% of seropositivity while in children with symptoms of grade-I it was 37.5% ($p = 0.0470$). They suggested that *T. canis* could act as a co-factor increasing the severity of the symptoms of bronchial asthma (25). However, further future studies with anti-parasitic treatment is needed to confirm this relationship..

One of the main limitations of our study is being cross-sectional and the low number of cases. Another limitations the detection of infection of *T. canis* with serology, which cannot differentiate between recent and past infections.

5. CONCLUSION

In this study,, we found a significantly positive serology of *Toxocaracanis* in asthmatic children especially in more severe diseases. To confirm the etiologic role of *Toxocara* in asthma, however, more advanced studies are needed.

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- **Conflict of interest:** none declared.

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