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ENTEROPARASITES, RESPIRATORY ALLERGY AND OTHER SIGNS AND SYMPTOMS IN CHILDS AND YOUTH POPULATION OF RECÔNCAVO OF BAHIA – BRAZIL

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Research

Author: Ana Lúcia Moreno Amor

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Carlos Henrique Araújo Fonsêca, Bruno Carvalho Marques, Leonardo Bispo Reis, Darcy Andrade Cardoso Lima, Luiz Henrique Silva Mota, Raoni dos Santos Andrade, Glauber Andrade dos Santos, Ana Lúcia Moreno Amor

Healthy Science Center – University Federal of Recôncavo Bahia – Santo Antônio de Jesus, Bahia, Brasil.

CORRESPONDENCE AUTHOR

Ana Lúcia Moreno Amor
Centro de Ciências da Saúde – Universidade Federal do Recôncavo da Bahia – Avenida Carlos Amaral, s/n. CEP: 44574-490 - Santo Antônio de Jesus, Bahia, Brasil. Telefone: +557536324598.
Email: ana_amor@ufrb.edu.br

CONFLICTS OF INTEREST

There are no conflicts of interest for any of the authors.

ABSTRACT

Respiratory allergies may develop at any age, but the onset are more frequent in childhood and juvenile population due to genetic factors and to development of the immune system, which may presents as rhinitis and/or asthma. In Brazil, asthma is the second cause of hospital admission in children aged four to nine years old and the third in adolescents. Exposure to pathogens, particularly helminths, and their products are common in developing countries, and it appears to protect against the development of autoimmune and allergic diseases in experimental and human models. Based on these data, the present study investigated the presence of allergic conditions, infection by intestinal parasites and symptomatology on the juvenile population of the rural area of Santo Antônio de Jesus (Bahia - Brazil), from July to October, 2015. A questionnaire was applied to evaluate asthma and allergic symptoms and the parasitological feces exam was performed in 47 individuals. The study identified 81% of the positive samples for at least one parasite species; 45% polyparasitism; and the prevalence to *Endolimax nana* (48%) and hookworms (39%); eczema as the predominant allergic manifestation (34%) and headache, fatigue after physical activity, urticaria, itching in the head and nervousness as the most frequent signs and symptoms. The prevalence of enteroparasites, respiratory allergy and the symptoms associated with each of them are present in the studied population, and it may be related not only to the infection, but also to the presence of previous or overlapping diseases.

Keywords: Allergy, Enteroparasit, Children, Adolescents

INTRODUCTION

Enteroparasitosis is a serious public health problem that affects mainly population from developing countries, especially those regions where missing basic sanitary structures (1). The prevalence of enteroparasites in a population is often used as an important indicator of the health situation and the housing conditions, since the most of the intestinal parasites are transmitted by water or food contaminated fecal material directly or after parasite development in soil (2). Besides, the consequences of parasitic diseases are

debilitating either mentally or physically, mainly in the child population, which is naturally more exposed when coming from communities whose socioeconomic conditions are precarious and has a less efficient immune system (3, 4).

The parasitic infections as helminthiasis contributed to increased morbidity statistics in Brazil and other parts of the world, due to the severity and non-specific symptoms such as diarrhea, vomiting, anemia, and other symptoms that make clinical diagnosis difficult (5). According to the World Health Organization (6), helminths transmitted by the soil are in the seventeen neglected tropical disease agents worldwide affecting mainly the lower social classes of underdeveloped countries. These diseases are related to several environmental changes, which may act as a preventive or transmitter agent and have an intimate association with human behavior.

On the other hand, parasitic infections, especially those caused by helminths, may have an important effect on the protection of allergic manifestations (7, 8, 9). In 1989, Strachan purpose the hypothesis of hygiene, which rightly brings a relation between being exposed to helminths and other pathogens and the reduction of allergic disorders (10). Allergic diseases have a high prevalence in the world population, with a consequent increase in direct and indirect costs to society (11). It has generally stimulated research to identify factors associated with these diseases, as well as to estimate their prevalence and incidence in order to propose and implement measures to mitigate these consequences (12).

There are several articles dealing with the effects of the protection that helminths can promote through immunomodulation in the host, experimental and epidemiological studies were able to prove and describe this mechanism (13, 14, 15). The protection has been explained by the ability of IL-10, especially derived from regulatory T cells, to inhibit Th2-path hyper stimulation by promoting a balance between Th1 and Th2 responses (16, 17, 18). In this way, chronic helminthic infections would be related to this phenomenon (19), especially the hookworms (20, 21).

