Original Article

Ascaris lumbricoides infection and parasite load are associated with asthma in children

Gerson Bragagnoli[1], Maria Teresa Nascimento Silva[2]

[1] *Unidade Acadêmica de Ciências da Saúde, Centro de Ciências Biológicas e da Saúde (CCBS), Universidade Federal de Campina Grande (UFCG), Paraíba, Brasil – Programa de Pós Graduação em Medicina e Saúde (PPgMS) – Universidade Federal da Bahia (UFBA), Salvador, Brasil*
[2] *Unidade Acadêmica de Ciências da Saúde, Centro de Ciências Biológicas e da Saúde (CCBS), Universidade Federal de Campina Grande (UFCG), Paraíba, Brasil*

Abstract

Introduction: Association between *Ascaris lumbricoides* infection and asthma is a controversial subject that has been studied by several authors based on the hygiene theory. This work contributes to better understanding this issue.

Methodology: This was a cross-sectional study involving 1,004 children from a neighborhood of low socioeconomic status in Campina Grande, Paraíba, northeastern Brazil. Asthma was diagnosed using the International Study of Asthma and Allergy in Childhood (ISAAC) questionnaire. Intestinal parasitosis was diagnosed by parasitological examination (the Ritchie technique), and parasite load determined by the Kato-Katz technique. The statistical analysis was descriptive, and hypotheses were tested according to odds ratios.

Results: A total of 260 children were infected with *A. lumbricoides*, and 233 had asthma. Light parasite loads were significantly associated with asthma (wheezing more than three times per year); p = 0.003, OR = 0.41(IC 0.22 – 0.75), while the heavy parasite loads were not; p = 0.002, OR = 2.37(IC 1.35 – 4.18). Similar results were observed in almost all the symptoms of asthma. No association was found with maternal educational level.

Conclusion: In children living in urban areas of low socioeconomic status, a light parasite load of *A. lumbricoides* is a protective factor against asthma and its symptoms. Meanwhile, heavy parasite load is a risk factor and contributes to the high prevalence of asthma and its symptoms among these children.

Key words: *Ascaris lumbricoides*; asthma; parasite load; asthma association.

J Infect Dev Ctries 2014; 8(7):891-897. doi:10.3855/jidc.3585

(Received 26 March 2013 – Accepted 22 July 2013)

Introduction

Asthma is a very common chronic disease in children. Its severity has increased in developed countries [1]. Parasitic infections are strongly associated with environmental factors [2]. Ascariasis is one of the most common parasitic diseases [3]. In a study conducted in 2002 in the Pedregal neighborhood in Campina Grande, Paraíba, Brazil [4-6], which was also the present study site, we found that the prevalence of ascariasis in children was 56%. These findings indicate that the absence of sanitary structures and disorderly occupation of the territory of urban centers favors the increase of intestinal parasitosis.

The association between asthma and ascariasis was initially proposed by Lynch [7]. Although several subsequent studies [8-12] have been published on this topic, the hygiene hypothesis, which associates the presence of infections with the absence of allergies, was only introduced in the late 1980s [13].

Though there has been a number of recent studies, this topic remains controversial. A meta-analysis shows that infection with *A. lumbricoides* does not usually protect against asthma [14]. However, a study using similar methodology found that helminthiasis, including ascariasis, is possibly a protective factor against asthma [15].

Studies conducted in northeastern Brazil [16] and in a rural area of Ecuador [17] showed an inverse relationship between helminthiasis and asthma. However, no association was found between asthma and ascariasis in Campina Grande [5].

In the present study, the parasitic loads of patients with ascariasis were evaluated to quantify the number of eggs as well as to associate them with asthma and its symptoms.

Methodology

A cross-sectional study was conducted in Campina Grande, Paraíba, Brazil, between January and November 2007. The study focused on children between two and ten years of age residing in the slum neighborhood of Pedregal, where there is overcrowding, low socioeconomic indices, and poor sanitation. This area has 2,655 families registered by the Family Health Program (PSF), according to data provided by the Municipal Health Department; thus, the estimated population is 10,706. There were 1,600 children between two and ten years of age, representing 14.9% of the residents.

