ORIGINAL ARTICLE

Atopic Dermatitis and its Correlation with Eosinophil Count and Serum IgE Levels - A Case Control Study

Swapna S. Khatu[1], Nitin D. Chaudhari[2], Nachiket M. Palaskar[3], Aditya R. Holani[4], Garima L. Balpande[5], Mahak Kukreja[6], Gaurav H. Khandait[7] and Rajvardhan M. Bagane[8]
Department of Dermatology[1, 2,3,4,5,6,7,8] Smt. Kashibai Navale Medical College and General Hospital, Off Mumbai-Banglore Highway, Narhe, Pune-411041, Maharashtra, India.

Abstract:

Introduction:

Atopic dermatitis (AD) is a chronic, highly pruritic inflammatory skin disease, and is one of the most common skin disorders in children. The main immunological abnormalities are excessive formation of IgE with a predisposition to anaphylactic sensitivity, some decrease in susceptibility to delayed hypersensitivity, abnormalities in expression of surface molecules in antigen presenting cells, and dysregulation of cytokine mediators. This study was conducted to demonstrate positive correlation of the severity of atopic dermatitis with the absolute eosinophil count and serum IgE levels.

Materials and Methods:

It was a hospital-based case-control, non-interventional study that was conducted in the department of dermatology of a tertiary care hospital over a period of 18 months. Total 61 patients of endogenous eczema were studied. The statistical package for social sciences (SPSS) for Windows version (16.0) was used to analyse the data (SPSS Inc., Chicago, IL). Statistical significance was declared at $p < 0.05$ or mentioned otherwise.

Results:

Out of 61 patients, 29 were diagnosed with atopic dermatitis and 32 had non-atopic childhood eczema. Mean age of onset of atopic dermatitis was 4.7 yrs. Male to female ratio of 1.41:1 was observed.

As severity of eczema increased, serum IgE levels and eosinophil count also increased significantly in atopic patients.

Discussion and Conclusion:

Eosinophil counts and serum IgE levels are valid prognostic indicators for atopic dermatitis. As eosinophil count is a simple and inexpensive test when compared to serum IgE levels, it can alone be used as a prognostic indicator in patients with atopic dermatitis especially in resource restricted settings.

Key Words: Atopic dermatitis, Eosinophil, IgE

Introduction:

Atopic dermatitis (AD) is a chronic or chronically relapsing highly pruritic inflammatory skin disease, and is one of the most common skin disorders in children.[1]The rash is characterized by itchy papules (occasionally vesicles in infants) that become excoriated and lichenified, and typically have a flexural distribution.[2,3,4,5] The disorder results in significant morbidity and adversely affects the quality of life.[6] Not only are patients affected by the social stigma of a visible skin condition, but the intense itching characteristic of the disease often leads to skin trauma and significant sleep disturbances.

Atopic dermatitis is a chronic relapsing eczematous skin disease characterized by pruritus and inflammation and accompanied by cutaneous physiological dysfunction, with a majority of the patients having a personal or family history of "atopic diathesis".

The term "atopic diathesis" refers to the presence of allergic rhinitis, bronchial asthma or AD.

The definitive diagnosis of atopic dermatitis requires the presence of all three of the following features: pruritus, typical morphology and distribution, and chronic and chronically relapsing course.[7] The pathogenesis of atopic dermatitis is not completely understood. However, the disorder appears to result from the complex interaction between defects in skin barrier function, immune dysregulation, and environmental and infectious agents.[8,9,10] Skin barrier abnormalities appear to be associated with mutations within or impaired expression of the filaggrin gene, which encodes a structural protein essential for skin barrier formation. The skin of individuals with atopic dermatitis has also been shown to be deficient in ceramides (lipid molecules) as well as antimicrobial peptides such as cathelicidins, which represent the first-line of defense against many infectious agents. These skin barrier abnormalities lead to transepidermal water loss (passage of water from inside the body through the epidermal layer of the skin to the surrounding atmosphere) and increased penetration of allergens and microbes into the skin. The infectious agent most often involved in atopic dermatitis is *Staphylococcus aureus*, which colonizes in approximately 90% of AD patients. Defective innate immune responses also appear to contribute to increased bacterial and viral infections in patients with atopic dermatitis. This interplay of factors leads to

