Original Article

Clinico-immunological profile and their correlation with severity of atopic dermatitis in Eastern Indian children

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Abstract

Objective: To study the clinical features, absolute eosinophil count, and total immunoglobulin E (IgE) level and their association with severity of atopic dermatitis in Eastern Indian children (Bihar). **Design:** Prospective hospital-based study. **Settings:** Pediatrics out-patient Department (OPD) and Dermatology OPD of a Tertiary Care Teaching Hospital located in Rohtas District of Bihar. The study was carried out over a period of 2 years during January 2010 to December 2011. **Participants:** One hundred and thirty two children aged 0 month to 15 years were diagnosed with atopic dermatitis. **Main Outcome:** Demographic profile, common clinical features, absolute eosinophil count, and total IgE level and their correlation with severity of atopic dermatitis in Eastern Indian children. **Results:** Out of a total 1829 pediatric patients aged 0 month to 15 years with some pediatric dermatoses, 132 (7.21%) had atopic dermatitis. Of 132 patients, 57 (43.2%) were boys and 75 (56.8%) were girls, with a male to female ratio 1:1.3. Of these 29 were infants and 103 were children. Two (62.1%) patients belonged to rural area whereas 50 (37.9%) belonged to urban area. Personal history, family history (up to third degree relatives), and both personal and family history of atopy were present in 43.18%, 33.34%, and 12.1% of the subjects respectively. Majority (89.4%) of patients had onset before 5 years of age. In infantile Atopic dermatitis (AD), mean age ± SD at onset was 5.2 months ± 3.01 months. In infantile group, 8 (27.6%) had mild, 14 (48.3%) moderate, and 7 (24.1%) had severe atopic dermatitis. Infantile AD had statistically significant higher SCORing Atopic Dermatitis (SCORAD) index score in all three grades of severity of the disease. One hundred and three patients had childhood AD, out of which 40 (38.8%) were boys and 63 (61.2%) were girls, with a male to female ratio 1:1.57. In childhood AD, mean age ± SD at onset of the disease was 3.47 years ± 3.02 years. Sixty three (61.1%) belonged to rural area whereas 40 (38.9%) were from urban area. One hundred and thirty (98%) patients presented with itching. Ninety two (69.7%) patients had high absolute eosinophils count (AEC) with mean ± SD of 1004.1 ± 596.2 (range 325-2510). Eighty seven (65.9%) patients had increased total serum immunoglobulin E (TsIgE) with mean ± SD value of 1127.11 IU/ml ± 731.69 IU/ml (range: 125-2680 IU/ml). **Conclusion:** Epidemiological data on atopic dermatitis in India are mainly hospital-based, true-point prevalence in community is still scanty**.** Although the prevalence of AD is considered to be increasing, it still remains low in comparison to developed countries. In Indian children, the disease is relatively milder than children of developed countries. This study identified that both AEC and TsIgE increased significantly in about 66% patient and directly correlated with the severity of the AD.

Key words: Absolute eosinophil count, atopic dermatitis, Eastern Indian children, total serum immunoglobulin E

Access this article online	
Quick Response Code:	Website: www.jnsbm.org
	DOI: 10.4103/0976-9668.127296

INTRODUCTION

Atopic dermatitis (AD) is a chronic or chronically relapsing eczematous skin disease that is also called as atopic eczema and characterized by itching, dry, inflamed, and easily irritated skin accompanied by cutaneous functional dysfunction. There is no laboratory "gold standard" for the diagnosis of AD. The diagnosis of AD is based on

a constellation of signs and symptoms.[1] It arises as a result of complex interplay between various genetic, immunologic, and environmental factors. Atopic dermatitis has a strong familial basis. Twin studies have shown that monozygotic twins have about 86% risk to develop AD if the twin partner has the disease, whereas there is only 21% disease risk in dizygotic twins.[2] The genetic predisposition of atopy causes a systemic expansion of Th2 cell activity, leading to increased secretion of Interleukin (IL) IL-5, IL-4, IL-13, and IL-3 which causes eosinophilia, increased immunoglobulin E (IgE), and increased growth and development of mast cell.[3] The prevalence of AD has been increasing over the past 30 years. Changes in environmental pollutants, breast feeding pattern, increased awareness, and urbanization are some of the reasons cited for this change.[4] There are many published research on natural history, epidemiology, etiopathogenesis, clinical patterns, and management of AD in Indian Literature, but no published research on clinico-immunologic profile and their correlation with severity of AD in Indian children. In this study, we have studied the clinical and immunological profile of AD and tried to correlate with severity of atopic dermatitis in Eastern Indian children.