A total of 1,582 (98%) International Study of Asthma and Allergy in Childhood (ISAAC) (asthma module) [18] questionnaires were filled by parents or guardians during home visits. Before completing the standard ISAAC questionnaire, a term consent statement was read and explained until no more doubt existed on the part of the legal guardian. Containers for collecting fecal material were also distributed during those visits. Despite great efforts by researchers and health agents, only 1,195 (74.7%) fecal samples were collected, and of these, only 1,004 had their addresses confirmed and were geo-referenced for further studies.

Although one previous study had considered only one wheezing a year to assess the prevalence of asthma [19], the present study characterized as asthmatic children who had three or more episodes of wheezing in the past 12 months. This criterion was chosen because it tends to diminish memory errors. Other asthma symptoms in ISAAC constant were also analyzed. Stool testing was immediately performed using Ritchie's method [20]. The Kato-Katz technique [20,21] was used to determine the *A. lumbricoides* parasite load, which was rated as either light (0 to 5,000 eggs/g feces), intermediate (5,000 to 10,000 eggs/g of feces) or heavy parasitic load (over 10,000 eggs/g feces). Age, socioeconomic status, and maternal education were recorded in categories.

Statistical analyses were performed using SPSS (Statistical Package for Social Science) version 17 for Windows, applying the *t* test for continuous data and chi -square (χ^2) Pearson for categorical data, and the chi-square test (χ^2) linear trend. Where relevant, odds ratio (OR) and confidence intervals (CI) were also applied. The probability of incurring on type I error was considered up to 0.05% (statistically significant at $p < 0.05$).

The study design and procedures were approved by the Ethics and Research Committee of the University Hospital Alcides Carneiro, Federal University of Campina Grande.

Results

The parasites (*i.e.*, protozoa and helminths) detected in the stool tests are tabulated in Table 1. *Schistosoma mansoni* eggs were not detected. Only 317 children (31.6%) had no infection. All children diagnosed with intestinal parasites were referred for evaluation and treatment to the University Hospital Alcides Carneiro (HUAC).

Table 1. Frequency of intestinal parasites and most prevalent co-infections with *A. lumbricoides* among children 2–10 years of age in Pedregal, Campina Grande, Paraíba, Brazil

Parasites found	Frequency	Percentage
Complex *Entamoeba histolytica/dispar*	464	41.3
Ascaris lumbricoides	260	23.1
Giardia lamblia	202	18
Trichuris trichiura	169	15
Hymenolepis nana	10	0.9
Enterobius vermicularis	6	0.5
Ancylostoma sp.	4	0.4
Strongyloides stercoralis	4	0.4
Taenia sp.	4	0.4
Endolimax sp.	1	0.1
TOTAL	1,124	100
Co-infection of *A. lumbricoides* with the most prevalent parasites		
Only *A. lumbricoides*	63	24.2
A. lumbricoides and complex *E. histolytica/dispar*	52	20
A. lumbricoides and *T. trichiura*	48	18.5
A. lumbricoides, *T. trichiura*, and complex *E. histolytica/dispar*	39	15
A. lumbricoides, complex *E. histolytica/dispar*, and *G. lamblia*	22	8.5
A. lumbricoides, *T. trichiura*, complex *E. histolytica/dispar*, and *G. lamblia*	15	5.8
A. lumbricoides and *G. lamblia*	13	5
A. lumbricoides, *T. trichiura*, and *G. lamblia*	8	3.1
TOTAL	260	100

Source: Survey data, 2012

Table 2. Associations between demographic data and the presence of *A. lumbricoides* with and without asthma in children 2–10 years of age in Pedregal, Campina Grande, Paraíba, Brazil

