

## Association of geohelminths infection and asthma in elementary school children in Kalibaru, North Jakarta

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### Abstract

**Background** Asthma inflammation process and geohelminth infection have the same immune response. Epidemiological studies in developed countries show the increased asthma prevalence and decreased geohelminth infection, while developing countries usually have low asthma prevalence but high geohelminth infection.

**Objectives** To determine asthma proportion in children with geohelminth infection and relationship between asthma and geohelminth prevalence of elementary school students in North Jakarta.

**Method** A cross sectional study was done in February 2009 at an Elementary School in North Jakarta. Asthma was diagnosed using ISAAC questionnaire which was answered by parents. We did fecal analysis using ether formaline test to establish geohelminth infection.

**Results** The proportion of students with asthma was 11.5% (33 of 286 children). Most of them were male, aged 6-10 years old, and well nourished. Geohelminth infection was found in 71.9% of the students. Most of children with geohelminth infection were male (55%), aged 6-10 years old (63%), and well nourished (64%). Proportion of asthma in children with and without geohelminth infection is 12.6% and 8.8%, respectively. Geohelminth infection consisted of ascariasis (80%), trichiuriasis (39%), and ankylostomiasis (9%). There was no significant relationship between asthma and geohelminth infection ( $P=0.357$ ), nor between asthma and ascariasis ( $P=0.202$ ), asthma and trichiuriasis ( $P=0.133$ ).

**Conclusions** The occurrence of asthma in children with geohelminth infection is 12.6% and there is no difference of asthma incidence among children with or without geohelminth infection. [Paediatr Indones. 2010;50:80-5].

**Keywords:** Asthma, geohelminth infection, ISAAC

Asthma is one of the most common chronic respiratory diseases in children.<sup>1</sup> The prevalence has been increasing in the last two decades, particularly in developed countries and urban areas which is suggested to be associated with various environmental factors.<sup>2</sup> Asthma results in negative impacts on patient's quality of life, such as frequent school absent as well as limitations in sports and overall daily living.<sup>1</sup> From 1975 to 1993, asthma morbidity in children aged 5-14 year old increased almost two folds.<sup>3</sup>

In developing countries, endemic helminthiasis remains as one of the main public health problems, among which ascariasis was the most common, affecting around 1.5 billion of people with prevalence around 36%.<sup>2-6</sup> The immune response elicited by allergic inflammation and helminthiasis shares common features, which are the elevation of IgE level, eosinophilia, mast cells, and dominant Th-2 response.<sup>2,3,7,8</sup> Epidemiologic studies in developed countries show that asthma is more prevalent compared to worm infections while different phenomenon occurs in developing countries in which asthma is relatively

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rare in the increase of worm infection. Those facts result in a hypothesis of inverse relationship between asthma and worm infection. However, there are still controversies regarding protective effect of worm infection on asthma development.<sup>2,5</sup> Some studies confirm the inverse relationship<sup>2,9</sup> showing lower prevalence of atopy in children with helminthiasis compared to those without (16.3% vs. 27%)<sup>10</sup> but some studies state that worm infections only associated with skin test reactivity but not with allergic symptoms.<sup>4,11</sup>

Although the prevalence of helminthiasis in Jakarta is variably high (36-90%)<sup>12</sup> and the occurrence of asthma is relatively low (1.6%-12.5%),<sup>13,14</sup> the presence of relationship between those two conditions in Jakarta remains unknown. The aims of this study were to assess the prevalence of asthma in children with helminthiasis and whether this was different from the prevalence of asthma in children without helminthiasis. In this study, asthma was assessed based on the ISAAC questionnaire<sup>15</sup> which had been proven to have moderate sensitivity (67.2%) and good specificity (92%).<sup>16,17</sup>

## Methods

This was a cross-sectional study carried out at the Kalibaru 06 Elementary School, North Jakarta in February 2009. Subjects were elementary school students in the the school which have high incidence of worm infection based on data from Kusuma Buana Foundation.

Sample size was calculated using the formula for estimating single population proportion<sup>18</sup> with  $\alpha=0.05$ , estimated prevalence of 12.5%, and accuracy of 5% revealing minimum sample size of 169 children. We included all students who did not consume any antihelminthic agents in the previous 1 month after parents gave informed consent, and excluded those with severe malnutrition or immunocompromised state.

After obtaining permission from the school principal, we performed history taking, physical examination and collected stool samples from every subjects. Parents were interviewed to answer the ISAAC questionnaires for establishing the diagnosis of asthma. Asthma was diagnosed if parents answered

“yes” to the following questions in the ISAAC questionnaire: “had you child experienced wheezing?” or “Did your child suffer from asthma?”.

Parasite stool analyses were performed in the Department of Parasitology, Medical School, University of Indonesia using formalin-ether concentration technique.<sup>19</sup> The presence of worm infections was defined if eggs were found in the stool specimen. Worm types were determined by the egg characteristics. Nutritional states were determined using ideal weight for height with weight for height 90% or above classified as well-nourished.<sup>20</sup>

Fisher’s exact or chi-square tests were used to evaluate the relation between asthma and worm infections. A P value of less than 0.05 was considered as statistically significant. Data was analyzed using SPSS software computer program version 15.0. This study was approved by the Ethics Committee Medical School University of Indonesia.

