

# Atopic Dermatitis and its Severity Correlation With Absolute Eosinophil Counts

Pandey S<sup>1</sup>, Jha S<sup>2</sup>, Pokharel NR<sup>3</sup>, Kadel A<sup>4</sup>

## ABSTRACT

**Background :** Atopic dermatitis is one of the common skin disease affecting children and adults. Atopic dermatitis is a common and difficult to manage allergic condition. Till date severity of atopic dermatitis is graded only by clinical findings, which has greater means of individual variation, so a laboratory value may uniform the grading and eosinophils are always thought to be associated with allergic conditions.

**Objectives :** To assess the severity of atopic dermatitis by peripheral blood eosinophil count and SCORAD index, and also to explore relationship between personal history of atopy, family history of atopy, severity of disease and absolute eosinophil count

**Material and Method :** This study is a hospital based Cross sectional descriptive study conducted in the Department of Dermatology, Venereology and Leprology of Nepalgunj Medical College Teaching Hospital, Kohalpur between March 2017 to February 2018. Total of 53 patients fulfilling the criteria of UK refinement of Hanifin and Rajka's criteria for atopic dermatitis presented to the OPD of dermatology department at Kohalpur were included in the study.

**Result :** A total of 53 patients were enrolled, mean age of the patients was 6.08 (SD 2.83) years and mean age of onset of disease was 2.95 (SD 1.57) years. Mean AEC was 537.17 (SD 343.92)/mm<sup>3</sup> and higher mean AEC was significantly (P<0.001) associated with greater severity of disease and similarly presence of personal history of respiratory atopy was also significantly (P<0.001) associated with higher mean AEC. Per patient AEC and severity of disease according to SCORAD index showed reasonable positive correlation (r=0.514 and P<0.001).

**Conclusion:** Severity of disease and presence of respiratory atopy are important factors determining peripheral blood eosinophilia in AD patients. Although larger studies are required to replicate these findings.

**Key Words:** Atopic dermatitis, SCORAD index

## INTRODUCTION

Atopic dermatitis (AD) is an inflammatory, chronic or chronically relapsing, non-contagious and intensely pruritic skin disease often occurring in families with other atopic diseases (bronchial asthma, allergic rhino-conjunctivitis)<sup>1</sup>. The clinical manifestations of atopic dermatitis vary with age; three stages can often be identified. In infancy, the first eczematous lesions usually emerge on the cheeks and the scalp. Scratching, which frequently starts a few weeks later, causes crusted

erosions. During childhood, lesions involve flexures, the nape, and the dorsal aspects of the limbs. In adolescence and adulthood, lichenified plaques affect the flexures, head, and neck. In each stage, itching that continues throughout the day and worsens at night causes sleep loss and substantially impairs the patient's quality of life<sup>2</sup>. It is one of the common skin disease with a prevalence of 10% to 20% in children and 1% to 3% of adults<sup>3</sup>. AD is a paradigmatic skin disease that is the product of a complex interaction between various susceptibility genes, defects in skin barrier function, a specific immunologic response, and a clear interaction with infectious agents and the host environment<sup>4</sup>. Two hypotheses concerning the mechanism of atopic dermatitis have been proposed. One holds that the primary defect resides in an immunologic disturbance that causes immunoglobulin E (IgE) mediated sensitization, with epithelial-barrier dysfunction regarded as a consequence of the local inflammation. The other proposes that an intrinsic defect in the epithelial cells leads to the barrier dysfunction; the immunologic aspects are considered as an epiphenomenon<sup>2</sup>. Management of disease consists of skin care, identification and elimination of flare factors, anti-inflammatory agents<sup>5</sup>. The role of eosinophils in AD is

- 
1. Dr. Sumit Pandey
  2. Dr. Smita Jha
  3. Dr. Nitesh Raj Pokharel
  4. Dr. A. Kadel

## Address of Correspondence:

Dr. Sumit Pandey  
Department of Dermatology  
Nepalgunj Medical College & Teaching Hospital  
Kohalpur, Banke  
Email: sumitpandey207@yahoo.com

suggested by the presence of peripheral blood eosinophilia, increased level of serum and urinary eosinophilic granular proteins in AD patients and eosinophilic infiltrates in AD lesions. It is further supported by information that links AD to cytokines and chemokines associated with production, recruitment, and activation of eosinophils<sup>6</sup>.