Demographic characteristic		*A. lumbricoides*					With asthma		Without asthma		
		Yes		No		*p* value					*p* value
		s	%	n	%		n	%	n	%	
Gender	Female	117	22.6	401	77.4	**0.013**	26	37.1	91	47.9	**0.122**
	Male	143	29.4	343	70.6		44	62.9	99	52.1	
Age group	< 3 years	64	23.2	212	76.8	**0.094**	23	32.9	41	21.6	**0.003***
	4–6	84	24.8	255	75.2		28	40	56	29.5	
	> 6 years	112	28.8	277	71.2		19	27.1	93	48.9	
Household income	< 1 MW	129	28.2	329	71.8	**0.079**	41	58.6	88	46.3	**0.034***
	1 MW	112	24.6	343	75.4		27	38.6	85	44.7	
	2 MW	18	22	64	78		2	2.9	16	8.4	
	≥ 3 MW	1	11.1	8	88.9		0	0	1	0.5	
Maternal education	Illiterate	59	44	75	56	**0.000**	17	24.3	42	22.1	**0.48**
	Primary school Incomplete	178	26.3	498	73.7		48	68.6	130	68.4	
	Primary school completed	9	13.8	56	86.2		2	2.9	7	3.7	
	Middle School Incomplete	12	9.8	110	90.2		3	4.3	9	4.7	
	Middle school completed	2	28.6	5	71.4		0	0	2	1.1	
Age (years)	Average	5.88	-	5.51	-	**0.043**	4.,93	-	6.,23	-	**0.000**
	DP	2.682	-	2.534	-		2.,51	-	2.,66	-	

(*) P value obtained $\chi 2$ test for linear trend. SM = minimum wage. Source: Survey data, 2012

Table 3. Association between asthma and co-infections of *A. lumbricoides* in children 2–10 years of age in Pedregal, Campina Grande, Paraíba, Brazil

Co-infection	Asthmatic (with more than 3 wheezing episodes per year)				
	Yes	No	Total	*p* value	OR (95% CI)
Only *A. lumbricoides*	17 (27.0)	46 (73.0)	63	0.99	1.00 (0.53–1.90)
A. lumbricoides and complex *E. histolytica/dispar*	9 (17.3)	43 (82.7)	52	0.08	0.50 (0.23–1.09)
A. lumbricoides* and *T. trichiura	**20 (41.7)**	**28 (58.3)**	**48**	**0.011**	**2.31 (1.20–4.45)**
A. lumbricoides, *T. trichiura*, and complex *E. histolytica/dispar*	12 (30.8)	27 (69.2)	39	0.557	1.24 (0.59–2.62)
A. lumbricoides, complex *E. histolytica/dispar*, and *G. lamblia*	4 (18.2)	18 (81.8)	22	0.396	0.61 (0.20–1.90)
A. lumbricoides, *T. trichiura*, complex *E. histolytica/dispar*, and *G. lamblia*	5 (33.3)	10 (66.7)	15	0.56	1.38 (0.45–4.20)
A. lumbricoides and *G. lamblia*	2 (15.4)	11 (84.6)	13	0.336	0.47 (0.10–2.210
A. lumbricoides, *T. trichiura*, and *G. lamblia*	1 (12.5)	7 (87.5)	8	0.35	0.37 (0.04–3.130

Source: Survey data, 2012

Table 4. Associations of asthma symptoms and age groups with *A. lumbricoides* parasitic load in children 2–10 years of age in Pedregal, Campina Grande, Paraíba, Brazil

