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ORIGINAL ARTICLE

LEVEL OF SERUM IgE DURING ATOPY WITH AND WITHOUT INTESTINAL PARASITIC INFECTIONS IN THE UNIVERSITY OF GONDAR TEACHING HOSPITAL, NORTHWEST ETHIOPIA

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ABSTRACT

***Background**: Recent studies have showen that controversial associations of chronic helminthic infections with allergic diseases as having protective and predictive roles. Lots of conflicts in answering such questions have continually arisen in recent years. This study aimed to determine the prevalence of intestinal parasitic infections, atopy and serum IgE level.*

***Methods:** A total of 225 patients were randomly selected from the Dermatology Outpatient Department at the University of Gondar Hospital, Ethiopia, from January - March 2006. A modified questionnaire of international study of asthma and allergies in children (ISSAC) was used to assess atopy, and skin scratch tests were done for common allergens. Stool specimen was collected and examined by the formol-ether concentration sedimentation technique. The serum IgE levels were quantified by total IgE ELISA kit. Simple descriptive statistics were used to explain the findings.*

***Results:** The prevalence of atopy was 40.9% (95% CI = 35.9% - 46.7%). The prevalence of intestinal parasitosis was 36.9% (95% CI = 29.8% - 44.4%). Lower prevalence of atopy was observed in individuals infected with any parasite, A. lumbricoides, S. stercoralis, Hookworm, and S. mansoni. The mean serum IgE level for positive prick test, self-reported atopy, and atopy was 2893 IU/ml, 2909 IU/ml, and 2914 IU/ml, respectively. The mean serum IgE level was 2785 IU/ml, 2714 IU/ml, 1613 IU/ml, 4020 IU/ml, 4415 IU/ml, and 4627 IU/ml for any parasites, A. lumbricoids, hookworm, S. stercoralis, S. mansoni, and E. histolytica, respectively.*

***Conclusion:** The results demonstrate a high prevalence of atopy and intestinal parasitosis. Atopy was inversely related to A. lumbricoides, S. stercoralis, Hookworm, S. mansoni, and E. histolytica infections. Both atopy and intestinal parasites caused higher mean serum IgE which was seen in all study participants with self-reported atopy and in skin scratch test positive study participants. A. lumbricoides, S. stercoralis, Hookworm, S. mansoni, and E. histolytica caused a higher mean serum IgE than the control study participants. The increased serum IgE level showed in G.lamblia, H. nana, and E. vermicularis infections without affecting the occurrence of atopy needs further study.*

***Key words:** atopy, serum IgE, intestinal parasites.*

INTRODUCTION

Intestinal parasites are a major enteric pathogen of children in many regions of the world, infecting nearly one-third of the global population (1). In contrast to the infections, there is a large international difference in the prevalence of atopic allergic diseases that appear to be much lower in tropical regions, particularly among rural populations (1-3). Although intestinal parasitosis is associated with a great degree of morbidity and malnutrition in many parts of the world (3), recent studies showed a protective effect of chronic helminthic infections on allergic diseases (4) and inflammatory diseases (4). Both allergy and helminthic infections are associated with elevated levels of immunoglobulin E (IgE), tissue eosinophilia and augmented T helper 2 (Th2)

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responses (5). High levels of serum IgE have also been detected in protozoal infections (6, 7). Apart from intestinal parasites, the whole gut microbial ecosystem has been shown to have some contribution in determining the development of allergic diseases (8). The immunological mechanism underlying the negative relationship between atopy and parasitic infection has been the center of debates (9). The blocking effects on the Fcε type I receptor of mast cells by non-specific polyclonal IgE have been proposed as one mechanism of protection against allergic diseases in chronic helminthiasis (10). Doubtful results have been reported on the saturation of Fcε type I receptor by polyclonal IgE because of its nature of elasticity (11, 12).

Then, how are helminths and other infections protective against allergic diseases? Is there a real negative association between allergy and infestations and infections? Lots of conflicts in answering these questions have continually been arising in recent years (13-15), including the eminent hygiene hypothesis (16).

In Ethiopia, several studies have been reported on allergy, serum IgE level, and allergy-parasitic infections among pre-school children (17-20) and school children (21, 22), asthmatic patients (23), adults (24), and patients of different cases (25). However, there is no report on the assessment and associations of serum IgE level during atopy with and without intestinal parasitic infections in patients who attended for dermatological care. Therefore, the aim of the study is to determine the prevalence of intestinal parasitic infections, atopy, and serum IgE level in patients attending the Dermatology Clinic of the University of Gondar teaching hospital, northwest Ethiopia.

METHODS

***Study design, area, and study participants*:** A cross sectional study was conducted in the Dermatology Outpatient Department of the University of Gondar teaching hospital between January and March 2006. The study participants were selected from patients who came to get services for different cases.

