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ORIGINAL ARTICLE

Ascaris Lumbricoides Impact on House Dust Mite Sensitization and Bronchial Asthma Severity

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Abstract

Background: **Environmental allergens and intestinal parasites may share antigens that can modulate allergic immune responses. Cross-reactivity studies between common parasitic helminths and house dust mites impacting people are gaining popularity, especially in underdeveloped countries.**

Aim of the study: **The objective of this study is to study the relationship between *Ascaris lumbricoides* infection with or without treatment on mite sensitization as well as the pathogenic relationship between *Ascaris* and bronchial asthma, if any, and the consequent clinical implication on asthma severity.**

Patients and methods: **This study comprised 80 atopic asthmatic patients of moderate severity according to the Global Initiative for Asthma (GINA) guidelines classification in the outpatient clinic at Al-Hussein Hospital following their free and informed consent. They were classified into two groups: (group A) asthma patients without *Ascaris* infection and (group B) asthma patients with *Ascaris* infection. Total IgE, *Ascaris* antibodies, and specific serum IgE levels to house dust mites species *Blomia tropicalis* (Bt), *Dermatophagoides pteronyssinus (Dp),* and *Dermatophagoides farinae (Df)* were measured through enzyme-linked immunosorbent assay (ELISA). Following informed consent for scientific research from the Al-Azhar Ethics Committee for Scientific Research, patients and a control group were enrolled in this study.**

Results: **The findings revealed that there was a statistically significant difference between total IgE in patients with positive *Ascaris* antibodies and *Blomia tropicalis*-specific IgE.**

Conclusion: **In conclusion, asthma severity increased in Ascariasis patients associated with Blomia tropicalis.**

Keywords: Ascaris lumbricoides, Bronchial asthma, House dust mite

1. Introduction

It is estimated that approximately 1.5 billion people worldwide are infected with *Ascaris lumbricoides*. Oral contamination with embryonated eggs is the route of infection for humans, especially in low-income and unsanitary environments, where they are more likely to be infected at a young age. Increased serum levels of IgE production, a robust T-helper 2 (Th2) response, increased eosinophil cell count, and hypersecretion of mucus characterize immunity to *A. lumbricoides*, which is elicited by somatic and excretory−secretory antigens of larvae and gives protection by preventing intestinal parasite clearance and reinfection.[1]

Ascaris lumbricoides, a parasitic worm, is thought to infect about 1.5 billion individuals worldwide. Humans are most commonly infected through oral contamination with embryonated eggs, especially in low-income and filthy surroundings, where children are more likely to be exposed to parasites at an early age. Protection against *A. lumbricoides* is afforded by the immune system's reaction to the somatic and excretory-secretory antigens of larvae, manifested by high levels of IgE production, a powerful Th2 response, eosinophilia, and mucus hypersecretion.[2]

Whether infections with this parasite predispose to or guard against atopy is of scientific and practical relevance because most developing nations are located in the tropics, where inhabitants are

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naturally co-exposed to both *A. lumbricoides* and mites. Evidence from a number of research shows that mites are a major problem in the tropics for those with allergies,[3] where the climate is tropical. Six medically significant species can thrive,[4] mainly from *D. pteronyssinus* and *B. tropicalis* as the most abundant mites in the house dust.[5]

Although systematic reviews and meta-analysis found that *A. lumbricoides* was related to a considerably increased likelihood of asthma, the results are contentious.[6] Some population studies have found that infection is associated with an increased risk of IgE sensitization and asthma,[7] while in others it is protective.[8]

Allergies, which are very sensitive to allergen levels in the environment, are likely to differ between regions. This is likely why researchers have studied the impact of helminthic infections in the development of allergic disorders for so long. The studies that have been conducted in this area have gradually zeroed in on particular concerns and analyzed them utilizing a wide range of methodological approaches. The particulars of the Th2 mechanisms that are involved in the pathogenesis of parasite infections and allergies are among the most relevant aspects.[1] The role that allergies play in the body's defense against parasitic diseases[9] and the role that parasitic diseases play in the development of allergies and their clinical manifestations were studied in correspondence with Th2 activity.[10]

Although allergic disorders and helminth infections are separate medical conditions, studies conducted over the past several decades have shown that the two are linked. Both the nature of the connection and the underlying mechanisms are still up for debate. High levels of immunoglobulin E (IgE), eosinophilia, increase in mast cells, hyperresponsive mucus, and T cells that selectively release Th2 cytokines are all hallmarks of both these diseases.[11] Epidemiological studies demonstrate an inverse relationship between the frequency of allergic disorders and helminthiasis despite the fact that they both involve a similar immune response. Gold et al. (2005) found that whereas helminthic infections are on the decline in developed nations, they are widespread in rural areas and developing nations, and allergic disorders are on the rise in both.[12]

There is some evidence to support the hypothesis that helminth infections may confer a protective immunity against the development of allergy symptoms.[13] These as well as other pieces of epidemiological evidence point to a possible causal connection between helminthiasis and allergies. Chronic helminth infections have been shown to generate IgE responses that are cross-reactive to allergens found in home dust mites, which can result in reactions that are clinically irrelevant.[14]

Alternative Th2 responses have been hypothesized, with a focus placed on the role that IgG4, IL-10, dendritic cells, and other downstream components of the Th2 response played in the immunomodulatory capacity of helminths.