	Parasite load								
	Mild			Intermediate			High		
	n (%)	*p*	OR (CI)	n (%)	*p*	OR (CI)	n (%)	*p*	OR (CI)
Wheezing once	56 (53.3)	**0.03**	0.45 (0.27–0.76)	22 (68.8)	0.56	1.25 (0.56–2.78)	89 (72.4)	**0.01**	1.98 (1.17–3.33)
Wheezing in the last 12 months	34 (32.4)	**0.018**	0.53 (0.32–0.90)	13 (40.6)	0.94	0.97 (0.45–2.07)	60 (48.8)	**0.018**	1.82 (1.10–3.00)
Wheezing > 3 times/year	18 (17.1)	**0.003**	0.41 (0.22–0.75)	8 (25.0)	0.79)	0.89 (0.38–2.09)	44 (35.8)	**0.002**	2.37 (1.35–4.18)
Wheezing in the morning	21 (20.0)	**0.001**	0.39 (0.22–0.70)	11 (34.4)	0.67	1.18 (0.54–2.58)	49 (39.8)	**0.004**	2.17 (1.27–3.71)
Difficulty in speaking	21 (20.0)	**0.003**	0.41 (0.23–0.74)	11 (34.4)	0.6	1.23 (0.56–2.69)	47 (38.2)	**0.009**	2.02 (1.18–3.47)
Wheezing after workout	105 (40.4)	**–**	–	32 (100)	–	–	123 (47.3)	**–**	–
Dry cough at night	47 (44.8)	**0.07**	0.63 (0.38–1.04)	15 (46.9)	0.57	0.80 (0.38–1.69)	72 (58.5)	**0.032**	1.70 (1.04–2.79)
Age < 3 years	30 (46.9)	0.223	1.42 (0.80–2.51)	8 (12.8)	0.957	1.02 (0.43–2.40)	26 (40.6)	0.217	0.69 (0.39–1.23)
Age 4–6 years	**24 (28.6)**	**0.007**	**0.46 (0.26–0.82)**	13 (15.5)	0.283	1.51 (0.70–3.23)	47 (56.0)	0.54	1.67 (0.89–2.82)
Age > 6 years	51 (45.5)	0.141	1.45 (0.88–2.40)	11 (9.8)	0.288	0.65 (0.30–1.42)	50 (44.6)	0.454	0.82 (0.50–1.35)

Source: Survey data, 2012

Among the 260 children identified as carriers of *A. lumbricoides*, the frequencies of the most prevalent co-infections (Table 1) were established. Children with and without asthma had similar ages (Table 1).

In terms of demographic variables, two associations were made: one with the presence of *A. lumbricoides* and another with the presence of asthma among patients with ascariasis. The demographic data with the presence of *A. lumbricoides* showed statistical significance with gender ($p = 0.013$), maternal education ($p < 0.001$), and mean age ($p = 0.043$). Among children infected with *A. lumbricoides*, association with asthma showed statistical significance with age group ($p = 0.003$), household income ($p = 0.034$), and mean age ($p < 0.001$) (Table 2).

The association between the presence of *A. lumbricoides* and asthma among the studied children did not achieve statistical significance ($p > 0.05$). However, the significance found ($p = 0.09$) suggested a further study using the parasite load (Table 3). Regarding the associations of asthma with *A. lumbricoides* co-infections, only *Trichuris trichiura* co-infection ($p < 0.05$) was found to be significant.

The associations between the parasite loads of *A. lumbricoides* infection are shown in Table 4. Light parasite load was significantly associated with all asthma symptoms ($p < 0.05$; OR < 1) with a CI not containing the value 1, except for the symptom *cough at night*. In addition, heavy parasite load was significantly associated with all asthma symptoms ($p < 0.05$; OR > 1) and a CI not containing the value 1. Meanwhile, intermediate parasite load was not significantly associated with the risk of symptoms. The highest frequencies of symptoms were observed at heavy parasite load. Heavy parasite load was only significantly associated with ages three to six years ($p < 0.05$; OR = 0.46; CI = 0.26–0.82) (Table 4).

During the study period, oral use of immune-suppressive drugs (prednisone, prednisolone), or use of inhaled drugs (fluticasone and budesonide) was not made available by the Municipal Health department. Thus, the use of immune-suppressive drugs were not considered to be a confounding factor. The only drug used by children was salbutamol (β2 agonist), provided free by the government.

Discussion

The hygiene hypothesis was launched by David Stracham when he suggested that the frequent exchange of infections among siblings from large families could be responsible for the lower incidence of allergies among them, when compared to families with fewer children [22]. In a previous study, we observed a lower prevalence of allergic diseases in the Métis Indians compared with European descendants from northern Canada [23]. The authors suggested that the low frequency of infection in European descendants could be responsible for the high prevalence of allergic diseases. Subsequently, it was observed that in allergic diseases, there is a polarization of T lymphocyte responses and increased secretion of cytokines involved in the regulation of immunoglobulin E, mast cells, basophils, and eosinophils, ultimately leading to disease and inflammation [24].

This immune behavior has also been observed in the farming communities versus populations of major cities as well as in developing versus industrialized countries [10-13,25,26]. Similar results were found in studies associating allergic diseases with socioeconomic levels in Germany [27] and Sweden [28].

