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Original Article

Total serum IgE levels in soil-transmitted helminth infected children with atopy symptoms

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Abstract

Background High total serum immunoglobulin E (IgE) levels and eosinophilia are markers for atopy, but other factors may also play a key role in affecting atopy, such as intestinal parasitic infection. Helminthiasis has been associated with a reduced risk of atopy and asthma symptoms in areas with high prevalence of parasitic infections.

Objective To assess for associations between total serum IgE level and soil-transmitted helminthiasis (STH) infection, as well as between STH infection and allergy symptoms.

Methods We conducted a cross-sectional study on 84 consecutively-enrolled children, aged 7–13 years, in the Secanggang Subdistrict, Langkat District, North Sumatera Province. Subjects were enrolled into one of two groups, with or without STH infection. Total serum IgE measurements and stool STH examinations were performed in all subjects. Data on atopy or allergy symptoms were obtained by parental interview.

Results The 42 subjects with STH infection had significantly higher mean total serum Ig E levels than the 42 subjects without infection, 1,131.26 IU/mL and 744.76 IU/mL, respectively (P=0.029). We also found significant positive associations between STH infection and asthma symptoms (P=0.049), as well as eczema symptoms (P=0.044).

Conclusion Mean total serum IgE level is higher in STH-infected subjects than in those without infection. In addition, STH infection is positively associated with asthma and eczema symptoms. **[Paediatr Indones. 2014;54:149-54.]**.

Keywords: *total serum IgE, soil-transmitted helminth infection, atopy, children*

Soil-transmitted helminths (STH) are included in a list of the world's neglected tropical diseases. Soil-transmitted helminths or geohelminths, include the roundworm *Ascaris lumbricoides,* the whipworm *Trichuris trichiura,* the hookworms *Ancylostoma duodenale*, *Necator americanus,* and *Strongyloides stercoralis.*[1-4] The greatest numbers of STH infections occur in the tropical and subtropical regions of Asia, especially China, India, and Southeast Asia, as well as Sub-Saharan Africa.[5] Soil-transmitted helminths causes human infection through contact with parasite eggs or larvae that thrive in warm and moist soil. Adult worms may live for years in the human gastrointestinal tract.[3] Epidemiological studies conducted throughout developing countries point to school-aged children as the population at greatest risk for heavy infection of Ascaris and Trichuris.[5] In 1995, STH infection prevalence in the North Sumatera Province was 57- 90%.[6] Prevalences based on species infected were 46-75% for ascariasis, 65% for trichuriasis, and 20% for hookworms.[7] The capacity for common

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environmental allergens to stimulate IgE responses and lead to allergic disease has tended to overshadow the fact that helminthic parasites are possibly the most potent inducers of this immunoglobulin. Although there is some debate regarding the relationship between helminthic infection and the IgE response, there is evidence that the IgE antibody is an important component of immune protection against these parasites.[8] It has been proposed that education of the immune system by certain microbes and parasites can prevent the development of inflammatory diseases. Reduced infections due to improved health care and personal hygiene as well as decreased exposure to microorganisms and their products may lead to insufficient stimulation of the immune system.[9]

The similarities between the immune response against helminthic parasites and IgE-mediated allergic diseases had led to discussions about the relationship between parasites and allergy. There are five possible relationships: (1) worms are protective, (2) worms cause allergies, (3) people with allergies are more resistant to worms, (4) people with allergies are more susceptible to worms, or (5) there is no causal relationship.[10]

The aim of this study was to assess for associations between total serum IgE level and soil-transmitted helminthiasis (STH) infection, as well as between STH infection and allergy symptoms.

Methods

We conducted a cross-sectional study from August to September 2009 at two primary schools in Secanggang, North Sumatera. We performed stool examinations by the Kato-Katz thick smear technique[11,12] to assess for the presence and severity of STH infection in 183 students, aged 7-13 years with written parental consent. Children undergoing steroid therapy or with bleeding diathesis were excluded.

Subjects were divided into two groups: the helminthiasis and non-helminthiasis groups. Based on the formula for minimum required sample size, we consecutively selected 42 subjects for each group. Subjects of both groups underwent measurements of total serum IgE levels using 2 mL of venous blood specimens. Data on atopic or allergy symptoms were obtained by interviewing parents. Children with STH infection based on stool examination results were treated with a single dose of 400 mg albendazole. This study was approved by Ethics Committee of the University of North Sumatera Medical School.

To identify the presence of STH infection we used Kato-Katz methods for stool examination. Eggs per gram (EPG) were determined by calculating the number of eggs found in all microscopic slide fields, then multiplying by 24. Subjects were classified into categories of infection type, single species or mixed infection, as well as infection severity: mild, moderate, or severe infection. The 1987 World Health Organization (WHO) Expert Committee criteria were used to classify the severity of *A. lumbricoides* and *T. trichiura* infection. For *A. lumbricoides*, the criteria were 1-4,999 EPG for mild infection, 5,000-49,999 EPG for moderate infection, and ≥50,000 EPG for severe infection. For *T. trichiura* the criteria were 1-999 EPG for mild infection, 1,000-9,999 EPG for moderate infection, and ≥10,000 EPG for severe infection.[13] Total serum IgE levels were determined by *VIDAS®* (bioMérieux, France), an enzyme-linked fluorescence immunoassay (ELFA), with a normal value of <200 IU/mL for children <15 years of age.