MATERIALS AND METHODS

This hospital-based prospective study was carried out in the Out-patient Department (OPD), of the Department of Pediatrics and the Department of Dermatology, at Narayan Medical College and Hospital, Jamuhar, Rohtas, Bihar, India, for a period of 2 years from January 2010 to December 2011. The Institute of Ethical Committee approved the study protocol. After taking informed written consent from parents of the every patient, all patients were enrolled on a pre-structured Performa and 2 ml blood in ethylenediamminetetraacetic Acid (EDTA) container and 5 ml blood in plain container were collected for laboratory investigations. This Performa included data on present age, age of onset, area of residence, personal and family history of atopy, seasonal variation, religion of the patient, mile stone development, socio-economic status of the parents, history of relapse, absolute eosinophil counts (AEC), and serum total IgE level.

A thorough clinical examination was carried out including measurement of height, weight, distribution of lesion, severity of skin lesion, and type of skin lesion. In every patient diagnosis of AD was confirmed after consultation with dermatologist. The eczema was categorized after a thorough clinical examination of the lesions. Atopic dermatitis was classified as acute, sub-acute, and chronic, according to stage of disease. Erythema, edema, vesiculation, and oozing were part of "acute AD" whereas "sub-acute AD" was defined as patches with minimal oozing, crusting and scaling, and dry, rough lichenified plaques with or without scaling denoted "chronic AD". The severity of the disease was assessed by SCORing Atopic Dermatitis (SCORAD) index.[5] SCORAD index is a clinical tool used to assess the extent and severity of eczema. The SCORAD index consist of the interpretation of the extent of the disorder, that is, the intensity, composed of six items (erythema, edema/papules, effect of scratching, oozing/crust formation, lichenification, and dryness), and two subjective symptoms (itch and sleeplessness), the maximum score is 103 points. This is ok here to describe SCORAD.

Hemoglobin, total leukocytes count (TLC), differential leukocyte count (DLC), and absolute eosinophils count (AEC) was performed by automated hematology analyzer (XS 800i) (This model no, so no expansion required) sysmex, Japan. AEC was also rechecked manually after staining with Leishman's stain. An AEC more than 300 was considered as increased eosinophils count. Total serum immunoglobulin E antibody titre (TsIgE) was performed by Chemiluminescence Immunoassay (CLIA) method in IU/ml. An absolute eosinophil count (AEC) more than 300 was considered as high and more than reference normal range of TsIgE for different age group (0-1 year, 0.6-117 IU/ml; 1-5 year, 0.3-313 IU/ml; 5-10 year, 0.6-555 IU/ml; and 10-15 year, 1.4-481 IU/ml) was considered as high TsIgE.

Inclusion criteria

Children aged 0 month to 15 years diagnosed with atopic dermatitis.

Exclusion criteria

Patients of AD with any associated congenital skin disorder, immunocompromised disorder, and drug rashes.

Statistical analysis

Mean age of the patients expressed in mean ± SD. Data were analyzed using Open Epi Statistical Software version 2.3.1. Mean, standard deviation, odds ratio, and relative risk were calculated using appropriate statistical methods. $P < 0.05$ was considered statistically significant for any given measures.

RESULTS

Out of a total of 1829 pediatric patients aged 0 month to 15 years seen in our Department of Pediatrics and the Department of Dermatology, from January 2010 to December 2011, 132 children had atopic dermatitis. In this study the prevalence of atopic dermatitis was 7.21% of all pediatrics dermatoses in this age group. Of 132 patients, 57 (43.2%) were boys and 75 (56.8%) were girls, with a male to female ratio of 1:1.3. Eighty

two (62.1%) patients belonged to rural area whereas 50 (37.9%) to urban area. Among rural area patients, 30 (36.6%) were boys and 52 were girls with a male to female ratio 1:1.7, whereas in urban area, 27 (54%) were boys and 23 (46%) were girls with male to female ratio 1:1.2. Of 132 patients, 98 (74.2%) were Hindu, 30 (22.7%) were Muslims, and 4 (3.1) were of others religion. Socioeconomically, 34 (25.8%) were from high socio-economic group, 61 (46.2%) were from the middle strata, and 37 (28%) from the lower socio-economic strata. Personal history, family history (up to third degree relatives), and both personal and family history of atopy was present in 42.18%, 31.34%, and 11.1% of subjects respectively. One hundred and eight (81.8%) had history of relapse. One hundred and eighteen (89.4%) patients had onset before 5 years of age. The distribution of the patients according to age of onset is shown in Table 1.

