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Validation of the Diagnostic Criteria for Atopic Dermatitis in the Adult Thai Population

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SUMMARY Atopic dermatitis is a chronic inflammatory skin disorder, for which it is difficult to obtain epidemiologic findings. In a previous study, we suggested the following diagnostic criteria for atopic dermatitis in the adult Thai population: visible flexural dermatitis, a history of flexural dermatitis, a rash of more than six months duration and visible dry skin. However these criteria were not validated against physicians' diagnoses. In the present study, we validated these diagnostic criteria for atopic dermatitis in the Thai population in a clinical setting. A case-controlled study was performed on a total of 259 patients; 33 subjects with active atopic dermatitis, 26 with inactive atopic dermatitis, 100 controls presenting with an inflammatory skin disorder other than atopic dermatitis and 100 controls without any skin disease. Each patient was examined according to the above criteria. Sensitivity, specificity, relative value, positive predictive value, and negative predictive value were calculated for each individual criterion and for composite criteria. Our data confirmed that in order to achieve satisfactory sensitivity and specificity for diagnosing atopic dermatitis in Thai people older than 13 years, a patient must have a history of flexural dermatitis plus two or more of the other mentioned criteria.

Atopic dermatitis is a common chronic inflammatory skin disorder that is characterized by erythematous, eczematous, intense pruritic lesions and dry skin. The onset is usually in the early childhood and the condition is typically long-lasting with at least one-third of the patients having persistent disease throughout adulthood. The disease is often associated with asthma, allergic rhinitis, food allergy and secondary skin infection. Many studies have estimated the incidence of atopic dermatitis in the general population to be between 3% and 20%.[1-3] Recent studies of Thai children and adolescents with atopic dermatitis have reported a prevalence of 9%[4] and 9.4%[5], respectively. In recent decades the worldwide incidence of atopic dermatitis has seemed to increase steadily.[1,6,7]

Although the clinical picture of atopic dermatitis is well known for several years, there is no objective laboratory marker for the disease. Hanifin and Lobitz, with later revisions by Hanifin and Rajka, proposed major and minor diagnostic criteria for the diagnosis of atopic dermatitis.[8] However, these criteria are not suitable for population-based studies because of a lack of accurate definitions, and infrequent and non-specific findings. Some criteria needed invasive investigations. Thus, despite its frequency, precise epidemiologic findings of this disease are difficult to obtain.

Williams *et al.*[9] assessed the significance of the major and minor criteria for atopic dermatitis in order to develop a definition of atopic dermatitis that

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is sensitive, specific, reproducible, non-invasive, and applicable to a range of ethnic groups, and which is easy to perform in population-based and clinical studies. Their study included patients with atopic dermatitis and patients with other inflammatory skin diseases. All of the major and minor criteria were evaluated but invasive investigations such as skin prick tests, serum IgE and RAST tests, while testing for white dermographism, eosinophilia, and skin swabs were excluded. The sensitivity and specificity of 31 diagnostic criteria (13 historical and 18 physical signs) were tested. This study suggested that a good separation of atopic dermatitis cases from controls with other inflammatory dermatoses can be achieved through 6 characteristics: a history of flexural involvement, a history of a dry skin, onset before the age of 2 years, a personal history of asthma, a history of a pruritic skin condition, and visible flexural dermatitis.[9]

Because of some variations in the frequency, symptoms, and severity among studies about atopic dermatitis worldwide which may be explained by ethnic, racial, genetic, climate, environmental and pollution variations,[10-14] we previously used a study design similar to one used by the U.K. Working Party for validating diagnostic criteria for atopic dermatitis in Thai patients. A case-controlled study was performed to analyze the diagnostic value of atopic features in the Thai population older than 13 years.[15] Seventy patients with atopic dermatitis and seventy exactly age-matched and sex-matched controls with an inflammatory skin disease other than atopic dermatitis were recruited from the out-patient division of the Dermatological Department, Faculty of Medicine, Siriraj Hospital, between October 1997 and September 2000. We reported that our diagnostic criteria for atopic dermatitis in the adult Thai population were visible flexural dermatitis, a history of flexural dermatitis, a rash of more than six months duration and visible dry skin.[15]

In order to validate the diagnostic criteria of the U.K. Working Party for atopic dermatitis, these criteria were tested in an independent sample of 200 consecutive dermatology outpatients comprising all ages.[16] The combination of the diagnostic criteria achieved 69% sensitivity and 96% specificity when validated against physicians' diagnoses. Their studies suggested that the newly proposed criteria for atopic dermatitis performed reasonably well in hospital out-patient settings.