The collected data was processed, analyzed, and presented by SPSS version 15.0. Independent T-test was used to compare mean values of total serum IgE levels between the helminthiasis and non-helminthiasis groups. ANOVA was used to analyze mean total serum IgE levels among the categories of infection type and severity. Chi square test was used to assess for an association between STH infection and atopic or allergy symptoms with a significance level of $P < 0.05$.

Results

We examined stool specimens from 183 children, 114 of whom suffered from ascariasis and/or trichuriasis. None were infected with *N. americanus* or *S. stercoralis*. We enrolled and assigned subjects to one of two groups, the helminthiasis or non-helminthiasis groups of 42 children each. Total serum IgE level measurements were performed for both groups. **Table 1** shows the demographic characteristics of subjects.

Table 1 shows that malnutrition was more common in subjects with STH infection than those without infection.

Figure 1 shows that 57.1% of STH infections in the study subjects were mixed infections of *A. lumbricoides* and *T. trichiura*. In addition, half of the subjects in the helminthiasis group had severe infections.

Mean total serum IgE was significantly higher in the helminthiasis group than in the non-helminthiasis group (P= 0.029) (**Table 2**).

Table 3 shows that there was no significant difference in mean total serum IgE levels between

Table 1. Characteristics of subjects

Characteristics	Helminthiasis group	Non-helminthiasis group
Mean age (SD) , years	10.3 (1.54)	10.3 (1.54)
Gender, n (%)		
Male	16 (38.1)	18 (42.9)
Female	26 (61.9)	24 (57.1)
Nutritional status, n (%)		
Normal	22 (52.4)	32 (76.2)
Mild to moderate malnutrition	19 (45.2)	9 (21.4)
Severe malnutrition	1 (2.4)	1 (2.4)
Helminth species, n		
A. lumbricoides	42	-
T. trichiura	18	-

Table 2. Distribution of atopy symptoms and total serum IgE levels

Variables	Helminthiasis group n=42	Non-helminthiasis group n=42	P value
Atopy symptoms	27	18	0.049
Asthma, n			
Allergic rhinitis, n	36	35	0.763
Atopic dermatitis/eczema, n	21	12	0.044
Mean total serum IgE (SD), IU/mL	1,131.3 (891,2)	744,8 (692,1)	0.029

Table 3. Distribution of total serum IgE levels based on infection type and severity

Variables	Mean total serum IgE(SD) IU/mL	P value
Type of infection		0.380
T. trichiura infection only	967.1 (994.3)	
A. lumbricoides and *T. trichiura*	1,222.5 (834.2)	
Severity of infection *		0.280
Mild	1,039.9 (1,022.6)	
Moderate	1,003.4 (772.5)	
Severe	2,500.0	

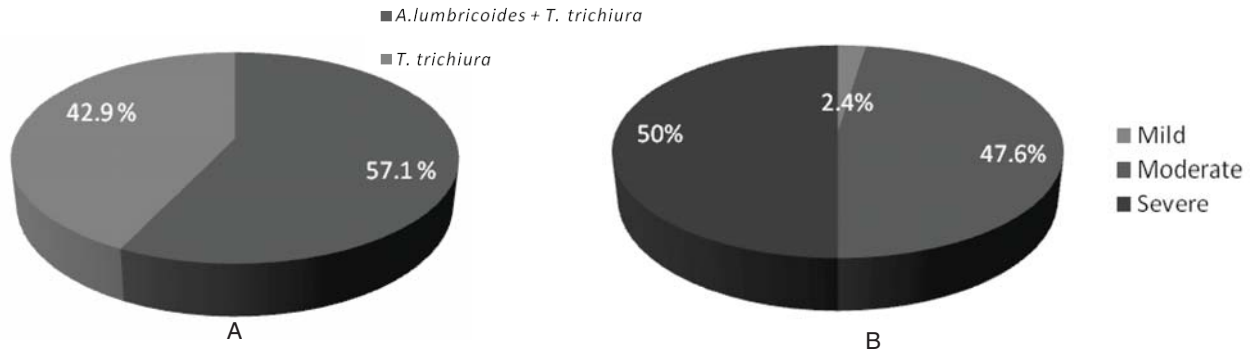

Figure 1. Distribution of (A) infection type and (B) infection severity

the single species infection (*T. trichiura)* and mixed infection, although total serum IgE levels were higher in children with mixed infection. Also there was no significant difference in mean total serum IgE levels among categories of infection severity, although the highest mean level was found in children with severe infection.

Discussion

Our study compared total serum IgE levels between an STH-infected or helminthiasis children (42 subjects) and uninfected or non-helminthiasis children (42 subjects), and analyzed the presence of symptoms of atopy or allergic disease (eczema, allergic rhinitis, and asthma) associated with STH infection.