It is widely accepted that house dust mites (HDMs), including *Blomia tropicalis* (Bt), *Dermatophagoides pteronyssinus (Dp)*, and *Dermatophagoides farinae (Df)*, are significant contributors to the development of allergy disorders around the world.[15] However, the most common causes of helminthiasis are helminthic parasites, e.g. hookworms and *Ascaris lumbricoides (Al)* that may be found all over the world.[11]

House dust mites contribute to allergy responses especially bronchial asthma, so it is considered to be one of the major causative factors for the development of the disease.

Isolation and characterization of IgE-binding antigens from the agents that are responsible for the disease are necessary steps in the process of elucidating the molecular and immunological mechanisms that are involved in the pathogenesis of both allergic disorders and helminthiasis. To this point, certain helminthic antigens, such as tropomyosin, have[16] ABA-1-like protein[17], paramyosin[18] and glutathione-S-transferase.[19]

2. Patients and methods

This study comprised 80 atopic asthmatic patients classified according to the Global Initiative for Asthma ((GINA)) guidelines classification, selected from the outpatient clinic at Al-Hussein Hospital. Patients are known asthmatics and they attend the clinics for follow-up following their free and informed consent. They were classified into two groups: (group A) asthma patients without *Ascaris* infection and (group B) asthma patients with *Ascaris* infection. Total IgE, *Ascaris* antibodies (IgG), and specific serum IgE levels to house dust mites species *Blomia tropicalis* (Bt), *Dermatophagoides pteronyssinus* (Dp), and *Dermatophagoides farinae* (Df). Patient's serum samples were collected, 5 ml of venous blood was taken, and left to be clotted. Serum was collected and stored at −80 °C till the time of the assay. Serum samples were used to measure the specific IgE by enzyme-linked immunosorbent assay (ELISA) manufactured by Ridascreen Diagnostics, Darmstadt, Germany Art. No. A0041 Reagents and Art. No A0141 for Total IgE Reagents., while for *Ascaris* IgG kits from DRG International, Inc. USA Ref. No EIA-5854. Informed consent was obtained for scientific research from the

Al-Azhar Ethics Committee for Scientific Research before patients and a control group were enrolled in this study.

2.1. Statistical analysis

Continuous data, such as age, was displayed as mean and a standard deviation to simplify the display. In the case of qualitative data, such as sex, it was supplied in the form of percentages. Student's t-test was used to compare continuous data between two independent groups. For qualitative data Chi square test was used. The level of significance was set at 0.05, which is the smallest possible value. The statistical analysis was done using IBM SPSS Statistics, Version 22 for Windows.

3. Results

Table 1.

There is no statistically significant difference between the two studied groups regarding age Table 2, Fig. 1.

This table shows a statistically significant difference in total IgE between the studied groups regarding mite sensitization Table 3.

Table 1. Mean ± SD of age and total IgE of studied groups.

Age	Asthma with Ascaris ($n = 10$)	Asthma without Ascaris ($n = 70$)	*T* test	*P* value
Age (Mean ± SD)	39 ± 12	34 ± 10.5	1.3	0.17
Total IgE (Mean ± SD)	255.8 ± 244.9	210.8 ± 135.7	0.8	0.38

Table 2. Comparison between the studied groups in mite sensitization.

	Total IgE in Bt + ve	Total IgE in Df + ve	Total IgE in Dp + ve	ANOVA	*P* value
Ascaris + ve	474.5 ± 251	76.8 ± 48.1	143.3 ± 100.8	5.3	**0.03**
Ascaris -ve	259.7 ± 121	142.6 ± 74	180.5 ± 164	5.1	**0.008**

