

Association between previous enterobiasis and current wheezing: Evaluation of 1018 children

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ABSTRACT

The aim of this study was to investigate the association between parasitosis and allergy. We surveyed all children aged 4–12 years living in poor hygienic conditions in a shantytown of Istanbul. After obtaining data from the International Study of Asthma and Allergies in Childhood (ISAAC) and an additional questionnaire, performing a skin-prick test (SPT), and determining total IgE, stool and perianal tape specimens were obtained from 1018 participating children. The prevalence of past episodes of wheezing, current wheezing, asthma, and rhinitis was 31, 14.6, 10.7, and 26.2%, respectively. Parasitosis was present in 49.1%, *Enterobius vermicularis* (23.3%), being the most common. A history of treatment for enterobiasis was present in 37%. Comparison of children with and without current enterobiasis revealed no significant difference in allergic manifestations and SPT results, except for serum total IgE level ($p = 0.018$), whereas children with previous enterobiasis were more likely to have current wheezing ($p = 0.012$). Current wheezers were more likely to have previous enterobiasis ($p = 0.01$) and a higher maternal employment level ($p = 0.036$) when compared with those without. According to logistic regression analysis, covariables significantly positively related with current wheezing were previous enterobiasis ($p = 0.003$) and being ≤ 5 years of age ($p = 0.043$), whereas being the first child of the family ($p = 0.043$) was negatively related. A previous infection with *E. vermicularis* was found to potentiate current wheezing in a population living in a shantytown in Istanbul.

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The prevalence of atopic disorders has been increasing in the industrialized developed countries in the past few decades,¹ in contrast to the considerably lower prevalence of atopic diseases in developing countries.² Environmental factors associated with a rural, nonwestern lifestyle may have a protective effect on the development of atopic diseases.^{3,4} The “hygiene hypothesis” suggests that either lack of bacterial or viral infections contributes to insufficient stimulation of T helper (Th)-1,⁵ or lack of exposure to parasites results in differences in the quality of Th-2 stimulation and allergic response to environmental allergens.^{5–8}

Ecological epidemiology has found an inverse association between parasitosis and asthma. Countries with high asthma prevalence are more likely to be western, urban, and industrialized without parasitosis; whereas countries with low asthma prevalence are likely to be rural, nonurban, nonwestern, and with high rates of parasitic infections.⁹

In a number of studies, helminthic infections such as *Ascaris lumbricoides*^{4,10} and *Schistosoma hematobium*¹¹ were found to be negatively associated with atopy and asthma, whereas in other studies *Toxocara* and *Ascaris* infections^{12,13} were shown to be positively related. One of the immunologic mechanisms underlying the negative association between atopy and helminth infections is that helminthic infections not only stimulate IgE responses, but also induce a strong nonspecific Th-2/IL-4–dependent polyclonal synthesis of IgE.^{14,15} The nonspecific nature of this polyclonal stimulus can suppress allergic responses by reducing the production of allergen-specific IgE^{16,17} and by causing mast cell blockade.^{17,18}

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On the other hand, several studies have established a defect in proliferative responses to helminth antigens, suggesting that individuals with chronic helminth infections develop prominent anti-inflammatory networks attributed to IL-10 and TGF- β .^{19–21} More recently, it has been shown that IL-10 induced in chronic schistosomiasis was negatively associated with the outcome of skin test reactivity to mites.¹¹

It is likely that the relationship between infections with parasites and the development of allergy is a complicated one. The fact that mild and sporadic helminthic infections can nonspecifically potentiate IgE synthesis to environmental allergens and augment the reactivity to specific allergens and susceptibility to allergic disease also must be taken into account.^{12,13,22–24} To date, there is no conclusive evidence that parasitic infection protects against asthma development. Although some heterogeneity in outcome according to the various parasite species is to be expected, intensity and continuity of infections are suggested to be important factors influencing the progression to allergy.²⁵ The purpose of this study was to investigate the association between infection with parasites and allergic manifestations in children living in poor hygienic conditions in a shantytown in Istanbul.

