Original Article

Frequency of raised serum IgE Level in childhood atopic dermatitis

Ijaz Ahmed, Sarwat Nasreen
Department of Dermatology, Ziauddin University, Karachi.

Abstract

Objective: To see the frequency of raised serum IgE level in children with atopic dermatitis.

Methods: The study was conducted in the out patient department of Dermatology, "Ziauddin University", KDLB Campus Karachi, from 1st October 2005, till 30th September 2006. Patients belonging to both sexes, aged upto 15 years, clinically diagnosed as atopic dermatitis were enrolled. The clinical severity was graded as mild, moderate and severe forms. Sera of all these patients were tested for IgE levels by ELISA.

Results: The study comprised of 124 patients, including 73 males (59%) and 51 females (41%). A total of 86 patients (70%) had a raised serum IgE level from a cut off value of 87 IU/ml. A large number of patients suffered from moderate disease (47%), followed by mild form (33%) and severe disease (20%). Serum IgE levels were divided into 3 groups i.e. upto cut off value (87 IU/ml) accounting for 31%, followed by 88 to 1000 IU/ml (41%) and 1001 to 3000 IU/ml (28%). Of the severely affected 25 patients (20%), 20 (57%) had values ranging from 1001 to 3000 IU/ml while another 3 (6%) ranged less then 1000 IU/ml (P<0.001). Of those with moderate disease (47%), 13 patients (37%) had serum IgE levels ranging from 1001 to 3000 IU/ml, while 25 (49%) had levels less then 1000 IU/ml (P=0.24). Of those affected mildly (33%), 23 (45%) had values ranging from 88 upto 1000 IU/ml and 2 patients (6%) had levels from 1001 to 3000 IU/ml (P<0.001).

Conclusion: Majority of children suffering from atopic dermatitis have a raised serum level of IgE, which in turn correlates well with severity of the disease (JPMA 57:431:2007).

Introduction

Atopic dermatitis is a multifactorial disease, resulting due to an inter play of different exogenous and endogenous factors in genetically predisposed subjects. The International Study of Asthma and Allergies in Childhood showed that there was marked variation in the global prevalence of atopic dermatitis.[1] A child with atopy produces IgE antibodies after exposure to common environmental allergens.[2] Type I allergy represents the genetically determined immune defects that leads to an excessive formation of immunoglobulin E (IgE) antibodies against innocuous environmental allergens in these subjects.[3,4] IgE titers inturn correlate well with the severity of atopic dermatitis. Elevated serum IgE level occur in about 80 percent of patients with atopic dermatitis and are directed against a wide variety of antigens e.g. pollens,

moulds, foodstuff, house dust mites (HDM) and bacterial antigens. Patients with atopic dermatitis often show positive Prick test and RAST to food allergens such as egg, milk, wheat, fish, Soya and peanuts.[5-9] In children, IgE mediated food sensitivity is more commonly associated with atopic dermatitis than in adults. Several factors have been identified that suggest the occurrence of food allergy in infants and children with atopic dermatitis.[2] Approximately 40% of infants and young children with moderate to severe atopic dermatitis have food allergy.[6-10]

Despite a strong association of atopic dermatitis with raised serum level of IgE, to our knowledge no relevant study has been published in our country. The current study was aimed to observe the frequency of raised serum IgE level in children with atopic dermatitis and to correlate the serum levels with severity of the disease.

Patients and Methods

The study was conducted in the outpatient department of Dermatology, "Ziauddin University", Kemari Campus Karachi, from 1st October 2005, till 30th September 2006. Patients belonging to both sexes and aged upto 15 years were included in the study however, infants were ruled out. Patients with any other dermatological and systemic problems were also excluded. After a detailed history and clinical examination, a clinical diagnosis of atopic dermatitis was made based on Hanfin and Rajika's diagnostic criteria.[11] Only clinically diagnosed cases of atopic dermatitis were registered. The clinical severity was graded as mild (localized chronic forms with <10% of the body surface area involved), moderate (disseminated lesions over trunk and extremities), and severe forms (e.g., more generalized eczema). The enrolled patients were also studied age wise. A written consent was taken from the parents for the study. In addition to routine investigations, any relevant investigations where required were carried out as well. These included scraping for fungus, swabs for culture and sensitivity, patch test, biopsy and histopathology. Sera of all these patients were tested for IgE levels by ELISA and their levels were graded to correlate with severity of the disease. A similar number of age matched controls were also investigated. All the findings were recorded on a preformed proforma. The results were compiled, tabulated and analyzed, using chi square test for association between disease severity and serum IgE levels..

