Total Serum IgE and SCORAD in children with atopic dermatitis in Qatar

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Abstract

Design: A prospective study to determine the level of IgE and SCORAD in children with AD.

Setting: Dermatology clinic Hamad General Hospital.

Patients: A total of 140 patients with AD were recruited (84 male and 56 female)

Methods. Patients were assigned an AD symptom score (SCORAD) and were screened for levels of serum IgE. The patients were subdivided by age into four groups: Group 1 (n=26) less than one year, Group 2 (n=43) preschool children less than four years, Group 3 (n=54) from four to seven years, Group 4 (n=17) more than seven up to twelve years.

Results: The SCORAD showed proportional increase with age among different groups the highest SCORAD was noticed in Group 4, IgE level was positive in only 42.1 % of the cases. The IgE level showed a significant positive correlation with SCORAD in Groups 1 and 4.

Conclusions: Clinical severity of atopic dermatitis increase with age especially in the older children as the mild and moderate cases tend to resolve, IgE level is correlated with the clinical severity only in infants and children beyond the age of seven years.

Introduction

Atopic dermatitis (AD) is a multifactorial, polygenic skin disorder that affects up to 20% of preadolescent children in Western countries[1] and is commonly viewed as immunologic in pathogenesis.[2,3] Atopic dermatitis (AD) or atopic eczema is a chronically relapsing, pruritic, exanthematous dermatosis of uncertain etiology that is characterized primarily by an allergic diathesis as well as erythema, oozing, crusting, excoriations, lichenification, and dehydration of involved skin surfaces[4].

Onset occurs at approximately 2 to 3 months of age, and the disease may persist, with periodic exacerbations and remissions, into adulthood. Sites predisposed to rash change with growth and development. The face primarily is involved in infants; extensor areas of the body are affected more commonly by age 10 months; and lesions are located predominantly on the flexor surfaces, antecubital and popliteal fossa, and neck in older children and adolescents. Spread to other areas may occur in severe cases[5].

The etiology of AD has not been fully elucidated, but it has been suggested that both genetic and environmental factors play a role in its genesis. Although a genetic linkage for AD has not yet been identified, clinical observations do suggest a hereditary basis for the disease. Recently, it has been shown that the prevalence of atopic eczema in children is approximately 60% with one affected parent and approaches 80% with two affected parents[6].

It also has been reported that nearly 40% of patients have at least one first-degree relative who has AD. Studies of twins have shown a very high degree of concordance of AD in monozygotic compared with dizygotic twins. Several genodermatoses, including icthyosis vulgaris, Netherton syndrome, Wiskott-Aldrich syndrome, and Bruton agamma-globulinemia, also are associated with AD. Environmental factors, including contact irritants and allergens, climate, sweating, aeroallergens, microbial organisms, certain foods, and stress/psyche, all have been shown to trigger AD in susceptible individuals.[7,8]

Contact irritants and allergens (eg, soaps, solvents, wool clothing, mechanical irritants, detergents, preservatives, perfumes) compromise the integument, creating inflammation, irritation, and a portal of entry for further environmental insult. The threshold for pruritus is lowered, and a fierce cycle of itching and scratching ensues, resulting in additional cutaneous damage. Similar changes occur with maceration from sweating and the drying effects of low humidity. Aeroallergens, including the house dust mite (*Dermatophagoides pteronyssinus*), molds, pollen, and dander, may induce eosinophilia and elevated levels of immunoglobulin E (IgE), leading to increased histamine release from IgE-activated mast cells and elevated activity of the Th_2 immune system.[9-11]

This disorder is diagnosed primarily on clinical grounds, and treatment consists of removal of precipitating factors, antibiotic coverage, rehydration of the stratum corneum, and topical anti-inflammatory therapy. Affected infants typically are fussy from sleep depriva-

tion because of pruritis and often are uncomfortable, are fretful, and may not eat well.[9] Older children who have severe atopic eczema frequently are asthenic and may have difficulties at school. Although anti-inflammatory therapies, such as topical glucocorticoids, and more recently, topical immunosuppressive agents (eg, tacrolimus, ascomycin, mycophenylate mofetil), are considered mainstays of therapy in AD,[2] reliance on these drugs carries potential risks, particularly in children. Moreover, AD typically relapses or flares after discontinuation of anti-inflammatory therapy.[3]

SCORAD is an essential component of evidence-based medicine is the use of valid and reliable outcome measures in clinical trials. There is much confusion in the field of atopic eczema regarding how to best measure disease severity objectively. Accurate and appropriate measurements of health outcome form the basis of good evidence-based practice. Methods of assessing the effects of health care intervention are continually being sought, both for use in clinical trials and medical audit, and for guiding the allocation of health service resources.[4]