MATERIALS AND METHODS

Study Population

We surveyed all children aged 4–12 years living in Sultanciftligi, a shantytown in Istanbul, between July and September 2001. Sultanciftligi was founded within the last 20 years by immigrants from various rural areas of minor Anatolia. This area has a moderate Mediterranean climate, being hot with a humidity of 60–80% during summertime. The habitants of this area are all of very low socioeconomic level, living in extremely poor hygienic and low-standard housing conditions.

Study Design

Initially, the International Study of Asthma and Allergies in Childhood (ISAAC) and an additional questionnaire were filled out by an independent person performing a face-to-face interview. Then, a skin-prick test (SPT) was performed and blood was drawn for determination of serum total IgE. Finally, perianal tape and stool specimens were obtained for parasitological evaluation. All procedures for each patient were performed on the same occasion. The study was approved by the Ethics Committee of Marmara University. Written informed consent was obtained from parents of all participating children.

Questionnaires

The ISAAC questionnaire was used to obtain data on ever-wheezing/rhinitis, current (past 12 months) wheezing/rhinitis, and doctor-diagnosed asthma through face-to-face interview from parents by an independent person, usually the mother. Also, data on family history of atopy was obtained from the ISAAC questionnaire. Another questionnaire was filled out by the same person to obtain data on socioeconomic and environmental factors including number of siblings, birth order, indoor smoking habits of family members, and educational and employment status of parents, as well as other housing conditions. To define treatment for previous enterobiasis, parents were questioned if “they had ever noticed pinworms in stool or perianal area” and “whether any treatment had been prescribed for that.” In case of a positive response to both of those questions the child was accepted as having “a positive history of treatment for previous enterobiasis.”

SPT and Serum Total IgE

SPT was performed with 15 common aeroallergens including *Dermatophagoides farinae*, *Dermatophagoides pteronyssinus*, *Alternaria*, *Aspergillus* mix, *Cladosporium*, *Penicillium* mix, *Candida albicans*, Betulaceae, mixture of 4 cereals, mixture of 12 grasses, Salicaceae, composites, feather mixture, cat hair, and dog hair (Stallergenes, S.A., France). Histamine and dihydrochloride saline were used as positive and negative controls. A wheal size ≥ 3 mm was considered positive. Subjects with one or more positive reactions were considered atopic. Blood was drawn for determination of serum total IgE level (Immulite method; Euro/DPC, Llnberis, United Kingdom). Samples were frozen at -20°C until analysis.

Diagnostic Tests for Intestinal Parasites

Accompanying parent(s) of all participants were supplied by a taped glass slide for perianal tape test and by a collection box for fresh stool sample. They were also taught how to perform an early morning perianal tape test by two of the investigators. They were instructed to work together with one parent getting access to the perianal area and the other handling the tape and then placing the specimen on the glass slide. Perianal tape specimens were examined for the presence of *Enterobius vermicularis* eggs. Collected feces samples were examined for the presence of eggs and larvae by the sedimentation technique using both unstained and Lugol-stained stool specimens. Stool specimens and perianal tapes were examined by the Microbiology Department of Marmara University.

Classification of Allergic Manifestations

The participant was defined as (1) ever wheezer, (2) current wheezer, (3) doctor-diagnosed asthma, (4) ever rhinitis, and (5) current rhinitis if the answer was yes to the following questions from the ISAAC:

1. Have you ever had wheezing or whistling in the chest at any time in the past?
2. Have you had wheezing or whistling in the chest in the past 12 months?
3. Have you ever had asthma?
4. Have you ever had a problem with sneezing or a runny or blocked nose when you did not have a cold or the flu?
5. In the past 12 months, have you ever had a problem with sneezing or a runny or blocked nose when you did not have a cold or the flu?

Also, subjects with one or more positive reaction on SPT were considered as SPT⁺ or atopic.

Statistical Analysis

Statistical analyses were performed by the Statistical Package for the Social Sciences (SPSS) program (release 10.0; SPSS, Inc., Chicago, IL). Differences between groups were tested for significance with the chi-square test, *t*-test, and Mann-Whitney *U* test. Risk factors with a value of $p < 0.20$ in univariate analyses were included as a covariable in logistic regression analyses. A value of $p < 0.05$ was considered significant.