In 1980s Hanifin and Rajka proposed list of characteristic feature (criteria) of AD to establish unity in the clinical concept of AD<sup>7,8</sup>.

It is said that Charles Darwin who propounded the 'theory of evolution' suffered from atopic dermatitis and that the legendary dermatologist Hebra treated him<sup>9</sup>.

In 1994, the UK Working Party refined Hanifin&Rajka's criteria into a concise and validated set of survey-based diagnostic criteria useful for the purposes of epidemiologic studies<sup>10-12</sup>.

SCORAD index is defined as sum of objective parameter and subjective parameter in which objective parameters includes extent of area involvement (A) and intensity of symptoms (erythema, oedema, population, excoriation, lichenification, oozing/crusting & dryness (B). The subjective parameters (C) include pruritus and sleeplessness. The extent of body surface area involvement is calculated by rules of nine, and the extent is graded (0-100 cm<sup>2</sup>). The intensity of each symptom is graded as (0-3). Subjective symptoms are graded as 10 cm visual analogue scale. According to the SCORAD index formula generated by European Task Force on Atopic Dermatitis (ETFAD) is  $A/5 + 7B/2 + C$ . where A= area (0-100), B= intensity of symptoms (0-18), C= subjective symptom (0-20)<sup>13</sup>.

Eosinophils are cells of the immune system that are most commonly known for their role in defense against parasites and, along with basophils and mast cells, as mediators of allergy and asthma. They are derived from CD34+ hematopoietic progenitor cells in the bone marrow and represent approximately 1–6% of white blood cells. They can persist in the circulation for 8–12 h and in tissue for 8–12 days in the absence of stimulation<sup>6</sup>. Under the physiologic conditions, the skin does not harbor eosinophils<sup>14</sup>, but in disease like AD, eosinophil can be found in lesional skin. Proliferation, immigration, and local activation of eosinophils are characteristic features of AD. T cell activation by antigen-presenting cells leads to production of Th2 cytokines, such as IL-4, IL-5, and IL-10, that support humoral immunity and eosinophil functions<sup>6</sup>. Eosinophilia (i.e., more than 500 eosinophils per microliter of blood) has been shown to be present in most patients with AD and correlate

with the disease activity<sup>15</sup>. Also, more recent studies suggested that peripheral blood eosinophilia could be used as a diagnostic tool in differentiating atopic AD from non-atopic AD<sup>16</sup> and that AD patients with other symptoms of atopy and family history of atopy have increased blood eosinophilia.

Another potentially important role for eosinophils in AD is based on the study that showed Th2 cytokines can stimulate eosinophils to produce IL-12<sup>17</sup>. Therefore; eosinophils may promote a switch from a Th2-like immune response, in acute lesions, to a Th1-like immune response, in chronic lesions of AD<sup>18</sup>.

From all these evidences we can draw a fair inference that eosinophils and its granular proteins plays an important role in pathogenesis and activity of disease in atopic dermatitis patients.

## MATERIALS & METHODS

This study is a hospital based Cross sectional descriptive study conducted in the Department of Dermatology Venereology & Leprology, Nepalgunj Medical College Teaching Hospital Kohalpur, between March 2017 to February 2018. Informed consent was taken from all the patients or parents of the patient (if age of the patient is less than 18 years) included in the study. Before initiating the study the proposal of the study was submitted to the Institutional Review Board. The will of the subjects was fully respected and those who did not give consent for participation were excluded from the study. A written consent was taken from each patient after explaining the relevant details of the study, its importance and implications. Confidentiality was maintained to utmost. Detailed history was taken and detailed clinical examination, investigation was performed, and the details were recorded. Altogether 53 patients were included in the study. The severity of atopic dermatitis was stratified as minimal, mild, moderate and severe as per the SCORAD index. Patients on steroid use were excluded from the study. The correlation between the severity of atopic dermatitis and absolute eosinophil count was estimated using the Karl Pearson's correlation coefficient. Similarly correlation of eosinophil count was done with other variables including personal and family history of atopy using SPSS 20.0 version and tables and graphs were made.

## RESULTS

A total of 53 atopic dermatitis patients were included in the study. The age of the patients ranged from 1.5 to 13 years with the mean age of 6.08 ±2.83 years as shown in the figure 1 below. Among the 53 patients of atopic dermatitis, there were

40 (75.47%) males and 13(24.53%) females as shown in figure2. Age of the patient at the onset of the disease ranged from 9 months to 6 years with mean age  $2.95 \pm 1.57$  years.