Sampling and sample size determination: All of the patients who visited the Dermatology Outpatient Department of the hospital during the study period were included in the study. Thus, out of 250 patients, data were collected from 225 eligible ones who were aged 15 years and above.

Socio-demographic and clinical data: A structured questionnaire containing questions about socio-demographic data, self reported respiratory symptoms of seasonal wheeze and/or rhinitis, recurrent or chronic flexural dermatitis, history of drug intake, and family history of allergic diseases were administered by physicians after the questions were translated into the local language. The following questions, taken and modified from the International Study of Asthma and Allergies in Childhood (ISAAC) module(26), were asked and clarified by a physician to appraise self or family history of atopy in each subject.

1. Have you had wheezing or whistling in the chest in the last 12 months?
2. Have you had a problem with sneezing or a runny or blocked nose in the last twelve months when you did not have cold or the 'flu?
3. Have you had an itchy rash that was on and off affecting one of the following places at any time: the folds of the elbows, behind the knees, in front of the ankles, under the buttocks, or around the neck, ears or eyes in the last twelve months?
4. Did any of your parents complain about one of the above symptoms or diagnosed to have asthma, hay fever, or eczema?

Skin scratch test: Skin scratch tests were done for five common types of allergens on the inner side of the forearm. The allergens used were mite extract (*Dermatophgoides pteronissimus*), dog fur, egg white, *Candida albicans*, and a mould Penicillium (Torii Pharm. Co. Ltd., Japan)**.** Fifty percent of glycerin and 5% of saline solution were used as negative control (Torii Pharm. Co. Ltd., Japan). The area to be tested was cleansed with alcohol and a gentle scratch was done with a lancet onto which drops of the allergens were added. The results were read after 20 minutes and considered positive (reactive) if there was a raised wheal or erythema at least 3mm wider than the control reaction (27). Study participants who had taken any antihistamines, sodium cromoglycate, or beta adrenergic blocking drugs within the preceding three weeks of the test were excluded. The atopy considered in our study was either self-reported in the last twelve months or detected in the positive skin scratch test.

Stool examination: Stool specimens were collected in clean stool cups and processed following standard procedures (28). The specimens were examined by direct microscopy in 0.85% saline to detect motile trophozoites. The formol-ether concentration technique was also employed to detect ova, larva and cysts of intestinal parasites. Two experienced laboratory technologists independently evaluated the stool microscopy of the patients. The direct microscopy

and formol-acetone concentration methods were used by considering as gold standard for trophozoites and ova, larva and cysts of intestinal parasites, respectively.

Determination of serum IgE levels: As previously described (29), the serum IgE levels were quantified by total IgE ELISA kit (IBL Immunobiological Laboratories, Hamburg, Germany) in accordance with the manufacturer's instructions. In brief, blood was drawn before the allergen / skin scratch/ tests were done and 10 ml serum samples or standard IgE were d pipetted in duplicates into wells of microtiter plates precoated with monoclonal mouse antihuman IgE antibody together with peroxidase conjugated antihuman IgE. After incubation for 30 min at room temperature, the plates were rinsed with diluted wash buffer to remove unbound material. Then a substrate solution (tetramethylbenzidine) was pipetted and incubated for 15 min to induce the development of color.

The reaction was terminated by the addition of a stop solution, and the resulting dye was measured in a spectrophotometer (Model 680 Microplate Reader, Bio-Rad Laboratories Inc., Japan) at a wave length of 450 nm against the substrate blank. The IgE concentration of the samples was read from a standard curve. Mean values of two separate determinations from each sample were used as serum IgE level of a particular study subject.

Statistical analysis: The data was entered, and analyzed using Epi Info for Windows 2000 Version 3.3. Simple descriptive statistical tests were used to explain the findings. Pearson chi-square was used to test the distribution of atopy in parasite infected and non-infected study participants.

Ethical consideration: Ethical approval for the study was obtained from the Ethics Committee of the University of Gondar, Ethiopia and the University of Tokushima, Japan**.** Specimens were taken and skin scratch test was done after consent was obtained from each study participant**.** Patients' clinical evaluation was managed following the routine patient management system of the Dermatology Clinic of the hospital, Gondar University. Emergency medical kit (availability of oxygen, facility for intravenous cannulation and intravenous fluids for rapid infusion in case of hypotension) and adrenaline for intramuscular injection were ready for managing a possible anaphylaxis. Participants were observed in the centre for at least 20 minutes following completion of the skin prick test for possible emergency management. A trained physician handled the skin prick test. However, none of the participants showed an emergency case for the test. A new sterile needle was also used for every prick to avoid cross contamination.

RESULTS

Demography**:** A total of 225 study participants with the mean age of 35 years (range 15-18 years) were included. Among these, 133(59.1%) were female.