RESULTS

A total of 1018 children (48% girls and 52% boys; mean $\pm$ SD, aged 7.9 ± 2.6 years) were identified and participated in the survey. Because there are no reliable census data on the number of children living in Sultanciftligi, the precise response rate is not known, but anecdotally there were few refusals. Questionnaire information was obtained from parents of all participants. Of these, 1007 children (98.9%) were skin-prick tested, and blood was drawn from 955 children (93.8%) for total IgE measurements. Perianal tapes and stool specimens were obtained from 1004 (98.6%) and 997 (98.1%) children, respectively.

According to the results of the ISAAC questionnaire, prevalence of ever-wheezing, rhinitis, current wheezing, and doctor-diagnosed asthma was 31, 26.2, 14.6, and 10.7%, respectively. A positive history of treatment for previous enterobiasis was present in 37%. The remaining characteristics obtained from the ISAAC and the additional questionnaires are summarized in Table 1. A positive perianal tape or stool examination was present in 49.1% (490/997) of subjects. The most common parasite was *E. vermicularis*, which was present in 23.3% of the cross-sectional sample, followed by *Blas-tocystis hominis* (22.4%) and *Giardia intestinalis* in 13%.

Table 1 Characteristics of 1018 children

Characteristic	
Age (mean $\pm$ SD; yr)	7.9 $\pm$ 2.6
Gender M/F (n)	529/489
Ever wheezing (%)	31.0
Current wheezing (%)	14.6
Doctor-diagnosed asthma (%)	10.7
Rhinitis (%)	26.2
Current rhinitis symptoms (%)	23.9
Maternal atopy (%)	19.8
Paternal atopy (%)	13.5
Sibling atopy (%)	31.1
Siblings >2 (%)	54.4
Birth order ≤ 1 (%)	37.3
Income ≤ 150 euros/mon (%)	61.7
Maternal education ≤ 5 yrs (%)	91.0
Paternal education ≤ 5 yrs (%)	80.3
SPT Positivity (%)	8.1
Sensitivity to HDM (%)	6.2
Previous <i>Enterobius</i> infection (%)	37.0
Total IgE (median, range)	81.2 (2.9–5376)

Entamoeba coli, *Entamoeba histolytica*, *Hymenolepis nana*, *A. lumbricoides*, and *Trichuris trichiura* occurred in 2.2, 1.7, 0.3, 0.1, and 0.1% of the samples, respectively.

Association between Current Parasitic Infections and Allergic Manifestations

Children with and without intestinal parasites had the same frequency of allergic manifestations including ever/current wheezing, ever/current rhinitis, doctor-diagnosed asthma, and SPT positivity, but serum total IgE was significantly higher in children with intestinal parasites ($p = 0.001$; positive versus negative, median [range], 97.3 [2.9–5376 IU/mL] versus 69.2 [3.9–4789 IU/mL]). Furthermore, frequency of allergic manifestations and of SPT positivity did not associate with positive tests for *E. vermicularis*, *B. hominis*, and *G. intestinalis*. However, total IgE levels were significantly higher in groups positive for *E. vermicularis* ($p = 0.018$) and *Giardia* ($p = 0.02$) compared with children who tested negative (data not shown). Also, there was no significant difference in any of the manifestations compared between those with a positive and negative stool examination for *B. hominis* (data not shown).

Association between previous *Enterobius* Infection and Allergic Manifestations

Children with a history of treatment for previous enterobiasis were more likely to have current wheezing (59% versus 44%, respectively; $p = 0.012$), ever rhinitis (31.8% versus 23.2%, respectively; $p = 0.005$), and current symptoms of rhinitis (28% versus 21.2%,

Table 2 Comparison of risk factors of subjects with and without ever and current wheezing