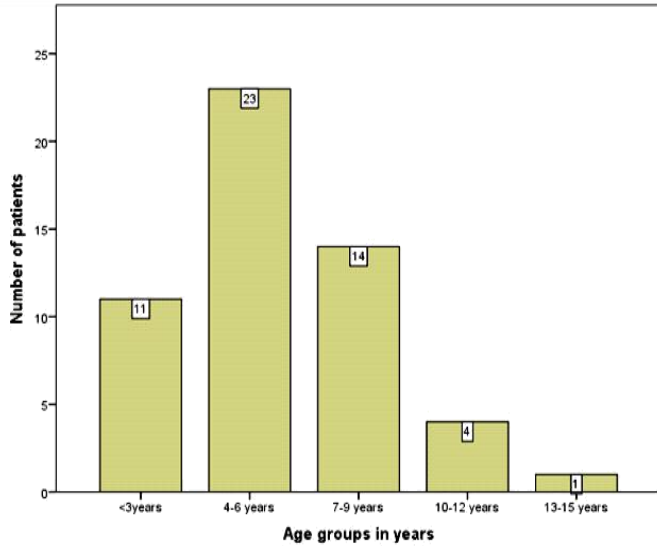


Figure 1

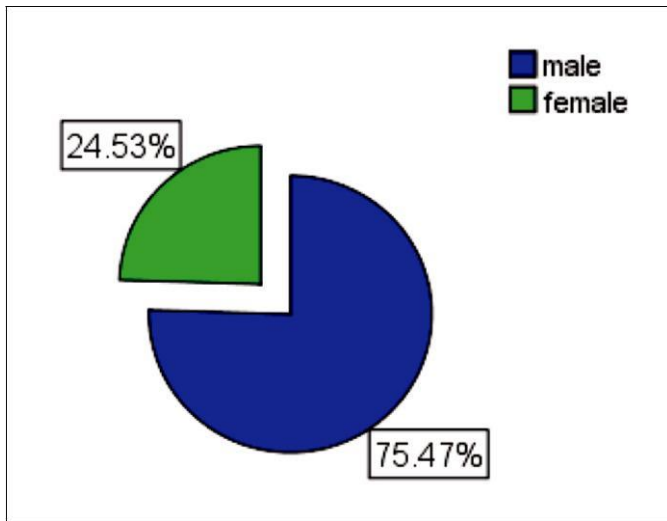


Figure 2

**Patients with personal history of atopy**

Among 53 patients, 31 patients (58.49%) had history of atopy. Among them 26 patients (49.05%) had allergic rhinitis and 5 cases (9.43%) were diagnosed cases of asthma. Remaining 22 patients (41.51%) did not have history of atopy as shown in fig 3

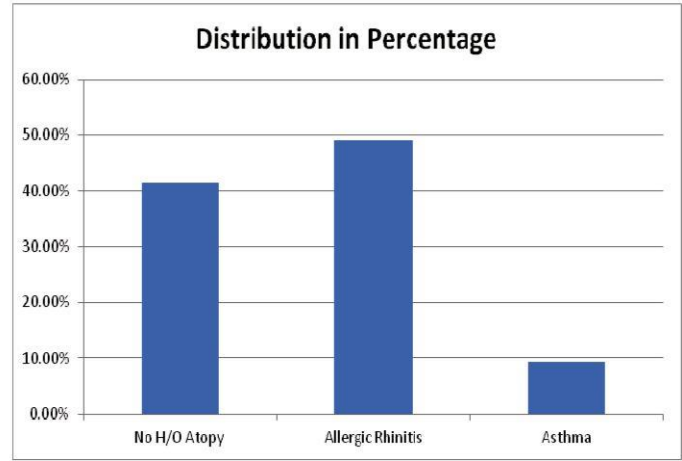


Figure 3

**Patients with family history of atopy**

In total of 53 patients 14 patients (26.41%) had family history of atopy and 39 patients(73.58%) did not have any family history of atopy . Among 14 patients with family history of atopy 9 patients (16.98%) had mother with history of atopy and 5 patients(9.43%) had sibling with history of atopy as shown in figure 4.