Thirteen atopic eczema severity scales have been described, but nearly all have not been adequately tested. It is also important to point out that just because a measure has been tested for the various attributes of a good scale, this does not mean that it is a good scale. For instance in the SCORAD index, serious interobserver variability has been demonstrated for many aspects of the scale. Although intraobserver variation may be more important in small single-center trials, in practice many clinical trials involve more than 1 center and hence consistency between observers is extremely important. It is therefore important to assess how well individual scales have performed as well as simply whether the scale has been tested.[12-15]

The large number of severity scales available for atopic eczema partly reflects the varying requirements of scales for different clinical situations. For example, indices such as SCORAD and SASSAD, which use an assessment of various combinations of clinical signs of atopic eczema in several body sites, result in wide scales that are probably best at detecting small changes in disease activity that might be useful in clinical trials. Other scales such as the Rajka and Langeland proposal and its refinement or the BCSS might be more suitable for broadly categorizing patients or for rapid assessments of disease severity for use in epidemiological studies or in health services research.[16-20]

In addition to the concept of different scales for different purposes, the properties of such scales require some consideration. It is unlikely that most scales are linear (ie, a change in the SCORAD index from 50 to 40 is not necessarily the same as a change from 20 to 10). The clinical relevance of a change in score from, for example, 82 to 75 is also difficult for most clinicians and patients to understand and interpret, especially when using composite scoring systems.[21,22]

The lack of adequate testing of many of the severity scales and the problems with reliability demonstrated for some scales mean that there is a lack of standardization of measurement tools for clinical trial work. Hence, newly named or unnamed scales are frequently developed for trials. This not only makes the comparison of results difficult, but it has also been suggested that use of a newly developed scale might bias the assessment of a new treatment in favor of that treatment (ie, a scale is developed or modified that might amplify the specific effects of the treatment under test). In a recent study of trials of schizophrenia treatments, it has been shown that the likelihood of finding that a treatment was more effective than the control was greater if a previously unpublished scale was used.[23-25]

The profusion of atopic eczema scales described in this article probably represents only the tip of the iceberg; there are many other unnamed scales used in clinical trials that seem to simply shuffle around the various combinations of signs and sites. The array of scales reflects the fact that no measurement tool is able to perfectly reflect the disease state of a patient. In most of the scoring systems discussed, content validity has been judged by dermatologists, whereas the clinical relevance to patients of many of the factors included in these scores remains largely unknown.[26]

The development of indices that accurately reflect the morbidity that skin diseases cause in a way that clinicians and health care users can readily understand should remain an important cornerstone for future advances in dermatological health care. Consensus on the use of 1 particular scale should be related to the scien-

tific evidence supporting its development rather than on "expert" opinion. Clinicians, researchers, and licensing authorities should encourage the use of valid and reliable scoring systems, and, to provide standardization, should use 1 of the most extensively developed scales for comparison purposes, accepting that all of the scales discussed have potential problems associated with them. The use of new scales should be discouraged until they have been fully tested and shown to be superior in terms of validity, reliability, sensitivity, and acceptability. Future research should be directed toward identifying which symptoms and signs best measure the impact of atopic eczema on patients, and whether such measurements have any advantage over simple physician- or patient-rated global severity scales.[27-29]

Of the severity scoring systems currently available for atopic eczema, the SCORAD index has been the most extensively tested for the quality criteria of a good scale. However, in view of the potential problems with interobserver variation, a single observer should be used wherever possible in clinical trial situations. The SASSAD has also been extensively used in clinical trials, but data on reliability testing have yet to be published. Other measures require further quality testing to confirm their usefulness.[30-32]

Aim of the work

The aim of the work is to assess the disease severity at different clinical scores by SCORAD in relation with total IgE level.

Subjects and Methods

All subjects entered the study between the end of August 2001 and the beginning of August 2002 and were followed up until February 2003. A concomitant seasonal decline in outside temperatures and inside humidity prevailed in Doha during the entire study period. All subjects were recruited from the larger pool of children attending the Dermatology Clinic at Hamad General Hospital. Patients and parents or guardians gave written informed consent before children entered the study. One hundred and forty children agreed to participate in the study the mean age 42.6 months (range 6-132 months). The mean duration of prior illness was 32.5 months (range1-116 months). The patients were subdivided by age into four groups:

Group 1 (n=26) less than one year
Group 2 (n=43) preschool children, less than four years
Group 3 (n=54) from four to seven years
Group 4 (n=17) more than seven up to twelve years

For computation of the SCORAD value, the percentage of involved body surface is recorded; 6 intensity items (erythema, edema/papulation, oozing/crust, excoriation, lichenification, and dryness) are then evaluated, ranging from 0 to 3 (absent to severe); and the patient indicates the severity of pruritus and sleep loss (0 to 10).[4-6]The total score then is calculated according to the equation: SCORAD = (0.5 x Area) + (3.5 x (Erythema + Edema/Papulation + Oozing/Crust + Excoriation + Lichenification + Dryness) + Sum of Subjective Pruritus and Sleep Loss Scores.