Risk Factors	Ever Wheezing			Current Wheezing		
	Positive (n = 314)	Negative (n = 694)	OR (95% CI)	Positive (n = 148)	Negative (n = 844)	OR (95% CI)
Age (%)	30.3	69.7	1.1 (0.8–1.5)	56.5	43.5	1.4 (0.9–2.3)
	32.9	28.7		48.0	52.0	
Male gender (%)	55.1	50.9	1.2 (0.9–1.6)	56.0	54.9	1.1 (0.7–1.7)
Number of siblings (%)	34.4	65.7	1.3 (1.0–1.8)*	49.6	50.4	0.9 (0.6–1.5)
	28.3	71.7		51.8	48.2	
Birth order (%)	32.5		1.1 (0.8–1.5)	43.6	56.4	0.7 (0.4–1.1)
				54.2	45.8	
Maternal atopy (%)	29.3	15.6	2.3 (1.6–3.1)*	31.7	27.8	1.2 (0.7–2.0)
Paternal atopy (%)	19.6	10.7	2.0 (1.4–3.0)*	20.6	18.8	1.1 (0.7–2.0)
Sibling atopy (%)	41.1	26.7	1.9 (1.4–2.3)*	46.4	35.8	1.6 (0.9–2.5)
Maternal smoking (%)	23.6	18.2	1.4 (1.0–1.9)*	25.0	22.4	1.2 (0.7–1.7)
Paternal education (%)	30.7	69.3	0.9 (0.6–1.3)	50.6	49.4	1.1 (0.6–1.8)
	32.8	67.2		50.0	50.0	
Maternal education (%)	30.6	69.4	0.8 (0.5–1.3)	50.0	50.0	0.8 (0.4–1.8)
	35.6	64.4		55.0	45.0	
Paternal employment (%)	29.0	71.0	0.8 (0.6–1.1)	50.0	50.0	0.9 (0.6–1.5)
	32.9	67.1		50.6	49.3	
Maternal employment (%)	30.9	69.1	0.9 (0.4–1.9)	49.3	50.7	0.1 (0.1–0.9)*
	34.5	65.5		88.9	11.1	
Income (%)	33.0	67.0	1.3 (1.0–1.7)	53.0	47.0	1.3 (0.8–2.1)
	27.6	91.5		46.5	53.5	
SPT positivity (%)	11.9	6.4	2.0 (1.3–3.1)*	14.3	11.2	1.3 (0.7–2.6)
Sensitization to HDM (%)	9.3	4.8	2.0 (1.2–3.4)*	11.6	8.5	1.4 (0.7–3.1)
Total IgE (median)	76 (4.9–4452)	82 (2.9–5376)		81 (5.6–3150)	71 (5.6–4452)	
Parasite (+) (%)	45.4	50.7	0.8 (0.6–1.0)	47.9	44.9	1.1 (0.7–1.8)
<i>Enterobius</i> (+) (%)	21.0	24.4	0.8 (0.6–1.1)	21.8	20.0	1.1 (0.6–1.9)
<i>B. hominis</i> (+) (%)	21.4	22.9	0.9 (0.6–1.3)	25.0	19.6	1.4 (0.8–2.4)
<i>G. intestinalis</i> (+) (%)	11.2	13.4	0.8 (0.5–1.2)	12.5	10.8	1.2 (0.6–2.4)
Previous hx. enterobiasis (%)	42.0	35.0	1.3 (1.0–1.8)*	50.0	30.0	1.8 (1.1–2.9)*

* $p < 0.05$, chi-square test.

Table 3 Comparison of risk factors of subjects with and without asthma and SPT positivity