The inverse relationship between helminth infections and the development of immune-mediated diseases is a cornerstone ofthe hygiene hypothesis and studies were carried outto elucidate the mechanisms by whichhelminth-derivedmolecules cansuppress immunological disorders (22). Important advances have occurred in understanding the parasite-host relationship, and some molecular and cellular mechanisms are already well defined. These mechanisms include the induction of regulatory cytokine production (IL-10 and TGF-) (23); CD4+ CD25+ Foxp3+ T cell (Treg cells) recruitment (24); blocking of IgE cross-linking by IgG4 (16); alternative macrophage activation inducing an anti-inflammatory phenotype (25) and an immune response shift (26). However, these mechanisms are variable depending on the parasite species or its products, experimental model, treatment protocol, among other factors (27, 28).

In view of the above, this study investigated infection by helminths, allergic manifestations and other signs and symptoms in a child population from the rural area of a municipality in the Recôncavo of Bahia - Brazil.

MATERIAL AND METHODS

Study design and location data of the area

The present work is a cross-sectional, descriptive study carried out with a segment of the resident population in the rural area (communities of Onha and Riacho Dantas) in the municipality of Santo Antônio de Jesus – Bahia - Brazil. This region was selected by the environmental characteristics, tropical climate, which predisposes the encounter of intestinal parasites as verified by previous works (9, 29). - The research period was from June 2015 to January 2016.

Samples and research tools

For the collection of data a unified instrument was used, built by the authors and applied in interviews during home visits in the form of a quiz, containing personal, socio-cultural, economic, housing and the health of the interviewees data.

For the questions related to allergic diseases (asthma, rhinitis and eczema), a standard questionnaire used by the International Study on Asthma and Allergies in Childhood (ISAAC) was applied (30).

The interviews were carried out on the same day of the first home visit, with the delivery of individuals kits [a fecal collection bottle (one per individual), properly identified; slides of glass with adhesive tape and wooden toothpick accompanied by illustrated instructions printed for correct collection].

Home visits occurred daily on the morning shift, from Monday to Saturday for a period of three months. We have visited 53 houses of the communities of Onha and Riacho Dantas.

Inclusion criteria

Participants in the study were: 47 residents of the rural communities of Onha and Riacho Dantas, who attended all the criteria for inclusion in this study: residing in the place, being between 0 and 19 (incomplete) years, signing the consent form, completion of the quiz, delivery of fecal material and parasitological evaluation.

Laboratory procedures

For the analysis of fecal samples, the parasitological methods (31) were: Hoffmann, Pons and Janer (spontaneous sedimentation); Baermann-Moraes and Kato-Katz which were carried out at the Parasitology Laboratory of the Food and Nutrition Security Center (SANUTRI) of the Health Sciences Center, Federal

University of Recôncavo of Bahia, with a reading of three slides per sample. The Graham method was used to analyze the slides of glass with adhesive tape.

Statistical analysis

The data and the statistical analyzes were tabulated and performed by the program SPSS for Windows 9.0, using the chi-square test to compare the prevalences of enteroparasites according to the age range, allergic condition and the presence of children's symptomatology researched. $p \leq 0.05$ were considered statistically significant.

Ethical Aspects and Informed Consent

The research was approved by the Committee of Ethics in Research with Human Beings of the Federal University of the Recôncavo of Bahia - Brazil. Participation and consent of the participants were obtained after clarification regarding the purpose of the research and express consent (signed or biometric signature) through the Informed Consent Form (of the responsible ones) and the Statement of Assent (public of 5 To 18 years), containing accessible language and information about the study. With the data tabulated, an educational action was carried out in the communities studied to read the results and explanation of the prophylactic measures pertinent to the parasites found in this population, as well as information about prophylactic measures for the allergic population. Participants were instructed to go to the basic health units of the neighborhood for medical care and prescription of treatment, when necessary.

RESULTS

The study found high positivity in the parasitological examination of feces of the population, where approximately 81% of the analyzed samples were positive for at least one parasite species (Figure 1A). Regarding the level of parasitism, polyparasitism predominated (45%) (Figure 1B).