Results

The study comprised of 124 patients, including 73 males (59%) and 51 females (41%). The minimum age of presentation was 1 year and maximum 15 years, the mean age being 7.2 ± 2.9 years. The family history of atopy was positive in 68% and personal history in 32% of the enrolled subjects. Maximum number of patients (66%) in the age group up to 5 years; followed by the 6-10 years group accounting for 29% and another 5% were 10-15 years old. The most frequent sites of involvement were cubital and popliteal fossae, 52% and 48% respectively. The other sites involved were face, neck, arms, hands, trunk, legs and feet.

Table. Association of diseaseseverity and serum IgE levels (IU/ml) cut off value 87 IU/ml (n=124).

Disease severity	Upto 87 IU/ml		88-1000 IU/ml		1000-3000 IU/ml		Total		P-value
	n	%	n	%	n	%	n	%	
Mild	16	42	23	45	2	6	41	33	<0.001
Moderate	20	53	25	49	13	37	58	47	0.24
Severe	2	5	3	6	20	57	25	20	<0.001
Total	38	31	51	41	35	28	124		

* Fischer exact test was used where cell value less than 5.

Table shows the disease severity with serum IgE levels, 86 patients (70%) had a raised serum IgE level considering the cut off value to be 87 IU/ml. The remaining 38 patients (30%) had a serum IgE level below 87 IU/ml. Only one member of the control group showed an elevated serum IgE level from the base line.

Serum IgE levels were divided into 3 groups i.e. upto cut off value (87 IU/ml) accounting for 31%, followed by 88 to 1000 IU/ml (41%) and 1001 to 3000 IU/ml (28%). The highest number of patients 58 (47%) suffered from moderate disease, followed by mild disease 41 (33%) and severe disease 25 (20%) patients.

Of the severely affected 25 patients (20%), 20 (57%) had high values ranging from 1001 to 3000 IU/ml while another 3 (6%) ranged less then 1000 IU/ml but more then 87 IU/ml (P<0.001). The remaining 2 patients (5%) had normal serum IgE levels. Among the 58 patients with moderate disease (47%), 13 (37%) had high serum IgE levels ranging from 1001 to 3000 IU/ml, while 25 (49%) patients had elevated levels between 88 and 1000 IU/ml (p=0.24). All the other 20 (53%) patients had normal serum IgE level. Of those affected mildly, 16 (42%) patients had normal levels of IgE, while 23 (45%) had values ranging from 88 upto 1000 IU/ml and 2 (6%) patients had elevated levels from 1001 to 3000 IU/ml (P<0.001) (Table).

Discussion

IgE responses play a critical role in the pathogenesis of atopic dermatitis as well as other allergic disorders.[12,13] IgE synthesis is in excess in atopic patients due to an inherent genetically determined immune defect in response to different environmental agents.[14-16] The two subtypes of T helper cells i.e. Th1 and Th2 control the production of IgE antibodies by a respective inhibitory and excitatory effect

on B-lymphocytes. However, in atopics, the excitatory effect of Th2 cells overcomes the inhibitory effect of Th1 cells leading to an excessive production of IgE antibodies.[17] The decreased number of Ts cells adds to the excessive production of IgE antibodies as these cells have an important inhibitory influence on B cells. These defects leading to the loss of inhibitory influence on B-lymphocytes are genetically determined. The antigens, which stimulate an excessive IgE synthesis include: egg white, cow milk, soya, wheat, rye, barley, pollens, HDM (House dust mite) and staphylococcus aureus.[18]