T cell responses in the skin (initially a predominantly T helper-2 [Th2] response and later a predominantly Th1 response) with resultant release of chemokines and proinflammatory cytokines (e.g., interleukin [IL]-4, IL-5 and tumour necrosis factor) that promote immunoglobulin E (IgE) production and systemic inflammatory responses, leading to pruritic inflammation of the skin. The main immunological abnormalities are excessive formation of IgE, with a predisposition to anaphylactic sensitivity, some decrease in susceptibility to delayed hypersensitivity, abnormalities in expression of surface molecules in antigen presenting cells, and dysregulation of cytokine mediators. The severity of atopic dermatitis has some positive correlation with the eosinophil count and serum IgE levels,[3,4] but this is not a consistent observation. Hence, we performed a study to elucidate the correlation between the severity of AD, the eosinophil count in the blood and the serum IgE levels. The main objective of this was; to evaluate clinical patterns of childhood eczema, to identify the cases of atopic dermatitis among patients of childhood eczema using Hanifin and Rajka's criteria and to study relation of serum IgE levels and eosinophil counts with the severity of atopic dermatitis.

Material and Methods:

It was a case-control, non-interventional study that was conducted in the department of dermatology of a tertiary care hospital over a period of 18 months. We included patients below 14 years of age, those diagnosed to have childhood eczema and patients willing to comply with study procedures. We excluded patients suffering from immunodeficiency disease, patients of eczema suffering from systemic illness, exogenous eczema, patients taking treatment for eczema and those who were not willing to comply to study procedures. Written consent was obtained from the subjects or their parents before enrollment.

After a detailed history and dermatological examination, patients were divided into 2 groups according to Hanifin and Rajka's criteria:-first group comprising patients of atopic dermatitis and control group comprising of non-atopic dermatitis patients. In those with atopic dermatitis, surface area of involvement and SCORAD (Scoring system designed by the European Task Force on Atopic Dermatitis to measure the severity of atopic dermatitis) index were calculated, epidemiological and clinical features of atopic dermatitis were studied and compared with controls. The total serum IgE levels and eosinophil counts were obtained in all patients (cases and controls). Relation between SCORAD index, serum

IgE level and eosinophil count in patients of atopic dermatitis was determined.

Hanifin and Rajka's Criteria:

Major Criteria:

Must have three of the following:

Pruritus, Typical morphology and distribution flexural lichenification in adults & facial and extensor involvement in infancy, Chronic or chronically relapsing dermatitis and Personal or family history of atopic dermatitis.

Minor criteria:

Must also have three of the following:

Xerosis, Ichthyosis / Hyperlinear palms / Keratosis pilaris, IgE reactivity, Early age of onset, Tendency for cutaneous infections, Elevated serum IgE, Tendency to nonspecific hand foot dermatitis, Nipple eczema /cheilitis, Recurrent conjunctivitis, Dennie – Morgan infraorbital folds, Keratoconus anterior subcapsular cataract, Orbital darkening, Facial pallor / erythema, Pityriasis alba, Itch when sweating, Intolerance to wool and lipid solvents, Perifollicular accentuation, Food hypersensitivity, Course influenced by environmental or Emotional factors, White dermographism.

SCORAD index:

It is a Scoring system designed by the European Task Force on Atopic Dermatitis to measure the severity of atopic dermatitis.

Five clinical signs viz. erythema, vesiculation, excoriation, crusting and edema are evaluated each of these signs with four scores: 0= absent, 1= mild, 2= moderate, 3= severe. It ranges from a minimum value of 0 to a maximum of 15.

Surface area of involvement of the disease was calculated using Wallace's Rule of Nine.

IgE Reference range & units:

<1 years: 00 - 29 IU/ml,1-2 years: 00 - 49 IU/ml, 2-3 years: 00 - 45 IU/ml,3-9 years: 00 - 52 IU/ml, Adults: 00 - 87 IU/ml.

Eosinophil count - 1- 6 %

The data were entered into SPSS version 21 for analysis. Data collected were coded and described as frequency and percentage for qualitative data and means and standard deviation for quantitative data. Statistical test used were Chi square test or Fisher test for nominal / non-parametric data, whereas for interval data- unpaired t test was used. Pearson's correlation coefficient was used to observe relationship between severity of atopic dermatitis, eosinophil count and serum IgE levels. We have included 74 cases of childhood eczema out of which 61 patients were included in case control study, 9 patients refused blood investigation and 4 samples were hemolysed.

Results:

A total of 74 cases of childhood eczema were enrolled out of which 61 patients were included in case control study, 9 patients refused blood investigation and 4 samples were hemolysed. Out of these 61 patients, atopic dermatitis was seen in 29 children (cases) andnon-atopic dermatitis in 32 children (controls).

1) Patterns of eczemas in both groups (cases and controls) were studied and most common type of eczema observed was pityriasisalba in 33 (44.6%) pediatric patients. (Table1)

2) Age of onset and duration of eczema- the mean age of onset of atopic dermatitis was found to be 57.45 monthsin cases and 65 months in controls; whereas the mean duration was 45.14 months in cases and 36.06 months in controls.