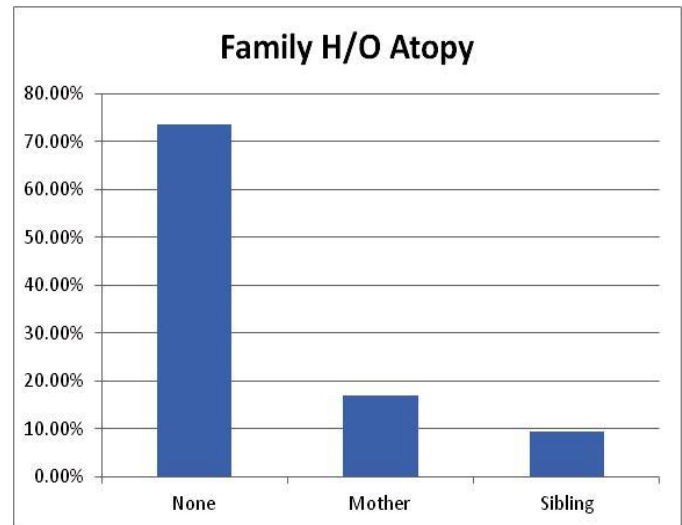
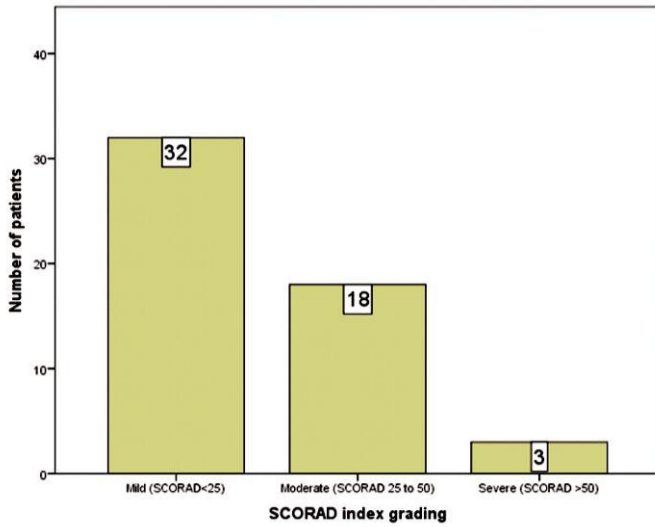


Figure 4

**SCORAD index and SCORAD grading**

SCORAD of the patients ranged from 9 to 58 with mean SCORAD value  $25.11 \pm 11.77$ . Among them 32(60.4%) patients had mild (SCORAD <25), 18(34%) patients had moderate (SCORAD 25 to 50), 3(5.6%) patients had severe (SCORAD>50) SCORAD grading. (Figure 5)



**Figure 5:** distribution of patients according to severity of disease based on SCORAD index

**Absolute eosinophil counts (AEC) on peripheral blood smear**

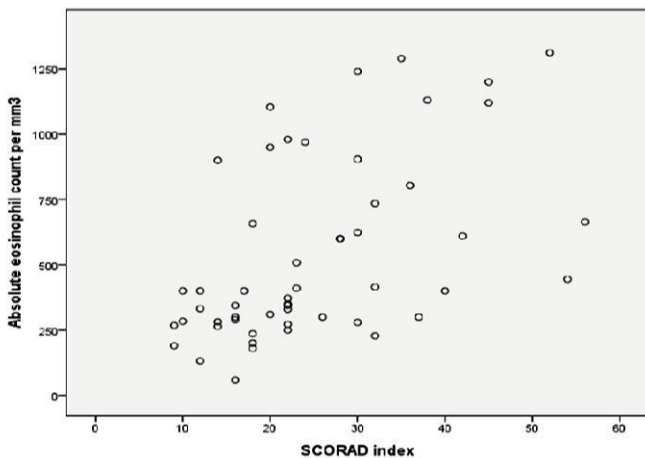
AEC on peripheral blood smear ranged from 58/mm<sup>3</sup> to 1312/mm<sup>3</sup> with mean eosinophil count 537.17±343.92/mm<sup>3</sup>. Percentage of eosinophil on peripheral blood ranged from 1% to 10% with mean percentage of 5.41±2.61%.

**Correlation and comparison of severity of disease and AEC with different aspects of disease**

Correlation of severity of disease (SCORAD index) with AEC. Correlation between severity of atopic dermatitis scored by SCORAD index and AEC showed reasonable positive correlation with Pearson correlation coefficient (r = 0.514) and P value 0.000831.