In children, IgE mediated food sensitivity is more commonly associated with atopic dermatitis than in adults. Several factors have been identified that suggest the occurrence of food allergy in infants and children with atopic dermatitis.[2] Elimination of suspected dietary factors responsible for excessive IgE synthesis results in decreased serum level of IgE against the particular antigen.[18]

About 80% of the patients with atopic dermatitis have an elevated level of serum IgE, which is directly proportional to severity of the disease. Normal persons may have similar increases in the serum IgE levels. On the contrary, atopic subjects may have normal levels of serum IgE.[19] Thus, it can be said that serum IgE may not be the primary stimulus to the signs and symptoms of atopic dermatitis but can exacerbate the disease. Moreover, the inflammatory disease is believed to be a consequence of IgE mediated release of mediators from the mast cells.[19]

In the current study, the IgE levels were raised in 70% of the patients, which is almost consistent with the reports in literature.[6-10] Somos Z et al[10] reported 63.6% of his patients having a raised serum IgE level and 85% of these cases had the response due to exogenous factors. Among the environmental factors responsible for the excessive antibody production, food sensitivity is more common in children then in adults.[6-10]

Total serum IgE level determination is a crude method for screening of atopic disease. Normal levels of serum IgE do not rule out the presence of atopic disease while elevated levels may in 20-30% of cases not be associated with atopic disease. Thus, it is difficult to set an exact level that always indicates atopy, below which it is always ruled out.

Zetterstrom O et al[20] determined that higher the serum IgE level, more likely is the presence of atopy. Laske N and Niggemann B[21] in their study also suggested that serum IgE levels correlate with the degree of eczema. The observations of our study were similar with serum IgE levels being raised in children with atopic dermatitis, which correlates well with the disease severity. Nomura I[19] and Schultz Larsen F[22] have also claimed the correlation of severity of the disease with serum IgE levels. However, most studies have concluded that the spread of IgE values is very wide and reliable upper limits distinguishing groups i.e. non-atopic and atopic could not be described. On the contrary, Weber M B et al[23] reported that although IgE levels were higher in severe atopic dermatitis, their study did not demonstrate a trend toward greater levels in patients with severe eczema as compared with mild eczema. Normal persons may have similar increases in the serum IgE levels.

The level of specific IgE to a food allergen is best used together with the clinical history in the diagnosis of IgE-mediated food allergy in such children.[24] A recent study by Bunkowski et al[6] indicated that serum IgE level might also be important in monitoring the severity of AD and to aid in the evaluation of treatment. Dhar S et al[25] claim that the duration of the disease or the chronicity of the eczema does not correlate with IgE levels. Moreover, the elevation of serum IgE is also confounded by association with other disease states such as parasitic diseases, neo-plastic diseases, as Hodgkin's disease, infectious diseases, allergic bronchopulmonary aspergillosis, HIV infection, and immune deficiency disorders as IgE myeloma, hyper IgE syndrome and Wiscott Aldrich syndrome.

Conclusion

Majority of children suffering from atopic dermatitis have a raised serum level of IgE, which in turn correlates well with severity of the disease.