The populations of developing countries or emerging economies, or those practicing traditional agriculture, have simple lifestyles that support the hygiene hypothesis [3,13]. Bacterial and viral infections, to which they are exposed during childhood, facilitate the development of the Th1 response, while stimulation of Th2 is due to helminth infections and allergic diseases [29]. The requirement to cause long-term infections may be the ability of the parasite to induce immunoregulatory mechanisms in the host, leaving him tolerant to parasites [3].

In large cities in developed countries, this immune chain is not triggered, allowing for the development of allergies [26]. The differentiating factors underlying these findings include the improvement of public health and the use of antibiotics and vaccines [30].

The co-infection of *A. lumbricoides* with the most common parasites was not associated with asthma, except for co-infection with *T. trichiura*. These results suggest that there could be a combined effect of two helminths contributing to the high risk of asthma. However, studies on co-infection and allergic diseases are scarce; therefore, further studies are required to better understand this interaction.

When associated with demographic characteristics, *A. lumbricoides* infection was weakly associated with asthma and its symptoms. When the infections were divided into three categories according to parasite load, it was evident that light parasite load constituted a protective factor against asthma and its symptoms. This finding is concordant with a recent review concluding that parasitic infections protect against

asthma [15]. Moreover, one should consider a study that evaluated the positive skin test immediate reading with aeroallergens in individuals infected with a light parasite load of *A. lumbricoides*, and it made no difference in those individuals without infection [31].

A heavy parasite load proved to be a risk factor for asthma and its symptoms, contradicting a review study that concluded that infection with *A. lumbricoides* provides no protection against asthma, but is not a risk factor, either [14]. In another study, individuals with heavy parasite loads had a lower prevalence of positive skin tests to aeroallergens in immediate readings [32]. The same result was found for heavy parasitic load for *S. mansoni* [31].

The data found in this work were obtained from populations with the same lifestyles, environments, and ethnicity, which may corroborate this immune behavior [26]. The children who participated in this study lived in a poor community with low socioeconomic status and were subjected to the same environmental conditions and lifestyle. Despite this, different parasite loads elicited different immune responses; a light parasite load of *A. lumbricoides* is a protective factor against asthma, whereas a heavy parasite load is a risk factor.

The explanation for the protective effect or not of helmintiasis against allergic diseases or lack thereof includes the age of the population, parasite load, time of exposure to the worm (chronic or acute), and helminth species [31]. Regarding the age of the population, there was a trend toward decreased asthma prevalence with increasing age. Light parasite load was only significantly associated with age between three and six years, which is the same age range reported in a study on atopy and socioeconomic status in Germany [27].

Maternal education was not associated with asthma among children with ascariasis in the present study. However, studies conducted in Duque de Caxias, Rio de Janeiro, reported the opposite [33].

Since the area of the present study was restricted, indicating that the children lived in the same environment, attended the same schools and nurseries, and routinely made use of anti-parasite medication prescribed by doctors of Primary Care Family Health (BHU), the present data may be biased by confounding variables. A long-term cohort study is required to further clarify the conditions of the parasitized children and their associations with atopic diseases.

Therefore, the results obtained indicate that maternal education had no role in the prevalence of asthma, and that the burden of low parasite infection by *A. lumbricoides* appeared to be a protective factor against asthma and its symptoms. Furthermore, the parasite load had heavy participation in the high prevalence of asthma and asthma symptoms among children between two and ten years of age living in urban areas with a low human development index.

The present findings contribute to the discussion about the existence of protective factors against atopic diseases in children parasitized by *A. lumbricoides*.

Acknowledgements

We thank Dr. Edgar Marcelino de Carvalho Filho for encouraging the research and the health workers of the Family Health Program, Campina Grande, Paraíba. This study was supported by the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES) program.

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Corresponding author

Gerson Bragagnoli
Rua João Alves de Oliveira, 179 apt. 701 – Centro
58400-117 Campina Grande, Paraíba, Brazil
Phone: 83-3321-2674/8807-2674
Fax: 2101-1233
Email: gersongb@terra.com.br

Conflict of interests: No conflict of interests is declared.