Protozoa were the main enteroparasites found. Among them, the non-pathogenic *Endolimax nana* and *Entamoeba coli* are the most frequent, followed by the pathogenic protozoa *Entamoeba histolytica* and *Giardia duodenalis*. Among the helminths, the main highlight is the finding of hookworms. The helminths *Enterobius vermicularis* and *Ascaris lumbricoides* appear as the second and third more frequent, respectively (Figure 1C).

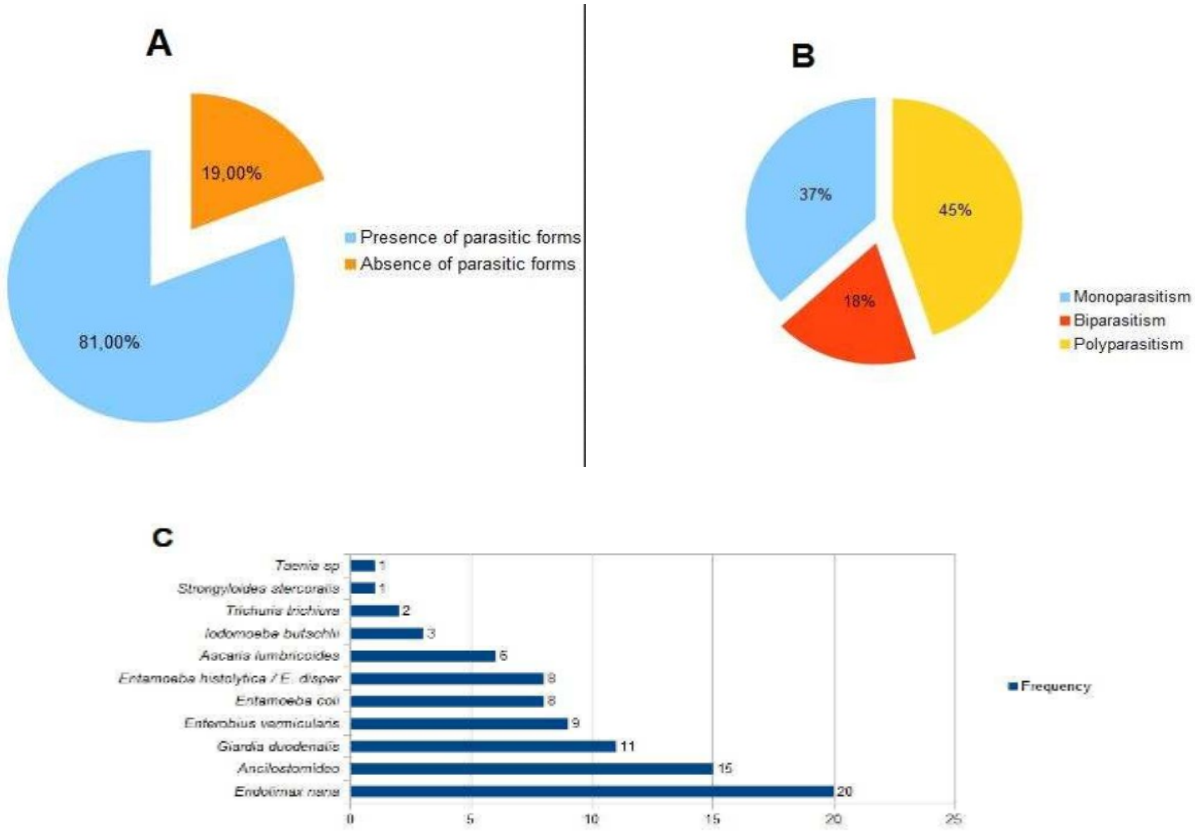


Figure 1 - Results of parasitological examinations performed in 47 individuals of children and adolescents living in rural areas of Santo Antônio de Jesus / BA, 2015: (A) percentage of positivity; (B) level of parasitism and (C) main species of parasites found, in global frequency, among 38 of the 47 individuals surveyed.