References

1. Michael SG, Andrew SK. Atopic disease in childhood. MJA 2005; 182: 298-304.
2. Cookson WO, Ubhi B, Lawrence R, Abecasis GR, Walley AJ, Cox HE, et al. Genetic linkage of childhood atopic dermatitis to psoriasis susceptibility loci. Nat Genet 2001: 27:372-3.
3. Casolaro V, Georas SN, Song Z, Ono S J. Biology and genetics of atopic disease. Curr Opin Immunol 1996; 8: 796-803.
4. Hopkin JM. Mechanisms of enhanced prevalence of asthma and atopy in developed countries. Curr Opin Immunol 1997; 9: 788-92.
5. Leung DY, Rhodes AR, Geha RS, Schneider LC, Ring J. Atopic dermatitis, atopic eczema. In Dermatology in General Medicine. Ed Fitzpatrick TB, Eisen AZ, Wolff K, Freedberg IM, Austen KF. 1993 4th Ed. McGraw-Hill, New York 1993; pp 1543.
6. Bunkowski R. Prevalence and role of serum IgE antibodies to the Staphylococcus aureus-derived super antigens SEA and SEB in children with atopic dermatitis. J Allergy Clin Immunol 1999; 103: 119-24.
7. Nissen D. IgE-binding components of staphylococcal enterotoxins in patients with atopic dermatitis. Ann Allergy Asthma Immunol 1997; 79: 403-8.
8. Paller AS. Atopic Dermatitis: In Current therapy in allergy, immunology and rheumatology; Fifth Ed Edited by Liechtenstein LM and Fauci AS. 5th Edition 1996; pp 83-6.
9. Sicherer S, Sampson H. Food hypersensitivity and atopic dermatitis: pathophysiology, epidemiology, diagnosis and management. J Allergy Clin Immunol 1999; 104:114-22.
10. Somos Z, Schneider I. Serum and secretary immunoglobulins in atopic dermatitis. Orv Hetil 1993; 134: 1359-61.

11. Hanifin JM, Rajka G. Diagnostic features of atopic dermatitis. Acta Dermatol Venereal 1980; Suppl 92: 44-7.

12. Leung DY. Pathogenesis of atopic dermatitis. J Allergy Clin Immunol 1999; 104:S99-108.

13. Leung DY. Role of IgE in the treatment of allergic diseases. Pediatric Res 1993; 33: 856-62.

14. Saeki H, Kawata S, Nakagowa H, Etoh T, Sawa S, Juji T. HLA and atopic dermatitis with serum IgE titers. J Allergy Clin Immunol 1994; 94 : 575-83.

15. Frue M. Atopic dermatitis: immunological abnormalities and its background. J Dermatol Scien 1994; 7:159-68.

16. Horseman HL, Harvima IT, Jarvii KA, Harrima RJ, Horseman HM. Mast cells are one major source of IL-4 in atopic dermatitis. Br J Dermatol 1994; 131:348-53.

17. Urisu A, Kondo Y, Wada E, Tsunita M, Yasaki T. Specific IgE antibody and serum ECP in children with atopic dermatitis alone. Acta Paediatr Jpn 1994; 36:146-9.

18. Agata H, Kondo K, Fukotomi O, Schneider S. Effect of elimination of diets on food specific IgE antibodies lymphocyte proliferation responses to food allergens in atopic patients; exhibiting sensitivity to food allergens. J All Clin Immunol 1993; 91:549-51.

19. Nomura I, Tanaka K, Tomita H, Katsunuma T, Ohya Y, Ikeda N, et al. Evaluation of the staphylococcal exotoxins and their specific IgE in childhood atopic dermatitis. J Allergy Clin Immunol 1999; 104: 441-6.

20. Zetterstrom O, Johansson SG. IgE concentrations measured by PRIST in serum of healthy adults and in patients with respiratory allergy. A diagnostic approach. Allergy 1981; 36: 537-47.

21. Laske N, Niggemann B. Does the severity of atopic dermatitis correlate with serum IgE levels? Pediatr Allergy Immunol 2004: 15: 86-8.

22. Schultz LF. The epidemiology of atopic dermatitis. Monogr Allergy 1993; 31: 9-11.

23. Hill DJ, Hosking CS, Reyes-Benito LV. Reducing the need for food allergen challenges in young children: a comparison of in vitro with in vivo tests. Clin Exp Allergy 2001; 31: 1031-5.

24. Weber BM, Petry V, Weis L, Mazzotti NG, Cestari TF. Evaluating the relation between pruritus, serum IgE levels and severity of clinical manifestations in atopic dermatitis patients. An Bras Dermatol 2005:80:365-96.

25. Dhar S, Malakar R, Chattopadhyay S, Dhar S, Banerjee R. Correlation of the severity of atopic dermatitis with absolute eosinophil counts in peripheral blood and serum IgE levels. Int J Dermatol 2005: 71: 246-9.