## Results

There were 330 children studied in the selected school, but only 303 children whose stool samples could be obtained. Among the 303 children, only 286 had the ISAAC questionnaires completely filled by their parents. Worm infection was positive in 218 (71.9%) children.

Subjects of this study consisted of 51.4% boys and 48.6% girls. Most subjects had age of 6-10 years old (66.1%), had good nutritional status (60.1%), 33 (11.5%) had asthma. See **Table 1**.

Among 303 subjects collecting stool samples, 218 (71.9%) were found to have worm infections, 54.6% were boys and the rest were girls. See **Table 1**. Details of the types of worms are presented in **Table 2**. Ascariasis was the most prominent worm infection in our study, followed by tricuriasis and ankylostomiasis. Most of the subjects were infected by single worm. Triple infection was found in only 6 students.

Out of 206 children with worm infections, 26 (12.6%) had asthma. There was no statistically significant difference in the occurrence of asthma between children having and not having worm infections. Asthma tended to be rarer in children without worm infection (**Table 3**). Based on the occurrence of ascariasis or trichuriasis, there was

**Table 1.** The proportion of asthma and worms in the study subjects

	Asthma		Worm	
	Yes 33 (11.5%)	No 253 (88.5%)	Positive 218 (71.9%)	Negative 85 (28.1%)
Sex				
• Male	23	124	119	37
• Female	10	129	99	48
Age				
• 6-10 years	25	164	138	52
• 11-14 years	8	89	80	33
Nutritional status				
• Undernourished	13	101	79	41
• Well-nourished	20	152	139	44

**Table 2.** Types of worm infection (n = 218)

Worm infections	N	%
Type of infections		
• Ascariasis	173/218	79.4
• Trichuriasis	85/218	38.9
• Ankylostomiasis	20/218	9.2
Amount of infections		
• Single infection	164/218	75.2
- Ascariasis	119/164	72.6
- Trichuriasis	35/164	21.3
- Ankylostomiasis	10/164	6.1
• Two infections	48/218	22.0
- Ascariasis – trichuriasis	44/48	91.7
- Ascariasis – ankylostomiasis	4/48	8.3
• Three infections	6/218	2.8

**Table 3.** The association between asthma and worm infections

	Asthma		Total	P value ( $\chi^2$ )
	Yes	No		
Worm infection				
• Yes	26	180	206	0.357
• No	7	73	80	
Ascariasis				
• Yes	23	147	170	0.202
• No	10	106	116	
Trichuriasis				
• Yes	6	78	84	0.133
• No	27	175	202	

also no significant difference in the prevalence of asthma.

There were some risk factors associated with asthma i.e., allergic history, number of household, smoker inside a house, and basic immunization. This study showed no significant relationship between asthma and those risk factors (data not shown).

## Discussion

This study shows the absence of association between worm infections and the occurrence of asthma in school-age children in North Jakarta. The use of ISAAC questionnaires could result in information bias although Riedler et al. found that it had the accuracy of 90% compared to objective measurements of bronchial hyperreactivity.<sup>21</sup> Praptiwi et al<sup>17</sup> found that the ISAAC questionnaire had moderately low sensitivity (67.2%) and high specificity (92%). The use of this questionnaire for establishing asthma diagnosis was one of the main limitation and could affect the results of this study. It would be better if asthma diagnosis was established based on the ISAAC questionnaire and spirometry evaluation.

Another limitation related to the study setting which was an elementary school with the highest heminthiasis prevalence located in a slum area in Jakarta. It meant that socioeconomic levels could be very homogenous and influence the results of this study considering hygiene hypothesis as one of factors influencing the occurrence of asthma.

The proportion of schoolage children with asthma was 11.5%, quite similar to the asthma prevalence in Jakarta which was found to be 12.5%<sup>14</sup> and higher than the overall prevalence in Indonesian children (1.6%).<sup>1</sup> Another studies using the ISAAC questionnaire and larger sample size found the prevalence of asthma of 3 to 6.7%, 3% in children aged 6-7 years and 5.2% in those aged 13-14 years.<sup>1</sup> The differences in prevalence might be caused by different diagnostic tools of asthma, subjects' characteristics, or sample size of a particular study.