Atopy**:** The prevalence of atopy (recurrent or chronic pruritic flexural skin condition, seasonal rhinitis, and self reported wheeze in the last 12 months or at least one positive skin scratch test) was 92(40.9%) (95% CI = 35.9% - 46.7%). Family history of atopy was reported in 10(4.4%) (95% CI = 1.9% - 8.6%) of the study participants.

Intestinal parasites**:** The prevalence of intestinal parasitosis was 83(36.9%) (95% CI = 29.8% - 44.4%), the most prevalent being infection with *Ascaris lumbricoides* 32(14.2%) followed by that of hookworm 25(11.1%), *Strongyloides stercoralis* 14 (6.2%), *Schistosoma mansoni* 10 (4.4%), *Entamoeba histolytica* 10(4.4%), *Giardia lamblia* 5(2.2%), *Hymenolepis nana* 4(1.8%), *Enterobius vermicularis* 4 (1.8%), *Trichiuris trichiura* 3(1.3%) and *Isospora belli* 1(0.4%). Dual infection was seen in 11.3% of the study participants. No case of three or more parasites was identified. The prevalence of atopy in study participants with parasites was compared with those without parasite which is summarized in (Table 1). Lower prevalence of atopy was observed among individuals infected with *A. lumbricoides* and *S. stercoralis*, *S. mansoni*, Hookworm, as well as in amoebiasis.

Serum imunoglobulin E**:** The total serum IgE level of the whole study population ranged from 69 IU/ml – 12202 IU/ml. The mean was 2151 IU/ml with a standard deviation of 917 IU/ml. The mean serum IgE level of the non-atopy, parasite negative group was 978 IU/ml (range: 69IU/ml – 8223 IU/ml with a standard deviation of 1779 IU/ml). The mean serum IgE level for positive prick test, self reported atopy, and atopy was 2893 IU/ml, 2909 IU/ml, and 2914 IU/ml, respectively. The mean serum IgE level for most prevalent parasites was measured and it was 2785 IU/ml, 2714 IU/ml, 1613 IU/ml, 4020 IU/ml, 4415IU/ml, and 4627 IU/ml for any parasite, *A. lumbricoids*, hookworm, *S. stercoralis*, *S. mansoni*, and *E. histolytica* respectively. The mean serum IgE level with respect to atopic status and parasite infection was compared with that of serum IgE in the non-atopy, parasite negative group and summarized in Tables 2 and 3.

Table 1- *Prevalence of atopy in parasite infected and non-infected study participants*

Parasites		Prevalence of Atopy n (%)			OR	CI	P-Value
		Yes	No.	Total			
Overall	Infected with any	39 (47.0)	44 (53.0)	83(100)	1.5	0.83-2.68	0.15
	Non-infected	53(37.3)	89(62.7)	142(100)			
Ascaris lumbricoides	*Infected*	9(28.1)	23(71.9)	32(100)	4.5	1.09-7.58	< 0.001
	Non-infected	15(7.8)	178(92.2)	193(100)			
Hookworm	*Infected*	11(44.0)	14(56.0)	25(100)	12.3	4.16-36.93	<0.001
	Non-infected	12(6.0)	188(94.0)	200(100)			
Strongyloids stercoralis	*Infected*	4(28.6)	10(71.4)	14(100)	9.0	1.93-40.4	<0.001
	Non-infected	9(4.3)	202(95.7)	211(100)			
Schistosoma mansoni	*Infected*	3(30.0)	7(70.0)	10(100)	11.1	1.86-62.5	<0.001
	Non-infected	8(3.7)	207(96.3)	215(100)			
Entamoeba histolytica	*Infected*	2(20.0)	8(80.0)	10(100)	10.5	1.19-78.6	<0.001
	Non-infected	5(2.3)	210(97.7)	215(100)			
Gardia lamblia	*Infected*	2(40.0)	3(60.0)	5(100)		not computed*	
	Non-infected	0(0.0)	220(100.0)	220(100)			
Hymenolopis nana	*Infected*	3 (75.0)	1(25.0)	4(100)		not computed*	
	Non-infected	2(0.9)	219 (99.1)	221(100)			
Enterobius vermicularis	*Infected*	2(50.0)	2(50.0)	4(100)		not computed*	
	Non-infected	1(0.5)	220(99.5)	221(100)			
Trichiuris trichiura	*Infected*	1(33.3)	2(66.7)	3(100)		not computed*	
	Non-infected	0(0.0)	222(100.0)	222(100)			
Isospora beli	*Infected*	1(100)	0(0.0)	1(100)		not computed*	
	Non-infected	0(0.0)	224(100.0)	224(100)			

** Due to low prevalence*

Table 2 - Mean serum IgE level of atopic study participants compared with controls