There was a significant difference in mean total serum IgE levels between the helminthiasis and non-helminthiasis groups, 1,131.26 IU/mL vs. 744.76 IU/mL, respectively (P=0.029). Children living in STH-endemic areas often have total IgE levels in excess of 10,000 IU/mL. The production of large amounts of polyclonal IgE during helminthiasis is thought to modulate immediate hypersensitivity reactions by inhibiting mast cell activity by saturation of the high affinity IgE receptor, also known as Fc epsilon RI (FcεRI), on mast cells and basophils.[14] A pediatric study demonstrated that IgE levels ranged from 40-5,000 IU/mL in 20 children with mild *A. lumbricoides* infection, 141-5,000 IU/mL in 20 children with chronic *A .lumbricoides* infection, and 60-975 IU/mL in children without *A .lumbricoides* infection.[15] Study on relationship between *A. lumbricoides* infection and atopic asthma in children from asthmatic families living in rural China showed IgE levels that ranged from 2.0 to 10,137.5 IU/mL, and there was relationship between positive stool examinations for *A. lumbricoides* and total IgE levels.[16]

Helminth antigens are potent inducers of IgE production and can stimulate IgE responses in almost all individuals.[17,18] Despite increased IgE level along with continuous exposure to helminth parasites, the role of IgE in an anti-helminth protective immune response is not fully understood.[17] People living in STH-endemic areas tend to have high levels of polyclonal IgE, due to chronic helminth exposure. It has been suggested that high levels of polyclonal IgE are a helminth defense mechanism against the effects of anti-parasite IgE. Nonspecific IgE may saturate FcεRI receptors on basophils and mast cells, preventing antigen triggering of mast cell degranulation.[18]

We found that 27/42 children in the helminthiasis group and 18/42 children in the non-helminthiasis group had asthma symptoms. As such, Chi square test revealed a significant positive association between STH infection and asthma symptoms (P=0.049). A Costa Rican study reported an association between sensitization to *A. lumbricoides* and asthma severity (airway hyperresponsiveness and hospitalization caused by asthma) (OR = 3.08; 95% CI 1.23 to 7.68; P=0.02).[19] Another study on school-aged children in Taipei reported a negative association between *Enterobius* infestation and asthma and rhinitis, which could in part be attributed to a protective effect of pinworm infestation on development of allergic symptoms.[20] In addition, a study in rural China reported an association between *A. lumbricoides* infection and increased risk of childhood asthma and atopy (OR = 1.85; 95%CI 1.37 to 2.49; P <0.001).[16] A South Brazil study on 1,982 children showed that helminth infection can simultaneously induce airway-related symptoms and attenuate atopic disease.[21] All STH parasites with a pulmonary phase of larval migration are capable of causing an asthma-like syndrome (Löeffler's syndrome), that is characterized by breathlessness, cough, and eosinophilia.[14] A study in Brazil on patients with high risk for intestinal helminth infection concluded that in patients with respiratory allergy and increased total serum IgE levels, the quantification of anti-ascaris IgE can be more useful and more insightful than parasitological stool examinations.[22]

In our study, 36 children in the helminthiasis group and 35 children in the non-helminthiasis group had rhinitis symptoms. We found, however, no association between STH infection and rhinitis symptoms (P=0.763). A questionnaire-based study on a pediatric population in Ecuador also reported no significant relationship of rhinoconjunctivitis symptoms to *A. lumbricoides* infection.[23] A cross-sectional study in Taiwan demonstrated that children with pinworm infection before or during first grade of primary school had lower risk for rhinitis diagnosis during school period compared to children without pinworm infection.[20] Nonetheless, questionnaire-

based studies for rhinitis symptoms in school-aged children could lead to mistakes in the classification of rhinitis symptoms. As such, in the future we need better epidemiological tools for more accurate identification.

We found that 21 children in the helminthiasis group and 12 children in the non-helminthiasis group had eczema/atopic dermatitis (P=0.044), but no significant association between STH infection and rhinitis symptoms (P=0.763). A population-based study of 4,169 East German children revealed an inverse association between *A. lumbricoides* infection and questionnaire-diagnosed eczema (adjusted OR=0.45; 95%CI 0.33 to 0.60).[24] A study on primary school children in Cuba reported that recent *A. lumbricoides* infection provided protection against atopic dermatitis, but past infections of pinworm and hookworm were risk factors for allergic rhinoconjunctivitis and/or atopic dermatitis.[25]

Various results among studies pointed to some factors that may involved in preventing atopy, such as intensity of infection, frequency of infection, timing of infection, and the species involved. There is the possibility that single, short term, and mild infections have stimulation effects, while frequent and severe infection suppress allergen responses.[9, 26]

In conclusion, total serum IgE levels are higher in children with STH infection than in uninfected children. Soil-transmitted helminth infection is associated with increased asthma and eczema symptoms, but it is not associated with allergic rhinitis.

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