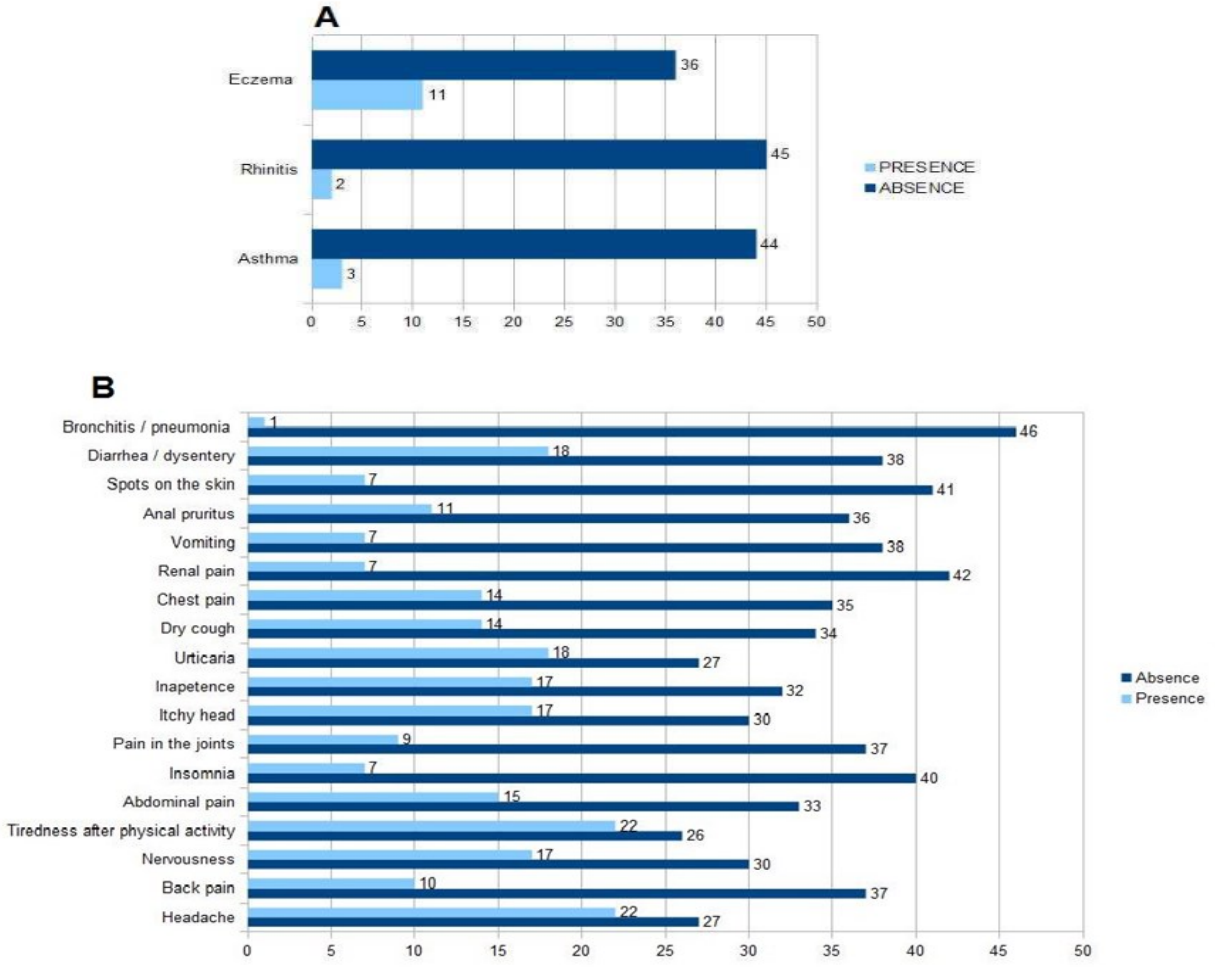
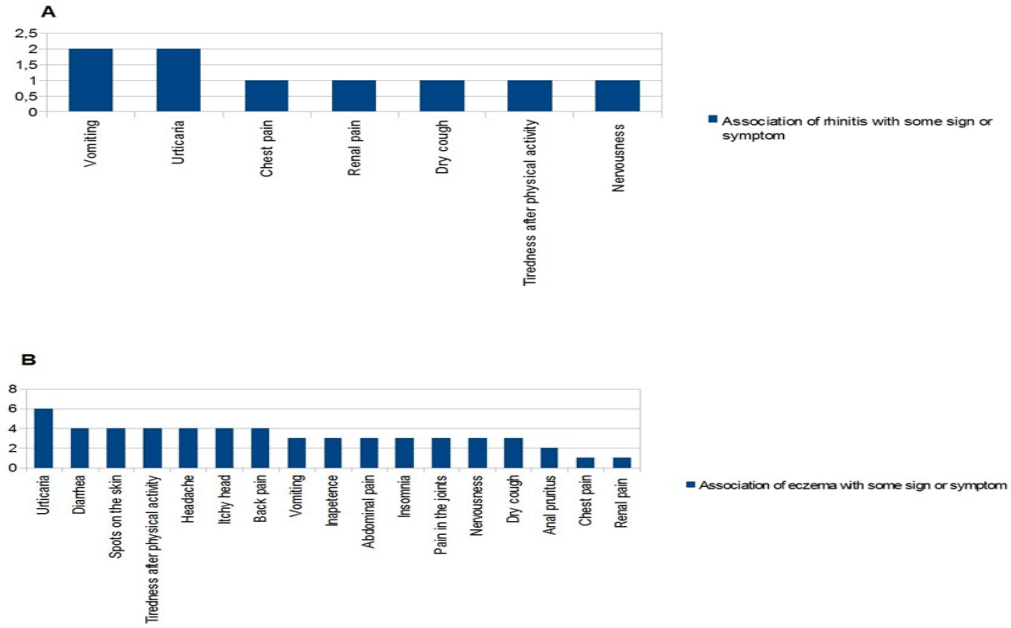