**Table1:** Correlation of SCORAD index and AEC

	SCORAD index	AEC	P value
<b>Pearson correlation</b>	1	0.532	0.000831



**Comparison AEC according to severity of disease**

Mean values of AEC of the patients were compared between the different severities of groups. Mean AEC values were higher in patients in severe category (807.00) as compared to those in milder categories. A subsequent analysis for statistical significance calculated by one way analysis of variance (ANOVA) showed the difference in mean values to be significant at a p-value of 0.004 (less than 0.05).

**Table 2:** Comparison of AEC according to severity of disease

Severity of disease	Mean value of AEC per mm <sup>3</sup>	P value
Mild	414.67±271.22	
Moderate	710.00±361.95	0.004
Severe	807.00±450.84	
<b>Total</b>	<b>537.17±343.92</b>	

**DISCUSSION**

Atopic dermatitis is a common and difficult to manage allergic condition. Once thought to be the disease of developed countries with rapid urbanization the prevalence of disease is increasing in developing countries like Nepal. Not many studies are done in regard to atopic dermatitis in Nepal. Different studies have suggested different age of onset for the disease. A study done by Illi S *et al* showed a total of 45% of all cases of atopic dermatitis begin within the first 6 months of life, 60% begin during the first year, and 85% begin before 5 years of age<sup>19</sup>. In another study from India mean age of onset of AD was 4.55 years<sup>20</sup>. In our study mean age of the patient at the onset of the disease was 2.95 (SD 1.75) years. In this study mean AEC on peripheral blood smear was 537.17 (SD 343.92)/mm<sup>3</sup> and higher values were associated with greater severity of disease and personal history of respiratory atopy with P value < 0.05. Patients with personal history of atopy showed significant association with higher severity of disease as compared to patients without personal history of atopy. However severity of disease and AEC were not significantly different between patients with and without family history of atopy. Also AEC count and severity of disease showed reasonable positive correlation with Pearson correlation coefficient (r = 0.514) and P value < 0.001. Although many exceptions exist where severe cases showed a normal eosinophil level and less severe cases showed higher eosinophil level. Similarly DharS *et al*<sup>20</sup> found significant difference in eosinophil count between AD and control group, they also found significant positive correlation between severity of disease and AEC.

Another study done by Tsuda *et al*<sup>21</sup>, evaluated the role of eosinophils in atopic dermatitis by correlating levels of serum eosinophil cationic protein (ECP), clinical activity, eosinophil count and IgE level found a positive correlation between the number of peripheral blood eosinophils and serum ECP levels in severe cases ( $r = 0.67$ ,  $p < 0.05$ ). Similarly more recent study from Taiwan showed positive correlation between SCORAD index and total eosinophil count ( $r = 0.489$ ,  $p < 0.001$ ), serum IgE ( $r = 0.317$ ,  $p = 0.028$ ), IL-16 ( $r = 0.321$ ,  $p = 0.026$ ) in acute exacerbation phase<sup>22</sup>. However, they did not mention role personal and family history of atopy in AEC, which also played a significant role in some of above mentioned studies and also in our study.

### CONCLUSION

The study demonstrate that blood eosinophil levels correlate with disease severity in patients with AD, although many exceptions exist where severe cases show a normal eosinophil level and less severe disease has higher eosinophil level. By correlating blood eosinophil levels with a personal history of respiratory atopy, we found that patients with atopic dermatitis and a personal history of respiratory atopy showed significantly higher eosinophil levels than patients without personal history of respiratory atopy. Thus, it is evident that the capacity for blood eosinophil elevation differs not only between the severities of disease but also between patients with and without history of respiratory atopy.

In summary, we conclude that severity of disease and presence respiratory atopy is important factors determining peripheral blood eosinophilia in AD patients.

### Limitations of the study:

There was no control group. Hence the AEC between AD patients and non-atopic dermatitis patients couldn't be compared.