Like the U.K. Working Party's, the purpose of our study was to validate diagnostic criteria for use in population-based and clinical studies of the Thai population.

MATERIALS AND METHODS

Using a study design similar to that used by the U.K. Working Party for validating diagnostic criteria for atopic dermatitis, patients who were older than 13 years were enrolled from the Dermatology Clinic at the Department of Dermatology, Faculty of Medicine, Siriraj Hospital, between October 2000 and September 2002.

Patients affected by active and inactive atopic dermatitis according to the criteria of Hanifin & Rajka, patients affected by other inflammatory skin disorders, and healthy controls were enrolled in the study. Every patient was asked about and examined for these criteria: 1) visible flexural dermatitis, 2) a history of flexural dermatitis, 3) a rash of more than six months duration, and 4) visible dry skin. Clinical diagnosis and other demographic features, including age and sex, were noted by a trained dermatologist.

The protocol and informed consent documents were reviewed and approved by the ethics committees of the Faculty of Medicine, Siriraj Hospital. Informed consent was obtained from all patients and the study protocol conformed to the 1975 Declaration of Helsinki.

Each criterion was analyzed for its sensitivity, specificity, relative value, positive predictive value, and negative predictive value using the SPSS/Win software package.

RESULTS

Two hundred and fifty nine subjects were recruited into the study. Of those, a total of 33 subjects (12.7%) had active atopic dermatitis, 26 inactive atopic dermatitis (10%), 100 patients had other inflammatory skin diseases (38.6%) and 100 patients were without any skin disease (38.6%). Age and sex of all patients are shown in Table 1. Of the 100

Table 1 Age and sex of patients with different clinical manifestations

Populations	Age (years)	Sex [n,(%)]	
		Male	Female
Patients without skin disorders	30.3	54 (54)	46(46)
Patients with inactive atopic dermatitis	27.2	9 (34.6)	17 (65.4)
Patients with active atopic dermatitis	28.2	8 (24.2)	25 (75.8)
Patients with other inflammatory skin disorders	36.9	54 (54.0)	46 (46.0)

Table 2 Sensitivity, specificity, relative value (RV), positive predictive value, and negative predictive value between patients with atopic dermatitis (active and inactive atopic dermatitis) and the other groups of patients (patients without any skin diseases and patients with other inflammatory skin diseases)

	Sensitivity (%)	Specificity (%)	Relative value	Positive predictive value	Negative predictive value
Individual features					
A	96.6	70.0	66.6	48.7	98.6
B	86.4	74.5	60.9	50.0	94.9
C	54.2	92.0	46.2	66.7	87.2
D	61.0	95.0	56.0	78.3	89.2
Composite of 2 criteria					
A and B	81.3	85.5	66.8	62.8	94.5
A and C	54.2	94.0	48.2	72.7	87.4
A and D	59.3	98.0	57.3	89.7	89.1
B and C	47.5	94.5	42.0	71.8	85.9
B and D	52.5	97.5	50.0	86.1	87.4
C and D	37.3	99.0	36.3	91.7	84.3
Composite of 3 criteria					
A, B and C	47.5	96.0	43.5	77.8	86.1
A, B and D	50.8	99.0	49.8	93.8	87.2
A, C and D	37.3	99.0	36.3	91.7	84.3
B, C and D	30.5	99.5	30.0	94.7	82.9
Composite of 4 criteria					
A, B, C and D	30.5	99.5	30.0	94.7	82.9
Composite criteria					
A plus 1 or more	91.5	83.0	74.5	61.4	97.1
B plus 1 or more	84.7	82.5	67.2	58.8	94.8
C plus 1 or more	54.2	92.5	46.7	68.1	87.3
D plus 1 or more	61.0	96.5	57.5	83.7	89.4
A plus 2 or more	74.6	95.0	69.6	81.5	92.7
B plus 2 or more	67.8	95.5	63.3	81.6	91.0
C plus 2 or more	54.2	95.5	49.7	78.0	87.6
D plus 2 or more	57.6	98.5	56.1	91.9	88.7
A and B plus 1 or more	67.8	95.5	63.3	81.6	91.0
A and C plus 1 or more	54.2	95.5	49.7	78.0	87.6
A and D plus 1 or more	57.6	98.5	56.1	91.9	88.7
B and C plus 1 or more	47.5	96.0	43.5	77.8	86.1
B and D plus 1 or more	50.8	99.0	49.8	93.8	87.2
C and D plus 1 or more	37.3	99.0	36.3	91.7	84.3

A = History of flexural dermatitis; B = Duration > 6 months; C = Visible flexural dermatitis; D = Visible dry skin.

patients with other inflammatory skin diseases, 41 had eczema/dermatitis (41%), 22 fungal infections (22%), 6 acne vulgaris (6%), and 31 had other inflammatory dermatoses (31%).