Figure 2 - Frequency of the health aspects of the population studied: (A) respiratory allergic manifestation (eczema, rhinitis and asthma) and (B) main signs and symptoms reported by the 47 individuals surveyed - Children and youths living in rural areas of Santo Antônio de Jesus / BA, 2015.



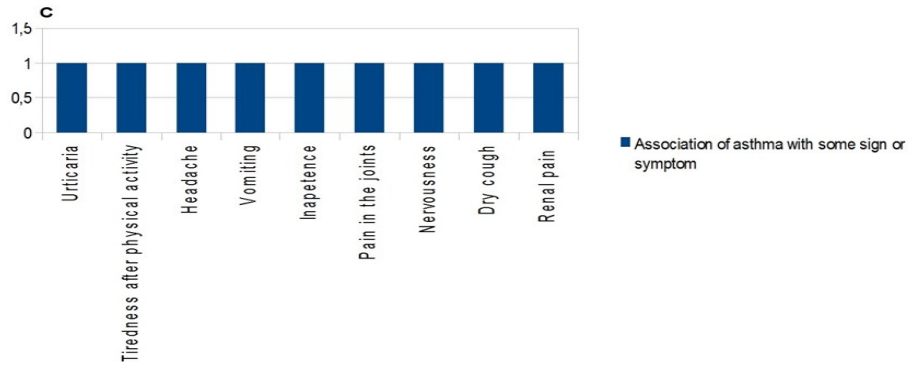


Figure 3 - Main signs and symptoms presented: (A) by the 2 individuals who reported rhinitis; (B) by the 11 individuals who reported eczema; (C) by the 3 individuals who reported asthma - Children and adolescents living in the rural area of Santo Antônio de Jesus / BA, 2015.

Table 1 - Associations with allergic manifestations in 47 individuals surveyed - Rural area of Santo Antônio de Jesus, Bahia, 2015: (A and B) Effect of parasite infection on asthma, allergic rhinitis and eczema; (C) Family and housing characteristics.

A

		Helminth		Protozoan		Both		Sample Negative		Total	
		n	%	n	%	n	%	n	%	n	%
ASTHMA	Yes	1	10	2	15,38	0	0	0	0	3	6,38
	No	9	90	11	84,62	15	100	9	100	44	93,62
RINITE	Yes	1	10	1	7,69	0	0	0	0	2	4,25
	No	9	90	12	82,31	15	100	9	100	45	95,75
ECZEMA	Yes	2	20	2	15,38	4	26,66	3	33,33	11	23,4
	No	8	80	11	84,62	11	73,34	6	66,77	36	76,6
TOTAL		10		13		15		9		47	

B

ALLERGIC MANIFESTATION		PRESENCE OF ONE OR MORE HELMINTHES		RP
		Yes	No	
ASTHMA	Yes	1	2	0,41
	No	24	20	
RINITE	Yes	1	1	0,87
	No	24	21	
ECZEMA	Yes	6	5	1,07
	No	19	17	