### REFERENCES

1. Darsow U, Lubbe J, Taieb A, Seidenari S, Wollenberg A, Calza AM, et al. Position paper on diagnosis and treatment of atopic dermatitis. *Journal of the European Academy of Dermatology and Venereology : JEADV*. 2005 May;19(3):286-95.
2. Bieber T. Atopic dermatitis. *The New England journal of medicine*. 2008 Apr 3;358(14):1483-94.
3. Schneider L, Tilles S, Lio P, Boguniewicz M, Beck L, LeBovidge J, et al. Atopic dermatitis: a practice parameter update 2012. *The Journal of allergy and clinical immunology*. 2013 Feb;131(2):295-9 e1-27.
4. Allergic triggers in atopic dermatitis. *Immunol Allergy Clin N Am*. 2010;30:289- 307.
5. Hoare C, Li Wan Po A, Williams H. Systematic review of treatments for atopic eczema. *Health technology assessment*. 2000;4(37):1-191.
6. Liu FT, Goodarzi H, Chen HY. IgE, mast cells, and eosinophils in atopic dermatitis. *Clinical reviews in allergy & immunology*. 2011 Dec;41(3):298-310.
7. Kefei k, Amy M P, Susan T N, Seth R S, C KD. Atopic dermatitis. Bologna: Dermatology. 1. Second ed: Mosby Elsevier.
8. Donald Y.M. Leung LFE, and Mark Boguniewicz. Atopic Dermatitis (Atopic Eczema). *Fitzpatrick's Dermatology In General Medicine*. 1. sixthed: McGraw-Hill Medical Publishing division. p. 1180-94.
9. D. S. Atopic Dermatitis. *IADVL Textbook Of Dermatology*. 1: Bhalani Publishing House Mumbai, India. p. 527-44.
10. Williams HC, Burney PG, Hay RJ, Archer CB, Shipley MJ, Hunter JJ, et al. The U.K. Working Party's Diagnostic Criteria for Atopic Dermatitis. I. Derivation of a minimum set of discriminators for atopic dermatitis. *The British journal of dermatology*. 1994 Sep;131(3):383-96.
11. Williams HC, Burney PG, Strachan D, Hay RJ. The U.K. Working Party's Diagnostic Criteria for Atopic Dermatitis. II. Observer variation of clinical diagnosis and signs of atopic dermatitis. *The British journal of dermatology*. 1994 Sep;131(3):397-405.
12. Williams HC, Burney PG, Pembroke AC, Hay RJ. The U.K. Working Party's Diagnostic Criteria for Atopic Dermatitis. III. Independent hospital validation. *The British journal of dermatology*. 1994 Sep;131(3):406-16.
13. Kunz B, Oranje AP, Labreze L, Stalder JF, Ring J, Taieb A. Clinical validation and guidelines for the SCORAD index: consensus report of the European Task Force on Atopic Dermatitis. *Dermatology*. 1997;195(1):10-9.
14. Kato M, Kephart GM, Talley NJ, Wagner JM, Sarr MG, Bonno M, et al. Eosinophil infiltration and degranulation in normal human tissue. *The Anatomical record*. 1998 Nov;252(3):418-25.
15. Kagi MK, Joller-Jemelka H, Wuthrich B. Correlation of eosinophils, eosinophil cationic protein and soluble interleukin-2 receptor with the clinical activity of atopic dermatitis. *Dermatology*. 1992;185(2):88-92.
16. Jenerowicz D, Czarnecka-Operacz M, Silny W. Peripheral blood eosinophilia in atopic dermatitis. *Actadermatovenerologica Alpina, Panonica, et Adriatica*. 2007 Jun;16(2):47-52.

- 17 Grewe M, Czech W, Morita A, Werfel T, Klammer M, Kapp A, et al. Human eosinophils produce biologically active IL-12: implications for control of T cell responses. *Journal of immunology*. 1998 Jul 1;161(1):415-20.
- 18 Kang K, Stevens SR. Pathophysiology of atopic dermatitis. *Clinics in dermatology*. 2003 Mar-Apr;21(2):116-21.
- 19 Illi S, von Mutius E, Lau S, Nickel R, Gruber C, Niggemann B, et al. The natural course of atopic dermatitis from birth to age 7 years and the association with asthma. *The Journal of allergy and clinical immunology*. 2004 May;113(5):925-31.
- 20 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 Jul-Aug;71(4):246-9.
- 21 Tsuda S, Kato K, Miyasato M, Sasai Y. Eosinophil involvement in atopic dermatitis as reflected by elevated serum levels of eosinophil cationic protein. *The Journal of dermatology*. 1992 Apr;19(4):208-13.
- 22 Wu KG, Li TH, Chen CJ, Cheng HI, Wang TY. Correlations of serum Interleukin-16, total IgE, eosinophil cationic protein and total eosinophil counts with disease activity in children with atopic dermatitis. *International journal of immunopathology and pharmacology*. 2011 Jan-Mar;24(1):15-23.



Pityriasis alba in a 7 year old boy  
with atopic dermatitis



Keratosis pilaris in right arm in a child  
with atopic dermatitis