Study participants	**Serum IgE level (IU/ml)**		
	Minimum	Maximum	Mean
*Control**	69	8223	979
Positive prick test	70	12202	2893
Self reported atopy	70	12202	2909
Atopy	70	12202	2914

**Controls are non-atopy, parasite negative individuals*

Table 3 *- Mean serum IgE level of parasite infected study participants compared with controls*

Parasites	n (%)	Serum IgE level (IU/ml)		
		Minimum	Maximum	Mean
*Controls**	69 (30.7)	69	8223	979
Any parasite	83(36.9)	70	12202	2785
A. lumbricoides	32(14.2)	80	11770	2714
Hookworm	25(11.1)	70	9923	1613
S. stercoralis	14(6.2)	188	11770	4020
S. mansoni	10(4.4)	184	11770	4415
E. histolytica	10(4.4)	378	12202	4627
G. lamblia	5(2.2)	183	8323	3466
H.nana	4(1.8)	190	6898	3009
E. vermicularis	4(1.8)	198	5338	2697
T.trichiura	3(1.3)	430	1005	717
I. belli	1(0.4)	937	937	937

*Controls are non-atopy, parasite negative individuals

DISCUSSIONS

The prevalence of self reported atopy and positive skin scratch tests in the study population was higher compared with other studies in developing countries, 32% of atopy in Estonia (30), 35.3% rural vs. 22.5% urban of skin prick test in Gambia (31), and 22.0% of allergic sensitization in Latin America (14), despite the very low socioeconomic status and expected poor hygiene of these areas. Nevertheless the figure is still lower than that seen in developed countries (32, 33). Previous studies in Ethiopia showed a lower prevalence of atopy (34), demonstrating that the general increase in prevalence of atopy is universal, not particular to developed countries as argued by other authors (35).

The relatively lower prevalence of intestinal parasitosis compared with the higher prevalence of atopy is a clue for the preventive role of parasitic diseases against atopic diseases (36, 37) or vice versa (38). In our study lower prevalence of atopy was detected in generally infected study participants and in study participants found to be infected with *A. lumbricoids*, hookworm, *S. stercoralis*, and *S. mansoni.* Why some parasites have preventive roles while others do not is a matter of dispute (2) and needs further investigation. Both opposite (39) and similar (40) results have been found out in other studies. Also, whether atopy prevents parasitic infection or parasites protect the development of atopy (or the other way round) can not be concluded from our study as it is a cross sectional survey.

Although IgE is an important mediator in parasitic (41) and atopic diseases (42), its production is influenced by some genetic factors (42). This could be the reason why the control group in our study had higher level of serum IgE compared with reference ranges from the rest of the world (43-45). Total serum IgE level is significantly higher in atopics than non-atopic controls. This shows that total serum IgE level is an important marker for the presence of atopic diseases even though it is not specific.

Most intestinal parasites are thought to increase total serum IgE concentration (46). Some parasites, such as *S. stercoralis* and hookworm increase total serum IgE concentration to a great extent and others like *T. trichiura* to a lesser extent (46). Likewise, in this study, we found a higher level of serum IgE in patients infected with *A. lumbricoids*, hookworm, *S. stercoralis*, and *S. mansoni*. *G. lamblia* is generally thought not to stimulate the IgE immunologic system (47). However, there are reports that identify allergic reactions and raised IgE level in such infection (8).

Our study showed a high level of serum IgE in amoebiasis, but not in giardiasis. There are few studies which showed a detectable rise in serum IgE in invasive amoebiasis without significantly affecting the total serum level (49). Some other studies showed normal or decreased serum IgE in amoebiasis (48, 49). A high level of serum IgE in *E. histolytica* infected study participants of our study might imply the immunoregulatory role of this protozoon in inflammatory and allergic diseases. The insignificant total serum IgE in some of the helminths, although still higher than the control, may be because of either the low prevalence of these helminths in the study population or due to early infection. Taken together, the presence of higher levels of serum IgE in some parasitic infections which did not show any protective role for atopy might indicate that polyclonal IgE is not the only factor that prevents the development of atopic diseases in infected patients.

In conclusion, the results demonstrate a high prevalence of atopy and intestinal parasitosis. The prevalence of atopy is inversely related to *A. lumbricoides, S. stercoralis*, Hookworm, *and S. mansoni*, and *E. histolytica infections*. Both atopy and intestinal parasites caused higher mean serum IgE. This higher level was seen in all study participants with self reported atopy and also in skin scratch test positive study participants. Intestinal parasites, mainly *A. lumbricoides, S. stercoralis*, Hookworm, *S. mansoni, and E. histolytica* caused a higher mean serum IgE than the control study participants. The increased serum IgE level showed in *G.lamblia, H. nana, and E. vermicularis* infections without affecting the occurrence of atopy needs further study.

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