C

		ASTHMA		RINITE		ECZEMA	
		Yes	No	Yes	No	Yes	No
Family history of allergic manifestation	Yes	0	9	1	2	2	6
	No	3	35	1	43	9	30
Presence of animal (dog or cat) at home	Yes	2	36	2	12	9	26
	No	1	8	0	33	2	10
Presence of wall or damp ceiling in the house	Yes	0	14	0	2	5	9
	No	3	30	2	43	6	27
Mattress lined with plastic and / or antiallergic cover	Yes	0	1	0	1	1	0
	No	3	43	2	44	10	36
Pillow lined with plastic and / or antiallergic cover	Yes	0	1	0	2	1	0
	No	3	43	2	43	10	36

Regarding the health aspect of the individuals, related to respiratory allergies, eczema was the predominant allergic manifestation in the questionnaire analysis: 34% of the study population reported having eczema at least once in their life, followed by asthma with 6.3% (Figure 2A). The main signs and symptoms presented by individuals during the last 15 days prior to the collection of information through the quiz were: headache, fatigue after physical activity, urticaria, itching of the head and nervousness (Figure 2B).

For individuals who reported having rhinitis as an allergic condition, vomiting and urticaria were the most frequent symptoms (Figure 3A); Individuals with eczema had urticaria, skin blemishes, headache, spinal pain, fatigue after physical activity and diarrhea as the main symptoms reported (Figure 3B); Regarding to asthma, the symptoms were urticaria, fatigue after physical activity, dry cough and others (Figure 3C).

Table 1A shows the absolute frequency of the number of individuals parasitized only with helminths or with protozoa or both and which presented some allergic conditions. Associating only with helminths: asthma (n = 1), rhinitis (n = 1) and eczema (n = 2). Table 1B presents the calculation of Prevalence Ratio (PR) between helminth infection, associated or not to protozoa, with allergic conditions, resulting in a PR of 0.41 for asthma, a result that suggests helminth protection, and which is repeated in rhinitis, where the PR value was 0.87. On the other hand, for eczema, the PR value was 1.07, indicating a risk ratio between those infected by helminths and the development of eczema.

Approximately 18% of the population who reported having eczema had a family history associated with allergic manifestations, a similar result for rhinitis, where 50% of the individuals (n = 1) reported having allergic relatives. The same was not observed for asthma, since individuals who reported having this allergic manifestation had no family history for that (Table 1C).

It is recorded that 81% of those who self-affirmed diagnosis for eczema reported having one or more domestic animals in their homes; 100% of the individuals affected by rhinitis and 66.7% of those with asthma, presented the same report (Table 1C). The presence of a wall or a damp ceiling in the residence is registered in 45% of the homes of those who reported having eczema. Not seen for rhinitis or asthma (Table 1C).

Among the individuals who presented asthma, none said to have a cover or lining with antiallergic properties for mattress or pillows, the same was repeated with the individuals who presented rhinitis, suggesting an important risk factor. Among those whose allergic manifestation was eczema, 90% did not have such lining partss (Table 1C).

DISCUSSION

This study found a high positivity of enteroparasites in the population studied, when compared to other studies using the children and youth population in Brazilian cities, where the positivity presented in the range of 45 to 66%, in Uberlândia - Minas Gerais (32), Crato - Ceará (4), and in municipalities of the Bahia backwoods (3), evidencing the great risk to the health of this population.

Parasitological findings, pathogenic and non-pathogenic parasites, helminths and protozoa, are directly related to other findings in the same municipality and reported in the work of Carvalho et al. (9). The total of polyparasitism with biparasitism presents a percentage higher than that of monoparasitism, suggesting that the contamination of the environment may be occurring in different ways and by different pathogens. It is important to highlight the protozoa carried by water, such as *Giardia duodenalis*, as well as positivity for helminths of the group of hookworms (geohelminths that infect humans by penetration / cutaneous, in other words, from contaminated soil) (33), requiring specific studies to better determine the factors involved in maintaining the local parasitic cycle.

The great positivity for *Endolimax nana*, hookworms and *Giardia duodenalis*, suggests contamination of the water sources used by this population, as well as environmental contamination of the soil or food ingested by the individuals, evidencing an important contamination of the home microenvironment, poor sanitary conditions and hygienic habits, contributing to the general high prevalence of positivity in this population, as presented in other studies, which is based on the literature on the prevalence of malnutrition in Brazil (2, 34, 35).