Risk Factors	Asthma			SPT Positivity		
	Positive (<i>n</i> = 108)	Negative (<i>n</i> = 899)	OR (95% CI)	Positive (<i>n</i> = 82)	Negative (<i>n</i> = 925)	OR (95% CI)
Age (%)						
≤5 yr	12.9	87.1	1.4 (0.9–2.1)	9.5	90.5	1.3 (0.8–2.1)
>5 yr	9.8	90.2		7.6	92.4	
Male gender (%)	55.6	51.7	1.2 (0.8–1.7)	56.1	51.1	1.2 (0.8–1.9)
Number of siblings (%)	13.5	86.5	1.7 (1.1–2.6)*	10.6	89.4	1.8 (1.4–2.8)*
≤2	8.4	91.6		6.2	93.8	
>2	6.8	93.2	1.2 (0.8–1.8)	8.0	92.0	0.9 (0.6–1.5)
Birth order (%)	10.1	89.9		8.4	91.6	
≤1	33.3	18.0	2.3 (1.5–3.5)*	19.5	20.0	0.9 (0.6–1.7)
>1	16.8	12.8	1.4 (0.8–2.4)	9.8	13.9	0.7 (0.3–1.4)
Maternal atopy (%)	48.0	29.0	2.3 (1.5–3.4)*	41.9	30.1	1.7 (1.0–2.7)*
Paternal atopy (%)	21.5	19.7	1.1 (0.7–1.8)	28.1	19.1	1.7 (0.9–2.8)*
Sibling atopy (%)	26.0	74.0	0.9 (0.7–1.4)	8.4	91.6	1.2 (0.7–2.3)
Maternal smoking (%)	27.0	73.0		6.9	93.1	
Paternal smoking (%)	26.0	74.0	0.8 (0.5–1.4)	7.6	92.4	0.5 (0.3–0.9)*
Maternal education (%)	29.5	70.5		14.0	86.0	
≤5 yr	26.0	74.0	0.9 (0.8–1.3)	8.0	92.0	0.9 (0.6–1.5)
>5 yr	26.2	73.8		8.3	91.7	
Paternal employment (%)	26.3	73.7	0.9 (0.4–2.1)	8.0	92.0	0.5 (0.2–1.6)
Housewife	27.6	72.4		13.8	86.2	
Regular job	11.4	88.6	1.2 (0.8–1.8)	7.7	92.3	0.9 (0.5–1.4)
≤150 euros/mon	9.7	90.3		8.9	91.1	
>150 euros/mon	15.7	7.2	2.4 (1.3–4.3)*			
SPT positivity (%)	13.9	5.2	2.9 (1.6–5.5)*			
Sensitization to HDM (%)	72 (5.8–1243)	81 (2.9–5376)		144.5 (2.9–3250)	77.9 (3.9–5376)*	
Total IgE (median)	43.9	49.5	0.8 (0.6–1.3)	50.6	48.9	1.1 (0.7–1.7)
Parasite (+) (%)	19.6	23.7	0.8 (0.5–1.3)	22.2	23.3	0.9 (0.5–1.6)
<i>Enterobius</i> (+) (%)	22.2	22.5	0.9 (0.6–1.6)	25.9	22.0	1.3 (0.7–2.1)
<i>B. hominis</i> (+) (%)	13.5	12.9	1.1 (0.6–1.9)	13.6	12.7	1.1 (0.6–2.1)
<i>G. intestinalis</i> (+) (%)	38.9	36.5	1.1 (0.7–1.7)	41.5	34.2	1.2 (0.8–1.9)
Previous hx. enterobiasis (%)						

**p* < 0.05, *chi-square test*.

Table 4 Logistic regression analysis of risk factors associated with current wheezing

Current Wheezing	OR	95% CI
Age (≤ 5 yr)	1.751	1.017–3.014
Sibling hx of atopy	1.359	0.812–2.276
Maternal employment (housewife)	0.123	0.014–1.061
Birth order (≤ 1)	0.575	0.336–0.982
Previous enterobiasis	2.164	1.298–3.608

Bold indicates values that are statistically significant.

respectively; $p = 0.010$) and had significantly higher total IgE levels (median [range], 90.7 [5.2–5376 IU/mL] IU/mL versus 74.3 [2.9–4452 IU/mL] IU/mL; $p = 0.017$). On the other hand, no significant difference was detected in the comparison of SPT positivity (9.2% versus 7.6%, respectively), doctor-diagnosed asthma, and ever wheezing of subjects with and without a history of previous enterobiasis.

Association between Allergic Manifestations and Risk Factors

Wheezing, Asthma, and Atopy. Univariate comparisons of subjects with and without ever wheezing, current wheezing, doctor-diagnosed asthma, and SPT positivity are presented in Tables 2 and 3. Risk factors with a value of $p < 0.20$ in univariate analyses were included as covariables in logistic regression analyses. Covariables included in this model for each analysis were as follows: age (≤ 5 years and > 5 years), sibling history of atopy, birth order (≤ 1 and > 1), history of previous enterobiasis, and maternal employment status (housewife and regular job) for current wheezing; sibling/maternal/paternal history of atopy, number of siblings (≤ 2 and > 2), maternal smoking, history of previous treatment for enterobiasis, SPT positivity, sensitivity to house-dust mites (HDMs), current parasitosis, paternal employment status (no regular job and regular job), and income (≤ 150 euro/month and > 150 euro/month) for ever wheezing; and sibling/maternal history of atopy, SPT positivity, sensitivity to HDMs and paternal education for doctor-diagnosed asthma and finally sibling history of atopy, maternal smoking and education level, number of siblings and log IgE for SPT positivity.