Very high prevalence of worm infection was found in our series. The prevalence of worm infection in Jakarta was reported to be around 36-90%,<sup>12</sup> while no data was available regarding the prevalence of worm infection in children with asthma. We found ascariasis, trichuriasis, and ankylostomiasis in 79.4%, 38.9%, and 9.2% of subjects respectively. A previous study in 1994 carried out in an elementary school in North Jakarta reported the prevalence of ascariasis, trichuriasis, and ankylostomiasis of 58.9%, 78.9%, and 0.26% respectively.<sup>12</sup> The high prevalence of worm infection despite several eradication measures might be caused by environmental (warm temperature and high humidity) and host factors (poor hygiene).<sup>22</sup>

Previous studies evaluating the association between asthma and worm infection reported inconsistent results. Some studies revealed an inverse relationship between asthma and worm infection,<sup>9,12</sup> while other studies did not.<sup>21</sup> Moreover some studies reported that worm infection could increase asthma symptoms.<sup>2,23</sup> In area with prevalent worm infection, people with worm infection had improved asthma symptoms while for those living in areas with low helminthiasis prevalence, the asthma symptoms increased.<sup>22</sup> This study was performed in high helminthiasis prevalence and theoretically continuous and chronic transmission of worm infections could suppress the appearance of allergic diseases.<sup>4,6</sup>

This study found no statistically significant association between ascariasis and asthma; it was similar to studies by Cooper and Scrivener.<sup>12,21</sup> On the other side, a meta-analysis reported the association between asthma and ascariasis (OR 1.34; 95%CI 1.05-1.71)<sup>23</sup> which was similar to the results of Palmer's study (OR 1.85; 95%CI 1.37-2.49;  $P < 0.001$ ).<sup>2</sup> These different results could be due to the cross-sectional design used in our study that could not reflect chronic exposures of worm infections which cause down-regulation of the Th-2 immune response.

Trichuriasis did not have significant association with asthma. Leonardi-Bee stated that there was no association between asthma and worm infections, except for ascariasis and ankylostomiasis.<sup>23</sup> This was in accordance with Cooper's and Scrivener's studies that found no association between trichuriasis and asthma.<sup>12,24</sup>

In ascariasis and trichuriasis that occur in early age persisting until toddlers with high parasite count in

the body, the prevalence of atopic and allergic diseases were reported to be low.<sup>4,6,8</sup> Several mechanisms could be responsible for this phenomenon. First, polyclonal IgE produced by a host in response to worm infections will bind to mast cell Fc receptors preventing the binding of other allergen-specific IgE. The second mechanism was the blocking of IgG4 antibody and the suppression of anti-inflammatory cytokines.<sup>4,6</sup> This study found no association between worm infections and asthma prevalence that could be due to several aforementioned study limitations, such as information bias caused by the questionnaires and low educational level of the respondents. Information bias might cause higher prevalence of asthma reported by parents resulting in no association between asthma and overall or any specific worm infection. Other factors could confound the results of this study considering that asthma has multifactor etiologies, such as the number of households, exposure to allergen (cigarette smoke), and gastrointestinal infections.<sup>1</sup> We could not control those factors in this study.

The risk of developing allergic disease is higher if one of parents have allergy. Sundaru reported the strong association between asthma in parents and that in children.<sup>14</sup> Koning et al<sup>24</sup> also stated that if one of the parents had allergic diseases then the children would have 20-40% risk of developing allergic diseases and this risk increased to 60-80% if both parents had allergic diseases. In this study, we found the prevalence of asthma of 42.4% in subjects with family history of allergy and no statistically different asthma prevalence between subjects with and without family history of allergy.

Viral and bacterial infections more easily spread between household members. The infection in early age will trigger Th-1 and suppress Th-2 maturation so that allergic response does not develop.<sup>25-27</sup> In this study, we found asthma in 97% of subjects with household members of more than three people although the asthma prevalence was not significantly different compared to that of those with household members less than three. We did not count the ratio between the number of households and the house size, as well as their activities, to predict the interaction and possibility of disease transmission among family members. The result of our study was different with that of Pararajasingam et al<sup>28</sup> reporting lower prevalence of asthma in children with more than four

household members compared to that of those with less than four although the result was not statistically significant.

Active and passive exposure to cigarette smoke have been proven to increase airway disorders including asthma and rhinitis. In this study we found higher prevalence of asthma (67%) in subjects with any active smoker inside their houses compared to that of those without. It was similar to other study on children aged 3-5 years showing higher prevalence of asthma if the mothers or parents smoked.<sup>29</sup>

Immunization could prevent a child from getting disease causing limited response of Th-1. Immunization was considered as one of risk factors of allergic disease since decreased microbial antigen could disturb adaptive immune response because efficient activation of dendritic cells did not occur.<sup>30</sup> In this study, 39.3% of subjects with complete immunization according to their age had asthma, but no statistically significant different prevalence between children having complete and incomplete immunization. Immunization is not the only factor affecting the occurrence of asthma and this study did not account for previous infections as well as antibiotic usage that also could influence the prevalence of asthma. A previous study also reported no significant association between atopic diseases and immunization coverage.<sup>30</sup>

In conclusion, the prevalence of asthma in our population is 11.5%, the prevalence of worm infection is 71.9% and the prevalence of asthma in children with worm infections is 12.6%. There is no significant difference in the occurrence of asthma between children having or not having worm infections. We recommend further cohort studies with larger sample size and more objective diagnostic tools to evaluate the association between asthma and worm infections.

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