Regarding to allergic diseases, the present study observed a prevalence of 34% of allergic individuals in the study population, this data was considered from the narrative of the subjects interviewed who reported having some allergic disease, that in this context, the most common was eczema. A study using the ISAAC quiz, the same as that used in this study, evaluated the prevalence of eczema and other allergies in seven Brazilian capitals, where a discordant result was observed, with a median prevalence based on medical diagnosis among 5.6%, in which Belém-Pará presented the highest rate, with 7.9% and Aracaju-Sergipe the lowest, with 3.4% (36). However, in the cohort study developed by Solé et al. (36), one can notice a large difference between the self-reported prevalence and the prevalence of medical diagnosis, where the self-reported rate of eczema averaged 9.1%, suggesting the need for new studies with the population studied here to explanation the high rate, since that sampling was for convenience, only for the diagnostic survey of the data presented here and discussed.

For the present study, the total prevalence of asthma self-reported by the population was 6.3%. In

in other Brazilian cities, such as Campinas - São Paulo a study revealed that asthma is the most common chronic disease in adolescents, with a prevalence of 7.59% (37), another study conducted in Salvador-Bahia resulted in a similar prevalence of 7.6% in the child and adolescent population (38) corroborating with the data obtained in the Recôncavo of Bahia as well as those of Sousa et al. (39), in São Paulo, which found a prevalence of 9.1% and Kuschnir et al. (40), whose work presented a result of 7.4% of asthma in Nova Iguaçu, Rio de Janeiro. In contrast, in the municipality of São José, Santa Catarina state, a result of 11.7% was found for asthma prevalence (41), showing that data may vary according to population and its characteristics. In Portugal, for example, a study was conducted with pre-school children where the prevalence found for asthma was 4.3% (42), presenting a lower percentage of cases of this inflammation when compared to the result of this study in a municipality in the Recôncavo da Bahia. In others European countries, for example Italy, the prevalence of asthma is higher, presenting 11.7% (43).

The increase in cases of asthma and other allergies in European and others developed countries can be explained on the basis of the theory of hygiene, thought by Strachan in 1989, who raised hypotheses about the increase of allergic conditions on the grounds, where children with pathogens, due to excessive hygiene and care, could influence the appearance of hypersensitivities (10).

This relationship to helminths and allergy, experimentally works have sought to show parasitic mechanisms that seem to influence the immune response of the host (17, 18, 44). Among the various mechanisms, the most known is based on the ability of certain helminth surface antigens such as those from hookworm and *Schistosoma manson*i to immunomodulate the predominantly Th2-type response, through stimulating Foxp3 T cells, also called regulatory CD4 + T cells (18, 44).

These cells modify the classical Th2 response to a modified Th2, maintaining certain characteristics as the high production of IL-4. However, T-reg cells stimulate the production of IL-10, which regulates the differentiation of Th2 cells, decreasing its population (17) and other anti-inflammatory cytokines, inhibiting the production of IgE, and producing IgG4 by the cells B, thus attenuating the Th2 response (45). However, the mechanisms by which helminths stimulate such an immunomodulatory response still remain obscure, with many hypotheses to be tested (46).

In this study, specifically, with the rural population of the municipality of Santo Antônio de Jesus, there was a protection relationship between the helminth infection and the allergic manifestations asthma and rhinitis, corroborating with the hypothesis previously described. Similar result was found by Pereg et al. (47) who analyzed the population of Ethiopian immigrants in Israel, where all of them were treated against helminths and there was a very large increase in the prevalence of asthma among children aged 8-17 years.

In the city of Salvador-BA, a study using the ISAAC quiz (round 2) analyzed 1,445 children living in poor neighborhoods of the city, where high prevalences of helminths such as *Ascaris lumbricoides* and low prevalence of allergic manifestations were found, suggesting helminth protection (48) and corroborating with the study done by Cardoso et al. (49), in the same city.

Another study carried out in Campina Grande, Brazil, evaluated the health status of 1,004 children with socioeconomic conditions similar to those of the present study, where there was a protective factor between helminth infections and the development of asthma (50). Carvalho et al. (9) carried out a study in Santo Antônio de Jesus - BA, where they found a relationship of protection between helminths and allergy, corroborating with data from this study (for asthma and rhinitis).