3) Sex Distribution- Among the cases, 58.60% were males and 41.40% were females; whereas in controls, 40.60% were males and 59.40% were females. Male to female ratio in atopic individuals was 1.41:1, with slight male predominance.

4) Prevalence of various types of eczema- we observed that P. alba (p=0.034) and foot eczema (p=0.00) were more common in atopic patients while pompholyx and prurigonodularis were more common in non-atopic patients. (Table 2)

5) Incidence of eosinophilia- we found that 72.4% of atopic patients showed eosinophilia, while only 25% of non-atopic eczematous patients showed evidence of eosinophilia, which was statistically significant ($p = 0.00$). (Table3)

6) Comparison of mean eosinophil count and serum IgE levels - we found that eosinophil count was significantly raised in patients with atopic dermatitis with a mean of 9.28%. Similarly, we observed that Serum IgE levels were raised in both atopics and non-atopics but levels were significantly higher in atopic patients ($p = 0.001$). (Table 4)

7) Relationship between SCORAD index and serum IgE levels - it was observed that as severity of eczema (SCORAD index) increases, IgE level increases with correlation coefficient of 0.7 which is statistically significant ($p = 0.001$). (Figure 1)

8) Relationship between eosinophil count and serum IgE levels - there was significant positive correlation between serum IgE levels and eosinophil count with a correlation coefficient of 0.5 ($p = 0.001$). (Figure 2)

Table No.1: Pattern of eczema in both groups (Cases and controls)

Type of eczema	Percentage of cases
Foot eczema	16.2%
Follicular eczema	6.8%
Hand eczema	1.4%
Hand Foot eczema	5.4%
Pompholyx	17.60%
Nummular eczema	21.60%
Nipple eczema	2.7%
Lichen simplexchronicus	6.8%
P. Alba	44.6%
Perioral dermatitis	5.4%
Prurigonodularis	9.5%

Table No. 2: Prevalence of various types of eczema

Type of eczema	Percentage of cases	Percentage of controls
Foot eczema	31	9.4
Follicular eczema	6.9	6.3
Hand eczema	0	3.1
Hand Foot eczema	3.4	3.1
Pompholyx	13.8	18.8
Nummular eczema	24.1	21.9
Nipple eczema	0	3.1
Lichen simplex chronicus	10.3	6.3
Pityriasis Alba	79.3	18.8
Perioral dermatitis	3.4	6.3
Prurigonodularis	3.4	15.6

Table No. 3: Incidence of eosinophilia

	Eosinophilia present	Eosinophilia absent
Cases	72.4%	27.6%
Controls	25%	75%

Table No. 4: Comparison of mean eosinophil count and serum IgE levels in cases and controls

	Mean Eosinophil count (%)	Mean serum IgE levels (IU/ml)
Cases	9.28	2509.03
Controls	3.09	254.56