Ever wheezing was positively associated with maternal (OR [95% CI], 1.65 [1.15–2.37]; $p = 0.007$), paternal (OR [95% CI], 1.77 [1.17–2.69]; $p = 0.007$), and sibling (OR [95% CI], 1.65 [1.20–2.26]; $p = 0.002$) history of atopy, and having ≤ 2 siblings (OR [95% CI], 1.53 [1.14–2.08]; $p = 0.005$) in logistic regression analysis (data not shown). Covariables that were significantly positively related with current wheezing were previ-

ous treatment for enterobiasis ($p = 0.003$) and being ≤ 5 years of age ($p = 0.043$), whereas being the first child of the family ($p = 0.043$) was negatively related (Table 4).

Doctor-diagnosed asthma was positively associated with sibling history (OR [95% CI], 1.83 [1.10–3.04]; $p = .001$) of atopy and negatively associated with a lower paternal employment level (OR [95% CI], 0.60 [0.39–0.93]; $p = 0.022$); meanwhile, sibling history of atopy (OR [95% CI], 1.83 [1.10–3.04]; $p = 0.02$), having ≤ 2 siblings (OR [95% CI], 1.68 [1.0–2.81]; $p = 0.048$) and log IgE level (OR [95% CI], 2.09 [1.37–3.19]) were the covariables significantly associated with SPT positivity in logistic regression analysis (data not shown).

Rhinitis

Univariate comparisons of children with and without ever and current rhinitis are presented in Table 5. Covariables included in logistic regression analyses were gender, sibling/maternal/paternal history of atopy, maternal/paternal smoking, history of treatment for enterobiasis, SPT positivity, sensitivity to HDMs, maternal education, and income for current rhinitis, and gender, sibling/maternal/paternal history of atopy, maternal smoking, income, history of a previous treatment for enterobiasis, SPT positivity, and current parasitosis for rhinitis.

Regression analysis of risk factors significantly associated with ever rhinitis were sibling history of atopy (OR [95% CI], 1.73 [1.25–2.38]; $p = 0.001$), maternal smoking (OR [95% CI], 1.81 [1.26–2.59]; $p = 0.001$), and male gender (OR [95% CI], 1.51 [1.11–2.05]; $p = 0.009$). Covariables associated with current rhinitis were maternal (OR [95% CI], 1.51 [1.03–2.23]), paternal (OR [95% CI], 1.72 [1.11–2.67]), and sibling history (OR [95% CI], 1.64 [1.18–2.29]), of atopy ($p = 0.030$, $p = 0.010$, and $p = 0.003$, respectively); maternal smoking (OR [95% CI], 1.73 [1.19–2.52]; $p = 0.004$); and male gender (OR [95% CI], 1.44 [1.05–1.98]; $p = 0.024$; data not shown).

DISCUSSION

This study evaluated the association between allergy-related phenomena and parasitic infections in 1018 children, aged between 4 and 12 years living in poor hygienic conditions. The prevalence rates of doctor-diagnosed asthma, rhinitis, and ever wheezing were found to be 10.7, 26.2, and 31%. A parasitologic evaluation was present in 49.1% of subjects; *E. vermicularis*, *B. hominis*, and *G. intestinalis* were the predominant parasites. In addition, a history of treatment for enterobiasis was obtained in 37% of all participating children. In univariate analyses treatment for previous enterobiasis was shown to be more frequent in subjects with ever and current wheezing and rhinitis. Further evaluation of the risk factors by multivariate analyses

Table 5 Comparison of risk factors of subjects with and without ever and current rhinitis