Considering the results obtained, there is an interesting fact about the association between being infected by helminths and the development of allergic processes, specifically for eczema. It can be noticed that, in the study population, there was no association between helminths and eczema, on the contrary, the value of PR = 1.07 suggests a increased risk, which is in agreement with previous experimental models named. However, although there is a great experimental theoretical basis and immunotherapies being developed using helminth antigens, certain epidemiological and experimental studies have shown that there is not always such a protective association.

Studies by Feary et al. (51, 52) corroborated Croft et al. (53) and in this present study, resulting no protection relationship between helminth infection and the development of some allergic manifestations.

On the other hand, a cohort study by Djuardi et al. (54) analyzed children from gestation to 4 years of age, performing IgE, IL-5 and skin tests to identify allergic conditions. The author concluded that there is no risk relationship between being infected with helminth and the development of allergic conditions, disagreeing with the findings of the present study for eczema.

According to Webb et al. (19), the association of parasite species may generate a cross reaction and decrease the immunomodulatory effect that helminths possess. A fact that is suggested is present in the study population that presented bi- and polyparasitism, in other words, parasite diversity involved in its level of parasitism. Considering the risk factors, the family history, which suggests atopy, is an important risk factor for the development of allergic diseases. Family history is a major factor in the development of allergies, which may be genetic or passed from mother to child through breast-feeding (55), and is often the main risk factor in

certain populations, as seen in the study of Morishita, Strufaldi, Puccini (56), where it was present in 65% of the cases. However, in the present study, the family history of allergic manifestations assumed an irrelevant role as a risk factor, corroborating Fogaça et al. (57), where the main factor was previous pneumonia (for asthma).

Environmental factors also contribute to the development of allergic diseases, among them the presence of domestic animals, which in this study was related to a considerable portion of cases of eczema. The association and the presence of domestic animals such as dogs and cats were related to cases of allergy in children in the city of Recife-Pernambuco-Brazil, suggesting it is a risk factor for the development of this morbidity (58). The use of anti-allergic covers for pillows and / or mattresses was an important risk factor in this population. No individual with asthma or rhinitis and only one with eczema reported having such protective equipment, which suggests a risk ratio. Many studies have been carried out to evaluate risk factors for respiratory allergies, many factors are controversial, however, there is agreement in literature regarding the use of these protective covers, with proven protection against aeroallergens (59), the which emphasizes the importance of the use by this population. As for the presence of mold or suggestive spots on the walls of the residence, this risk factor concerns the housing conditions of that population and has a strong connection with local ventilation and exposure to the sun, that is, it is assumed that there is no Ventilation, which predisposes to the appearance of so -called "mold" on the walls, an important factor for the development of allergies (60).

The main symptoms associated with positivity to intestinal parasites were headache, fatigue after physical activity, urticaria, itching in the head, nervousness, inappetence and abdominal pain. Similar data to those obtained by Carvalho et al. (9) in Santo Antônio de Jesus-Bahia and by Oliveira and Amor (61) in Araci-Bahia, in Brazilian cities. It shows the difficulty in the clinical diagnosis of allergic manifestations or positivity for enteroparasites, based only on the presence of signs and symptoms that seem specific, since individuals without these diagnoses may also present the same symptoms.

In summary, considering the prevalence of enteroparasites, respiratory allergy and various signs and symptoms associated or not with each other, it shows the health aspect of the population researched and that may be related not only to the parasitic infection, but also to the presence of previous or overlapping diseases.

CONCLUSION

The present study may conclude that, in the individuals studied, specifically the child and youth population of the rural area of Santo Antônio de Jesus-Bahia-Brazil, there was no association of protection between helminth infection and allergic conditions, in fact, it is possible to suggest a increased risk related to eczema. Because it is a convenience sample, it is suggested that new studies be carried out with this and other populations of the region, to better evaluate and identify the peculiarities of the same.

On the other hand, it is important to highlight the high prevalence of intestinal parasitoses in this population, a possible reflection of the precarious conditions of basic sanitation and socioeconomic conditions of the communities where they live. In this case, it is necessary to investigate the local environment in search for answers to the results obtained, besides promoting more health education activities and charge the competent authorities for better housing conditions.

CONFLICT OF INTEREST

The authors declare that they have no competing interests.

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Contact Us: SIFT DESK
Deerpark Dr, #75, Fullerton,CA,92831,United States. E-mail: helpdesk@siftdesk.org