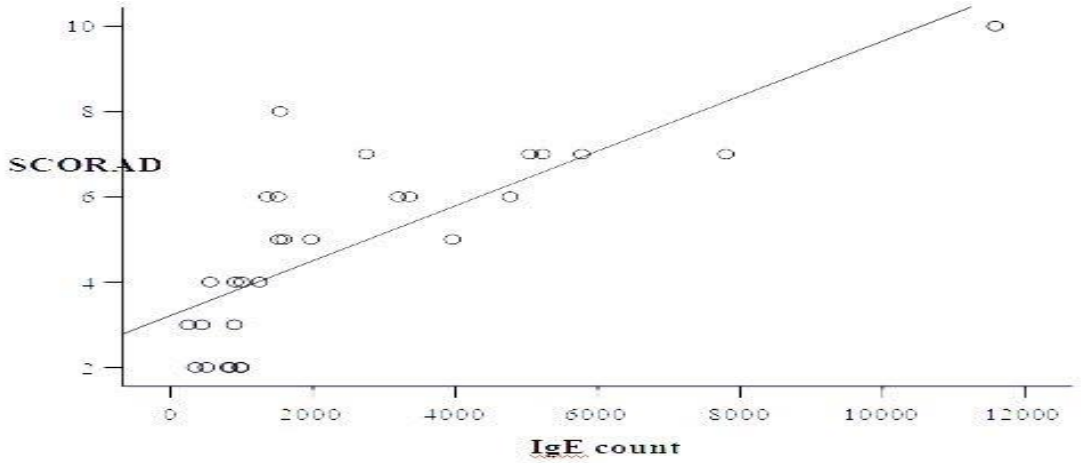

Figure 1: Relationship between SCORAD index and serum IgE levels

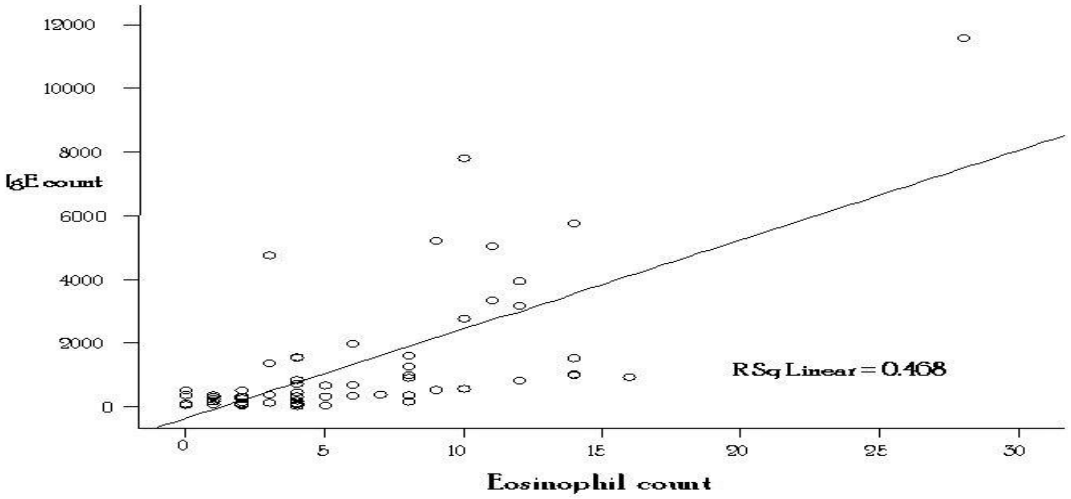

Figure 2: Relationship between eosinophil count and serum IgE levels.

Discussion:

Immunoglobulin E (IgE) has unique properties among immunoglobulin isotypes. It is present in human serum in very small amount; its serum concentration may increase several folds in response to specific stimuli. The levels are raised in allergic diseases like allergic rhinitis, allergic bronchial asthma, atopic dermatitis and urticaria.[11] A child with atopy produces IgE antibodies after exposure to some environmental allergens. Elevated serum IgE level occurs in around 80% of patients with atopic dermatitis and are directed against a variety of antigens e.g. pollens, moulds, foodstuff, house dust mites and bacterial antigens. Patients with atopic dermatitis show positive Prick test and RAST to food allergens such as egg, milk, wheat, fish, soya and peanuts. In atopic dermatitis the partial loss of the cutaneous barrier function, due to low ceramide levels and reduced filaggrin function, facilitates the transepidermal water loss and the penetration of environmental antigens, resulting in a specific, IgE-driven, allergic skin inflammation. IgE activates key effector cell types involved in allergic inflammation and its contribution to some of other allergic diseases in which patients are sensitized to allergens and have elevated levels of IgE have been investigated.[12]

In this study the mean age of onset of atopic dermatitis was 4.7 years. Sandipan Dhar et al[13] also found similar observation with a mean age of onset of 4.55 years. However, Basnet et al [11] found a higher mean age of onset at 9.03 years. In our study male predominance was seen with male to female ratio of 1.41:1.SandipanDhar et al[13] also found similar observation with predominance of males over females. In this study it was found that pityriasisalba and foot eczema were common in atopic patients while pompholyx and prurigonodularis were common in non-atopic patients. In this study 72.4% atopic patients showed eosinophilia, while only 25% of non-atopic eczematous patient showed evidence of eosinophilia. This revealed eosinophil count was significantly raised in cases of atopic dermatitis. Serum IgE levels were raised significantly in atopic patients, as severity of eczema (SCORAD index) increases with correlation coefficient of 0.7 which is statistically significant. As severity of eczema (SCORAD index) increases, eosinophil count increases with correlation coefficient of 0.3 which is also statistically significant. Body surface area involvement had no significant correlation with severity of eczema, serum IgE levels andeosinophil counts. There was a significant positive correlation between serum IgE levels and eosinophil counts. Ijaz Ahmedet al[14] found similar findings that children suffering from atopic dermatitis have a raised serum level of IgE, which in turn correlates well with severity of the disease.