Risk Factors	Current Rhinitis			Ever Rhinitis		
	Positive (n = 239)	Negative (n = 763)	OR (95% CI)	Positive (n = 265)	Negative (n = 746)	OR (95% CI)
Age (%)	24.0	76.0	1.1 (0.7–1.4)	25.5	74.5	0.9 (0.7–1.3)
Male gender (%)	23.7	76.3		26.5	73.5	
Number of siblings (%)	58.6	50.1	1.4 (1.1–1.9)*	59.3	50.0	1.5 (1.1–2.0)*
	24.4	75.6	1.1 (0.8–1.4)	27.0	73.0	1.1 (0.8–1.4)
Birth order (%)	23.1	76.9		25.5	74.5	
	24.0	76.0	1.1 (0.8–1.4)	26.2	73.8	0.9 (0.7–1.3)
	23.6	76.4		26.2	73.8	
Maternal atopy (%)	28.9	16.9	2.0 (1.4–2.8)*	27.7	17.0	1.9 (1.3–2.6)*
Paternal atopy (%)	20.9	11.2	2.1 (1.4–3.0)*	19.3	11.3	1.9 (1.3–2.8)*
Sibling atopy (%)	43.5	27.0	2.1 (1.5–2.8)*	43.8	26.5	2.2 (1.6–2.9)*
Maternal smoking (%)	28.4	17.3	1.9 (1.4–2.7)*	28.1	16.9	1.9 (1.4–2.7)*
Paternal education (%)	23.8	76.2	0.9 (0.7–1.4)	10.3	89.7	0.8 (0.5–1.3)
	23.4	76.6		12.8	87.2	
Maternal education (%)	23.4	76.6	0.7 (0.4–1.2)	10.6	89.4	0.9 (0.5–1.8)
	13.9	86.1		11.5	88.5	
Paternal employment (%)	23.2	76.8	0.9 (0.7–1.3)	8.5	91.5	0.6 (0.4–0.9)*
	24.4	75.6		13.0	87.0	
Maternal employment (%)	23.7	76.3	0.7 (0.3–1.5)	10.6	89.4	0.7 (0.2–2.8)
	31.0	69.0		14.3	85.7	
Income (%)	25.4	74.6	1.3 (0.9–1.7)	28.2	71.8	1.3 (0.9–1.8)*
	21.1	77.9		22.7	77.3	
SPT positivity (%)	11.4	7.3	1.6 (1.0–2.7)*	10.7	7.3	1.5 (0.9–2.5)
Sensitization to HDM (%)	8.1	5.7	1.5 (0.8–2.5)	7.3	5.8	1.3 (0.7–2.2)
Total IgE (median)	71 (2.9–4452)	84 (4.4–5376)		74.8 (2.9–4452)	82.9 (3.9–5376)	
Parasite (+) (%)	51.9	48.5	1.2 (0.9–1.5)	53.1	47.8	1.2 (0.9–1.6)
<i>Enterobius</i> (+) (%)	22.1	23.7	0.9 (0.6–1.3)	24.2	23.0	1.1 (0.8–1.5)
<i>B. hominis</i> (+) (%)	22.3	22.4	0.9 (0.7–1.4)	22.1	22.5	1.0 (0.7–1.4)
<i>G. intestinalis</i> (+) (%)	15.5	12.3	1.3 (0.9–2.0)	14.3	12.6	1.2 (0.8–1.8)
Previous hx. enterobiasis (%)	44.0	35.0	1.5 (1.1–2.0)*	44.1	34.0	1.5 (1.1–2.0)*

* $p < 0.05$, *chi-square test*.

revealed that previous treatment for enterobiasis was significantly associated with current wheezing. Although parental reporting of treatment for previous enterobiasis may be a flaw of this study, the report of direct observation of pinworms by parents strengthens the reliability.

In this study, allergic manifestations including ever wheezing, doctor-diagnosed asthma, ever rhinitis, and current rhinitis were determined according to parental responses to the ISAAC questionnaire and atopic status according to SPT positivity. Although univariate analyses revealed that history of a treatment for previous enterobiasis was significantly more frequent in ever/current wheezers and those with ever and current rhinitis symptoms, no association with asthma and SPT positivity, which account for the most valid variables of allergic manifestations, could be established. After analyzing by logistic regression analyses, among the allergic manifestations only current wheezing was significantly associated with previous enterobiasis.