Of 132 patients, 29 were infants (up to 1 year of age) of whom 17 (58.6%) were boys and 12 (41.4%) were girls with a male to female ratio 1.4:1. Mean age (SD) at onset was 5.2 (±3.01) months. Nineteen (65.5%) belonged to rural area whereas 10 (34.5%) were from urban area. In infantile group 8 (27.6%) had mild, 14 (48.3%) moderate, and 7 (24.1%) had severe atopic dermatitis. Infantile AD had statistically significant higher SCORAD Index score in all three grade of severity of the disease as shown in Table 2.

One hundred and three patients were in childhood group (1-15 year), out of which 40 (38.8%) were boys and 63 (61.2%) were girls, with a male to female ratio of 1:1.57. Mean age ± SD at onset of the disease was 3.47 years ± 3.02 years. Sixty three (61.1%) belonged to rural area whereas 40 (38.9%) were from urban area. Childhood AD had statistically significant lower SCORAD Index score in all three grade of severity of the disease. One hundred and thirty (98%) patients presented with complain of itching or pruritus as shown in Table 3.

Ninety two (69.7%) patients had high AEC with mean ± SD of 1004.1 ± 596.2 (range 325-2510). Among patients with increased AEC, mean (±SD) AEC in mild, moderate, and severe AD were 596.16 ± 135.57, 850.17 ± 406.17, and 1404.86 ± 438.31 respectively. On ANOVA analysis of the AEC in different severity, severe AD had statistically significant high AEC ($P < 0.0001$). Even within same group, patients with high AEC had statistically significant higher SCORAD Index score [Table 4].

Eighty seven (65.9%) patients had increased total serum immunoglobulin E (TsIgE) with mean ± SD value of 1127.11 IU/ml ± 731.69 IU/ml (range: 125-2680 IU/ml). Among patients with increased TsIgE, mean (±SD) TsIgE, in mild, moderate, and severe AD were 389.28 IU/ml ± 476.22 IU/ml, 831.37 IU/ml ± 745.27 IU/ml, and 1269.8 IU/ml ± 745.27 IU/ml respectively. On ANOVA analysis of the TsIgE, in different severity, severe AD had statistically significant high AEC ($P < 0.0001$). Even within-group patients with high TsIgE had statistically significant higher SCORAD Index score [Table 5].

Table 1: Age at onset of disease

Age (in year)	Number of patients (*N*=132)	Percentage
0-1	38	28.8
1-2	40	30.3
2-3	26	19.7
3-4	10	7.6
4-5	4	3
5-15	14	10.6

Table 2: SCORing atopic dermatitis index score (mean±SD) among infantile atopic dermatitis and childhood AD

Severity of AD	SCORAD index mean±SD		*P* value
	Infantile AD (<1 year)	Childhood AD (1-15 year)	
Mild	17.8±4.29	12.3±5.1	0.0065
Moderate	38.35±8.28	33.3±7.5	0.032
Severe	88.42±14.24	64.9±11.89	0.002

Statistical significance by two sample independent *t*-test and $P<0.05$ is statistically significant, SCORAD: SCORing atopic dermatitis, AD: Atopic dermatitis

Table 3: Common clinical presentation of atopic dermatitis

Clinical feature	No. of patients (*N*=132)	Percentage
Pruritus/itching	130	98
Chronic relapsing eczema	108	82
Family history of atopy	91	68.9
Excoriation of skin	86	65.1
Dryness of the skin	82	62.1
Flexural lichenification	64	48.5
Ichthyosis	46	34.9
Recurrent conjunctivitis	22	16.7

Table 4: SCORAD index score (mean±SD) in patients with normal absolute eosinophil count and high absolute eosinophil count among mild, moderate, and severe atopic dermatitis