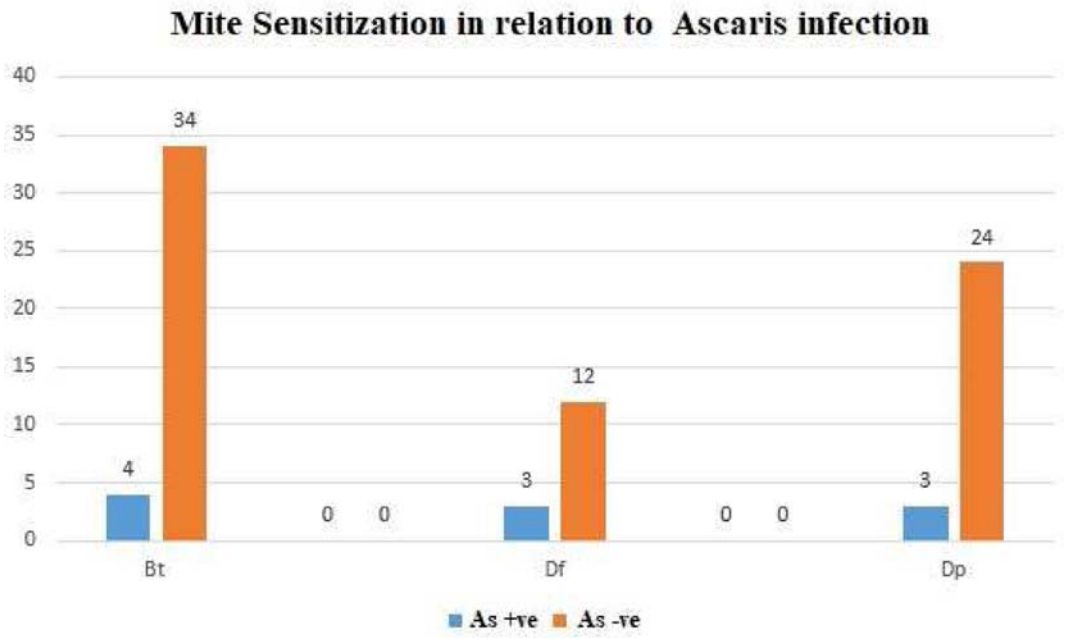

Fig. 1. Mite sensitization in relation to Ascaris infection.

Table 3. Comparison between Total IgE in different studied mite species.

	Ascaris + ve	*Ascaris* -ve	*t*-test	*P* value
Total IgE in Bt + ve	474.5 ± 251	259.7 ± 121	2.9	**0.0005**
Total IgE in Df + ve	76.8 ± 48.1	142.6 ± 74	1.4	0.17
Total IgE in Dp + ve	143.3 ± 100.8	180.5 ± 164	0.38	0.70

Table 4. Correlation between Ascaris infection and asthma severity.

Severity of asthma	*Ascaris* + ve	*Ascaris* -ve	Chi square	*P* value
Mild ($n = 35$)	5	30	0.84	0.65
Moderate ($n = 34$)	3	31		
Severe ($n = 11$)	2	9		

Table 5. Correlation between mite species and asthma severity.

Severity of asthma	Bt	Df	Dp	Chi square	*P* value
Mild ($n = 35$)	8	9	18		
Moderate ($n = 34$)	20	6	8	19.02	**0.001**
Severe ($n = 11$)	10	0	1		

This table shows a statistically significant difference in total IgE in *Ascaris*-positive and *Ascaris*-negative subjects with different mite species Tables 4 and 5.

4. Discussion

The estimation of IgE concentration in response to crude extracts is an essential method for establishing the sensitization profile of a particular population. It is also the first stage in the process of determining which allergens cause an individual's allergic reactions. The fact that allergic patients in this study consistently showed a high level of reactivity to HDM allergens is evidence that Bt, Dp, and Df allergens are clinically important as primary causes of allergic sensitization in asthmatic patients. The results obtained here are in agreement with ***Salvadore et, al,*** who studied early sensitization studies that were performed in the past indicating that Bt, Dp, and Df are important allergens that produce sensitization among allergic persons in the Philippines[20]

Moreover, the occurrence of *Ascaris*-specific IgE among individuals with respiratory allergy (73 %) was also reported in another tropical area by ***Medeiros and others.***[21]

Since several HDM species generally coinhabit their local environment (parallel sensitization) and dust mites have cross-reactive allergens, allergic persons often have numerous HDM allergen sensitizations. Regarding sensitization of ascariasis subjects to HDM allergens, our study agreed with the ***Gradette et. al.study,*** which found significant association between HDM and ascaris-specific IgE.[22]

In our results, total IgE in *Ascaris*-positive subjects is higher than that of *Ascaris*-negative subjects in patients sensitized to *Blomia tropicalis*. These findings agree with the ***Zakzukc et. al.*** findings who found that children who were allergic to *Ascaris* showed higher levels of the antibody IgE in response to the mite *B. tropicalis*. They used species-specific components to rule out the potentially confounding effect of cross-reactivity. They discovered that individuals who had IgE responses to ABA-1, which is a marker of nematode infection, also had increased IgE responses to Blo t 5 and Blo t 12, which are two allergens that are species-specific to *B. tropicalis*[23]

Regarding *Dermatophagoides pteronyssinus* and *Dermatophagoides farinae,* there is no statistically significant difference between *Ascaris*-positive and *Ascaris*-negative subjects, which mean there is no cross-reactivity between *Ascaris* and *Dp* or *Df*. These findings are in contrast with ***Buendía et, al,*** who confirmed that asthma risk variables included sensitivity to *Ascaris* and *Dermatophagoides pteronyssinus* extracts as well as a molecular component of *Ascaris*. As mites and *Ascaris* cross-react, chronic exposure to one may have increased primary sensitization from the other. *Ascaris* infection does not worsen bronchial asthma unless coupled with *Blomia tropicalis* as reported by the study carried out by ***Buendía et, al.***[24]

4.1. Conclusion

In conclusion, asthma severity increased in Ascariasis patients associated with *Blomia tropicalis*.

Statements

The authors have no conflicts of interest to declare that are relevant to the content of this article.

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The authors have no financial interest to declare in relation to the content of this article.

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