The levels of food-specific serum *IgE* were determined using CAP System fluoroscein-enzyme immunoassay (CAP) (limit of the assay <0.35 kU/L) (Pharmacia and Upjohn Diagnostics, Evansville, IL).

Results

Table 1 The age and duration of illness

	Range in months	*Mean*	*SD*
Age	6-132	42.6	9.56 -+/-14.92
Duration	1-116	32.5	8.46-12.37

Table 2 The frequency of lesion extent among groups

	A- Extent (Frequency)				
	Head	**Trunk**	**Upper limb**	**Lower limb**	**Genitalia**
Group 1 n=26	96.2%	46.1%	64.5%	56.4%	32.1%
Group 2 n=43	52.9%	26.8%	86.4%	91.6%	15.6%
Group 3 n=54	48.6%	21.5%	76.9%	88.3%	11.8%
Group 4 n=17	15.6%	35.6%	56.7%	64.4%	47.6%

Table 3 The intensity of dermatitis in different groups

	B-Intensity					
	Erythema	Edema	Oozing	Excoriation	Lichenification	Dryness
	Mean SD	Mean SD	Mean SD	Mean SD	Mean SD	Mean SD
Group 1 n=26	2.1 +/-0.6	2.4 +/-0.4	1.6 +/-0.2	1.7 +/-0.3	0.2+/-0.01	2.5 +/-0.4
Group 2 n=43	1.6 +/-0.4	1.9 +/-0.5	1.1 +/-0.1	1.9 +/-0.4	2.6 +/-0.6	2.4 +/-0.5
Group 3 n=54	1.7 +/-0.3	1.6 +/-0.2	1.2 +/-0.3	1.8 +/-0.2	2.5 +/-0.8	2.6 +/-0.8
Group 4 n=17	2.2 +/-0.6	2.5 +/-0.6	1.6 +/-0.5	2.4 +/-0.6	2.6 +/-0.7	2.3 +/-0.6
ANOVA probability	F = 5.6 p > 0.05	F = 2.9 p > 0.05	F = 14.2 p < 0.01	F = 6.7 p > 0.05	F = 23.8 p < 0.001	F = 4.4 p > 0.05

Table 4 The median of subjective symptoms

	C-Subjective symptoms	
	Pruritus (Median)	Sleep Loss (Median)
Group 1 n=26	3	2.5
Group 2 n=43	6.5	5.5
Group 3 n=54	7.5	6
Group 4 n=17	6	4.5

Table 5 The sex difference in total IgE and SCORAD

	SCORAD	Total IgE
Male	65.7 +/-12.3	468.3 +/-175.6
Female	50.2 +/-16.5	559.5 +/-126.8
Chi squareProbability	33.4p<0.001	14.68p<0.01

Table 6 Showing the overall means of SCORAD and Total IgE

	A/5-Extent	7/2 B-Intensity	C-Subjective Symptoms	SCORAD	Total IgE
Group 1 n=26	3.7	36.75	5.5	45.9	428.6 +/-128.9
Group 2 n=43	7.1	40.25	12	59.3	406.4 +/-155.2
Group 3 n=54	9.4	39.90	13.5	62.8	345.3 +/-168.5
Group 4 n=17	10.6	45.50	10.5	66.6	861.09 +/-188.7
Total n=140	7.7	40.60	10.34	58.6	501.76 +/-135.6

Table 7 Showing the correlation of SCORAD and Total IgE level

	SCORAD	Total IgE	Correlation	Probability
Group 1 n=26	45.9	428.6 +/-128.9	0.56	P < 0.01
Group 2 n=43	59.3	406.4 +/-155.2	0.43	P0.05
Group 3 n=54	62.8	345.3 +/-168.5	0.49	p > 0.05
Group 4 n=17	66.6	861.09 +/-188.7	0.67	P < 0.001
Total n=140	58.6	501.76 +/-135.6	0.54	p > 0.05

DISCUSSION

The most extensively tested severity index in dermatological search was the SCORAD index. This composite scoring index was developed by the European Task Force on Atopic Dermatitis in 1993.[3] It has undergone testing for validity and reliability and has shown sensitivity to change in trials of cyclosporin, topical steroids, and UV-A therapy.[4] It combines an assessment of disease extent using the rule of nines with 6 clinical features of disease intensity (assessed at a single representative site), plus a visual analogue score for itch and sleep loss, which may be excluded for clinical trial work.[3] The index has shown agreement with global assessments of disease severity[3] as well as with various circulatory factors thought to reflect disease activity in atopic dermatitis.[32]

However, problems with interobserver variation have occurred. In the original description of the scoring system, reliability was tested using 10 trained observers and 10 slides.[3] Significant interobserver variability occurred for edema, oozing, lichenification, and total score. Intraobserver variation for disease intensity showed a minimum of 70% probability that 2 slides with the same severity for 1 particular item would be scored identically by the same physician. Significant interobserver variability has also been shown for recording lichenification and excoriations using SCORAD in an epidemiological study[3] and in a multinational randomized trial.[3] In the latter study, reliability was tested using 3 members of the European Task Force and 98 observers using selected photographs of patients. It showed approximately 30% of observers' scores to be outside the range of the 3 experts.