In previous studies evaluating the association between parasitic infections and allergy, helminthic infections such as *A. lumbricoides*^{4,10} and *S. hematobium*¹¹ were shown to be negatively associated with atopy. On the other hand, in another study *Toxocara* seropositivity was shown to be positively related with allergen-specific IgE response.¹² It also was shown that infection with *A. lumbricoides* augmented atopy, asthma, and allergic reactivity.¹³

To our knowledge, there are a limited number of studies evaluating the effect of *Enterobius* infection on development of atopy. In a recent study of Huang *et al.*,²⁶ the prevalence of doctor-diagnosed asthma and allergic rhinitis was significantly lower in children currently infected with *E. vermicularis*. Furthermore, current enterobiasis was negatively associated with current asthma and rhinitis. This study also evaluated the effect of previous enterobiasis on development of allergic manifestations after 7 years of age. Those with enterobiasis at or before grade 1 were less likely to have a diagnosis of allergic rhinitis at 7 years of age, compared with the uninfected group. Meanwhile, in another study conducted by Herrstrom *et al.* the association between *E. vermicularis* and allergic disease in 4- to 10-year-old Swedish children was evaluated. Infestation with *E. vermicularis* was found significantly higher (37%) in those children with SPT positivity, compared with the nonallergic control group (23%).²⁷

On the other hand, in our study frequencies of asthma, SPT positivity, and ever and current rhinitis/wheezing were similar in those subjects with and without current enterobiasis, but current wheezing and rhinitis were found to be significantly more in those subjects with a history of treatment for previous enterobiasis. Moreover, current wheezing was significantly

associated with a history of treatment for previous enterobiasis in logistic regression analysis.

The population included in our study consisted of a group of children living in poor hygienic and low-standard housing conditions whereas the population included in the study of Huang²⁶ and Herrstrom²⁷ lived in a city with a lifestyle similar to Western societies. The contradictory effect of enterobiasis on the development of allergy in different regions indicates that this effect has to be considered in the context of other risk factors such as atopic status, genetic predisposition, other in-house environmental factors including number of siblings, allergen exposure, smoking status, etc. It is more likely that infections such as parasitosis before the establishment of allergic diseases would play a more important modulatory role than current infections.

On the other hand, in recent studies mild and sporadic helminthic infections were shown to augment reactivity to specific allergens and susceptibility to allergic disease.^{12,13,22-24} The intensity and chronicity of helminth infections are suggested to be important factors that may determine whether helminthes act as a risk factor or confer protection against allergic diseases.^{25,28}

In a previous study by Lynch *et al.* sporadic and light helminthic infections were shown to be associated with increased frequency of skin test reactivity and allergic diseases when compared with those with rare infections.²⁴ In another study, light helminthic infections were associated with the amplification of allergen-specific IgE responses and high skin reactivity, whereas heavily parasitized subjects were protected from atopic skin reactivity, despite a high degree of sensitization to mites.²⁹ This protective effect of parasites may be associated with the invasiveness of the organism. Because *E. vermicularis* is a noninvasive helminth with a life cycle restricted to the intestinal lumen, it can be speculated that long-term infestation with this helminth may be associated with increased frequency of allergic disease when compared with invasive helminths, which may confer protection against atopy. In our study population there was a strong correlation between previous and current enterobiasis (data not shown), which can be considered as long-term infestation with a noninvasive helminth. We have to acknowledge the weakness of our study with respect to the lack of criteria on the intensity of neither previous nor current enterobiasis.

In our study, although no association was shown between current enterobiasis and allergy, children infected previously were more likely to develop respiratory allergic diseases with ongoing symptoms. It can be hypothesized that being infected with *E. vermicularis* in early life is more likely to influence the progression to allergy, whereas a new infection in a child with already

established skin test reactivity and allergic disease is unlikely to have such an effect.

In conclusion, a previous infection with *E. vermicularis* was found to potentiate current wheezing in a population living in poor hygienic conditions. This questions the ameliorating effect of poor hygiene on the development of atopy. Extremely poor hygienic conditions could not be beneficial, but detrimental in this respect. The immunologic mechanisms and accompanying risk factors underlying the impact of enterobiasis on the development of allergic disorders in different geographical regions remains to be studied. To date, studies evaluating these associations have been conducted cross-sectionally or retrospectively. Prospectively designed studies evaluating the impact of early enterobiasis on the development of allergic manifestations in children are warranted.

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