Severity of AD	SCORAD index score (mean±SD)		*P* value
	Normal AEC (*n*=40)	High AEC (*n*=92)	
Mild (25)	9.84±6.67 (31)	11.8±7.05	0.0336
Moderate (13)	30.92±5.76 (46)	37.4±8.23	0.0024
Severe (2)	62.5±10.6 (15)	89.84±12.41	0.0007

Statistical significance by two sample independent *t*-test (two tailed) and $P<0.05$ is statistically significant, SCORAD: SCORing atopic dermatitis, AD: Atopic dermatitis, AEC: Absolute eosinophils count

Table 5: SCORAD index score (mean±SD) in patients with normal total serum immunoglobulin E (TsIgE) and high TsIgE among mild, moderate, and severe atopic dermatitis

Severity of AD	SCORAD index score (mean±SD)		*P* value
	Normal TsIgE (*n*=45)	High TsIgE (*n*=87)	
Mild (28)	8.52±5.87 (28)	12.07±6.93	0.043
Moderate (15)	30.6±4.79 (44)	36.72±7.68	0.006
Severe (2)	62.5±10.6 (15)	89.84±12.41	0.0007

SCORAD: SCORing atopic dermatitis, AD: Atopic dermatitis

DISCUSSION

Atopic dermatitis (AD) is a chronic or chronically relapsing eczematous skin disease that is also called as atopic eczema and characterized by itching, dry, inflamed, and easily irritated skin accompanied by cutaneous functional dysfunction. Eczema literally means to boil out (Ec-out, Zema-boil) and the term eczema and dermatitis are often used synonymously.

Atopic dermatitis has three phases. (1) Infantile phase (up to 2 years of age) primarily involved face, scalp, neck, and extensor surface of extremities with erythematous oozing papulo-vesiculous lesions. (2) In childhood phase (between 2 year and 10 years of age), the lesions are sub-acute, more scattered, and often localized in the flexor folds of the neck, elbows, wrist, and knees. (3) In adolescent and adult phase (more than 10 years of age), the lesions are primarily dry, lichenified, and hyperpigmented plaques were seen in flexor areas.

The prevalence of AD had been increasing over the past four decades in developed country and also in India.[4,6] Our study was a hospital-based rather than population-based, so the exact incidence of AD in the community could not be estimated, but these patients comprised 7.21% of all pediatric dermatoses in the study age group. A four-decade-old study from Bihar reported an incidence of 0.38% of the total number of out-patient attendees.[7] On contrary to our study, North Indian hospital-based study reported 28.46%[8] and 29.9%[9] of total pediatric dermatology patients. "Hygiene Hypothesis" can explain the relatively lower occurrence of AD in our study when compared with North Indian children because overall hygiene is poor and various infections in childhood is rampant in this part of the country because of poor socio-economic status. However, prevalence in Bihar also had increased over last four decades.[7] The reason for this increase is not known but probably increased environmental pollution, exposure to agricultural chemicals, decline breast feeding, earlier weaning, urbanization, increased awareness, better case detection technique, and improved quality of life are the factors that can explain increasing trend in occurrence of AD.

In previous studies carried out, there are contrast view regarding gender ratio, although most have reported a male predominance, with male to female ratio 2.13:1 for infants and 1.09:1 for children,[8] 2.25:1 for infants and 1.6:1 for children.[9] On the contrary, our study found that girls outnumbered boys, with a female to male ratio of 1.3:1, however, in infantile group, boys outnumbered girls with a male to female ratio 1.4:1. In childhood group, female to male ratio was 1.57:1. Our study result was comparable with study carried out by Rajka *et al.* who found female predominance with a female to male ratio of 1.5:1.[10]

Todd *et al.*[11] and Poysh *et al.*[12] found higher prevalence in urban areas than rural areas. In contrast to these findings, our study found higher prevalence in rural areas, with a rural to urban ratio of 1.64:1. This finding can be explained in view that our hospital caters to predominantly rural population. Our finding regarding religion was proportionate to the percentage population of different religion in Eastern India.