Very high eosinophil counts were common in severe cases of AD who had a personal or family history of respiratory atopy, while normal or moderately elevated counts were obtained in severe cases of ‘pure’ atopic dermatitis who had neither a personal nor a family history of respiratory atopy. It was suggested that disease severity and personal or family history of respiratory atopy are important factors in determining high blood eosinophil levels in atopic dermatitis.[15]

In atopic dermatitis, a Th1/Th2 imbalance has been reported, and interleukin (IL)-13 seems to play a pivotal role in the inflammatory network. The elevated IgE response and eosinophilia observed in patients with atopic dermatitis may reflect increased responses of type 2 T-helper (Th2) cytokines with a concomitant decrease in interferon-gamma (IFN-gamma) production. However, the cross-regulation of Th1/Th2 derivation and function in AD patients are incompletely characterized. Kumar et al[16] studied clinical features, absolute eosinophil count and total IgE level and their association with severity of AD. The study found that total IgE increased significantly in about 66% patient and directly correlated with the severity of the AD.

Limitations:
Due to small sample size, the alteration of eosinophil count and serum IgE levels with treatment could not be studied.

Conclusion:
Eosinophil counts and serum IgE levels are valid prognostic indicators for atopic dermatitis. Eosinophil count is a simple and inexpensive test when compared to serum IgE levels, it can alone be used as a prognostic indicator in patients with atopic dermatitis especially in resource restricted settings.

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Conflict of Interest - Nil

Sources of Support - Nil

References:

1. Krakowski AC, Eichenfield LF, Dohil MA. Management of atopic dermatitis in the pediatric population. Pediatrics. 2008;122:812–824.
2. Ohman S, Johansson SG. Immunoglobins in atopic dermatitis, with special reference to IgE. Acta Dermato-Venereologica 1974;54:193-202.
3. Ohman S, Johansson SG. Allergen-specific IgE in atopic dermatitis. Acta Dermato-Venereologica 1974;54:283-290.
4. Jones HE, Inouye JC, McGerity JL, Lewis CW. Atopic disease and serum immunoglobin-E. British Journal of Dermatology 1975;92:17-25.
5. Uehara M. Family background of respiratory atopy: a factor of serum IgE elevation in atopic dermatitis. Acta Dermato-Venereologica Suppl. (Stockh) 1989; 144:78-82.
6. McKenna SP, Doward LC. Quality of life of children with atopic dermatitis and their families. Current Opinion in Allergy Clinical Immunology 2008; 8:228–231.
7. Dhar S, Banerjee R. Atopic dermatitis in infants and children in India. Indian Journal of Dermatology, Venereology and Leprology 2010; 76:504-513.
8. Egawa G, Kabashima K. Multifactorial skin barrier deficiency and atopic dermatitis: essential topics to prevent the atopic march. Journal of Allergy and Clinical Immunology 2016; 138(2):350–358.
9. Nomura T, Kabashima K. Advances in atopic dermatitis in 2015. Journal of Allergy and Clinical Immunology 2016; 138(6):1548–1555.
10. Fonacier LS, Dreskin SC, Leung DYM. Allergic skin diseases. Journal of Allergy and Clinical Immunology 2010; 125: S138–S149.
11. Basnet B, Neupane S, Shrestha S. Serum IgE levels and severity of atopic dermatitis. Journal of Universal College of Medical Sciences 2015; 3:22-26.
12. Wang IJ, Lin TJ, Kuo CF, Lin SL, Lee YL, Chen PC. Filaggrin polymorphism P478S, IgE level, and atopic phenotypes. British Journal of Dermatology 2011;164: 791-796.
13. Dhar S, Malakar R, Chattopadhyay S, Dhar S, Banerjee R, Ghosh A. Correlation of the severity of atopic dermatitis with absolute eosinophil counts in peripheral blood and serum IgE levels. Indian Journal of Dermatology, Venereology and Leprology 2005; 71: 246-249.
14. Ahmed I, Nasreen S. Frequency of raised serum IgE level in childhood atopic dermatitis. Journal of Pakistan Medical Association 2007; 57(9):431-434.
15. Uehara M, Izukura R, Sawai T. Blood eosinophilia in atopic dermatitis. Clinical and Experimental Dermaotology 1990;15: 264-266.
16. Kumar MK, Singh PK, Patel PK. Clinico-immunological profile and their correlation with severity of atopic dermatitis in Eastern Indian children. Journal of Natural Science, Biology and Medicine 2014; 5 (1):95–100.

Address for correspondence: Dr. Aditya R. Holani , Department of Dermatology, Smt. Kashibai Navale Medical College & General Hospital, Off Mumbai-Banglore Highway, Narhe, Pune- 411041, Maharashtra, India.
Email: arholani93@gmail.com Mobile: +91 8983530746
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