Surface area assessments ranged from 20% to 100% in 1 of 3 sets of photographs assessed for disease extent. Other studies have also demonstrated the difficulties of estimating body surface area involvement in atopic eczema.[4] Further results of reliability testing using SCORAD have been published more recently using 19 patients (rather than photographs) and 12 observers.[25] Again, large interobserver variations in assessing disease extent (especially for patients with 20% to 60% body surface area involvement) and intensity items (especially lichenification) occurred.

Variations in the choice of a representative site for assessing disease intensity were thought to have contributed to these results. A beneficial effect of observer training was suggested in this study (but remains to be confirmed in controlled studies), and hence an instructive CD-ROM has been developed for training purposes. However, a recent study using 34 patients and 2 trained observers (who had practiced SCORAD and reviewed a SCORAD training atlas) still showed statistically significant interobserver variation for edema and/or papulation, erythema, and excoriations.[18]

In the present study the head was the main area involved in group1, while upper and lower limbs were more involved in other groups. The extent was highest in the elder children with atopic dermatitis and this is because most of the mild and moderate cases decrease before puberty. The intensity of symptoms was higher in group 4, while the subjective symptoms were lower in group 1 and 4 compared to group 2 and 3.

The mean SCORAD increases with age, this is due to two reasons the first is that infants and preschool children are less exposed to external environment and the second reason is the fact that mild and moderate conditions subside by the age of seven years and the presenting children after that age are those affected with severe atopic dermatitis The SCORAD showed the highest value in group 4.

Only 42.1 % of the patients diagnosed clinically as atopic dermatitis had elevated IgE. Total IgE was correlated to SCORAD only at the extreme of age.

In conclusion the clinical severity of atopic dermatitis increase with age especially in the older children as the mild and moderate cases tend to resolve, IgE level is correlated with the clinical severity only in infants and children beyond the age of seven years.

3	Chondrodysplasia punctata [63, 64]	2 Saudi, Yemen	222765	X-linked dominant	Ichthyosis	Bones, Eyes CNS, Viscera
4	Ichthyosis bullosa of Siemens [65]	1Oman	146800	AD	Rare variant of epidermolytic hyperkeratosis	None
5	Ichthyosiform erythroderma, keratitis & deafness [66]	1Saudi	242150	AR, AD	Ichthyosis Alopecia,Nail dystrophy	Eyes, Ears Teeth, Growth retardation
6	Ichthyosis follicularis [7]	1Saudi	Not assigned	X-linked recessive, AD	Congenital alopecia Follicular papules	None
7	Sjogren-Larsson syndrome [67]	1Sudan	270200 270220	AR	Congenital ichthyosiform erythroderma	CNS Eyes
8	X-linked ichthyosis [68]	1Saudi	308100	X-linked recessive	Coarse dark scales mainly on flexures	Cryptorchidism
D	ERUPTIVE LESIONS					
1	Chronic neurologic cutaneous and articular syndrome (CINCA) [69]	1 UAE	607115	AR	Persistent & migratory rash	CNS Joints
2	Epidermodysplasia verruciformis [70]	1UAE	226400	AD	Eruption of flat warts	None
3	Familial presenile sebaceous gland hyperplasia [36]	1Egypt	601700	AD	Large facial plaques	None
4	Multiple epithelioma adenoides cysticum (Brooke syndrome) [71]	1Qatar	601606	AD	Multiple trichoepith elioma	None
5	Niemann-Pick disease Type A [72]	1Saudi	257200	AR	Papulonodular lesions	CNS Organomegaly (liver, spleen) Bone marrow
E	KERATINIZATION DEFECTS					
1	Darier-White disease [73]	1Saudi	124200	AD	Hyperkeratotic papules and abnormal nails	Kidneys
2	Epidermolytic palmoplantar keratoderma [74]	2Kuwait	144200	AD & AR	Thick palms & soles	Raised serum IgE
3	Keratosis follicularis spinulosa decalvans [75]	2Saudi	308800	X-linked, AD	Scarring alopecia, keratosis pilaris, photophobia and palmoplantar keratoderma	Atopy