William found that prevalence of AD increases with improvement in socio-economic condition.[4] Similar finding was reported by Spergel *et al.* who found that the prevalence of AD had increased two to three folds during past three decades in industrialized countries due to improvement of socio-economic condition and improved life style.[13] In contrast to our study, 46.2% patients came from middle class, 28% from lower socio-economic class, and only 25.8% from upper socio-economic class, which was comparable with Indian study carried out by Sarkar and Kanwar, in which they found that majority belonged to middle class families (53.8% for up to 1 year and 57.57% onwards) whereas minority of patients was from low strata 15.55% for up to 1 year and 23.23% above 1 year.[8]

In our study, mean age (±SD) at onset was 5.2 (±3.01) months in infantile AD and 3.47 years ± 3.02 years in childhood AD, these were comparable with other Indian studies which recorded 4.2 months for infantile AD and 4.5 years for childhood AD,[8] 4.5 months for infantile AD and 4 years for childhood AD.[9] In the present study, 28.8% of children developed disease by the age of 1 year and 89.4% by the age of 5 years and only 10.6% developed after 5 years of age. In a study, Rajka found that 60% of subjects were having the onset of the disease in the first year of life and 85% by 5 years of age.[14] In a North Indian study they found 55.2% developed disease by 1 year of age and only 5.6% developed the disease after 6 years of age.[9] In our study, late presentation can be explained that

in rural areas milder disease often ignored especially during infancy in low socio-economic strata.

In the present study, 65.8% children had history of atopy, among which 42.18%, 31.34%, and 11.1% of children had personal history, family history (up to third degree relatives), and both personal and family history of atopy. Halbert *et al.* found that approximately 70% patients had family history of atopy.[15] Family history varied in different studies. In an Indian study, the personal or family history of atopy was observed in 54% and 65% respectively.[16]

In the present study infantile AD had statistically significant higher SCORAD Index score in mild, moderate, and severe AD with mean ± SD score of 17.8 ± 4.29 vs. 12.3 ± 5.1 ($P = 0.0065$), 38.35 ± 8.28 vs. 33.3 ± 7.5 ($P = 0.032$), and 88.42 ± 14.24 vs. 64.9 ± 11.89 ($P = 0.002$) respectively. Sarkar and Kanwar in a study from north India also reported that infantile AD was relatively more severe than childhood AD.[9]

In this study most common (98%) clinical presentation was itching. Face was affected in 76.8% patients in infantile AD and 56.8% patients in childhood AD. Our findings were comparable with findings of Dhar and Kanwar.[8]

In our study disease severity was assessed by SCORAD and we found 42.4%, 44.7%, and 12.9% patients had mild, moderate, and severe disease, which was almost comparable with other Indian study by Dhar *et al.*[16]

We found that 69.7% and 65.9% patients with AD had high absolute eosinophil count (AEC) and total serum IgE (TsIgE) respectively. Increased AEC and TsIgE level directly correlated with severity of the disease. Akadis *et al.* also found that systemic expansion of Th2 cell activity leading to release of IL-5, IL-4, IL 13, and IL-3 caused eosinophilia.[3] In a study, Leiferman has found that exact role of eosinophils and IgE antibodies in the pathogenesis of AD is not clear, but individual with AD has elevated eosinophils and IgE antibody level.[17] Wollenberg also has demonstrated that majority of cases are associated with a sensitization to environmental allergens and increased total IgE and eosinophilia, but about 30% of all cases lack increased total IgE.[18]

CONCLUSION

Epidemiological data on atopic dermatitis in India are mainly hospital-based, true-point prevalence in community is still scanty. Although the prevalence of AD is considered to be increasing, it still remains low in comparison to developed countries. In Indian children, the disease is relatively milder than children of developed countries. This study identified that both AEC and TsIgE increased significantly in about 66% patient and directly correlated with the severity of the AD. However, to confirm our findings, larger population study in future is needed. Our study had some limitation as this was a hospital-based study true-point prevalence in community could not be extrapolated.

WHAT IS ALREADY KNOWN IN AD?

Majority of patients with AD had increased AEC and total serum IgE antibody level.

WHAT THIS STUDY ADDS?

Higher AEC and TsIgE directly associated with severity of AD.

ACKNOWLEDGMENT

We wish to thank our Dean, Prof. Dr. M.L. Verma, Narayan Medical College and Hospital, Jamuhar, Sasaram, Bihar, India for allowing us to publish this study.

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How to cite this article: Kumar MK, Singh PK, Patel PK. Clinico-immunological profile and their correlation with severity of atopic dermatitis in Eastern Indian children. J Nat Sc Biol Med 2014;5:95-100.

Source of Support: Nil. **Conflict of Interest:** None declared.