Table 3 Sensitivity, specificity, relative value (RV), positive predictive value, and negative predictive value between patients with atopic dermatitis (active and inactive atopic dermatitis) and patients without any skin diseases

	Sensitivity (%)	Specificity (%)	Relative value	Positive predictive value	Negative predictive value
Individual features					
A	96.6	87.0	83.6	81.4	97.8
B	86.4	97.0	83.4	94.4	92.4
C	54.2	100.0	54.2	100.0	78.7
D	61.0	98.0	59.0	94.7	81.0
Composite of 2 criteria					
A and B	83.1	100.0	83.1	100.0	90.9
A and C	54.2	100.0	54.2	100.0	78.7
A and D	59.3	100.0	59.3	100.0	80.6
B and C	47.5	100.0	47.5	100.0	76.3
B and D	52.5	100.0	52.5	100.0	78.1
C and D	37.3	100.0	37.3	100.0	73.0
Composite of 3 criteria					
A, B and C	47.5	100.0	47.5	100.0	76.3
A, B and D	50.8	100.0	50.8	100.0	77.5
A, C and D	37.3	100.0	37.3	100.0	73.0
B, C and D	30.5	100.0	30.5	100.0	70.9
Composite of 4 criteria					
A, B, C and D	30.5	100.0	30.5	100.0	70.9
Composite criteria					
A plus 1 or more	91.5	100.0	91.5	100.0	95.2*
B plus 1 or more	84.7	100.0	84.7	100.0	91.7
C plus 1 or more	54.2	100.0	54.2	100.0	78.7
D plus 1 or more	61.0	100.0	61.0	100.0	81.3
A plus 2 or more	74.6	100.0	74.6	100.0	87.0
B plus 2 or more	67.8	100.0	67.8	100.0	84.0
C plus 2 or more	54.2	100.0	54.2	100.0	78.7
D plus 2 or more	57.6	100.0	57.6	100.0	80.0
A and B plus 1 or more	67.8	100.0	67.8	100.0	84.0
A and C plus 1 or more	54.2	100.0	54.2	100.0	78.7
A and D plus 1 or more	57.6	100.0	57.6	100.0	80.0
B and C plus 1 or more	47.5	100.0	47.5	100.0	76.3
B and D plus 1 or more	50.8	100.0	50.8	100.0	77.5
C and D plus 1 or more	37.3	100.0	37.3	100.0	73.0

A = History of flexural dermatitis; B = Duration > 6 months; C = Visible flexural dermatitis; D = Visible dry skin.

The analysis was done both using individual and composite criteria. The overall sensitivity, specificity, relative value, positive predictive value, and negative predictive value of patients with atopic dermatitis (active and inactive atopic dermatitis) compared to patients without skin diseases and to patients with other inflammatory skin disorders are shown in Tables 2, 3 and 4, respectively. The relative value (RV) was derived by the summation of sensitivity and specificity, and then subtracting 100.

When comparing patients with atopic dermatitis (active and inactive) to patients with other inflammatory skin disorders or patients without skin diseases, the highest overall relative value and negative predictive value was obtained by a history of flexural dermatitis (A) plus 1 or more of the three remaining criteria (Tables 2 and 3). However, these composite criteria had a lower relative value than a history of flexural dermatitis plus 2 or more of the three remaining criteria when compared to patients with other inflammatory skin disorders (Table 4).

Table 4 Sensitivity, specificity, relative value (RV), positive predictive value, and negative predictive value between patients with atopic dermatitis (active and inactive atopic dermatitis) and patients with other inflammatory skin diseases

	Sensitivity (%)	Specificity (%)	Relative value	Positive predictive value	Negative predictive value
Individual features					
A	96.6	53.0	49.6	54.8	96.4
B	86.4	52.0	38.4	51.5	86.7
C	54.2	84.0	38.2	66.7	75.7
D	61.0	92.0	53.0	81.8	80.0
Composite of 2 criteria					
A and B	83.1	71.0	54.1	62.8	87.7
A and C	54.2	88.0	42.2	72.7	76.5
A and D	59.3	96.0	55.3	89.7	80.0
B and C	47.5	89.0	36.5	71.8	74.2
B and D	52.5	95.0	47.5	86.1	77.2
C and D	37.3	98.0	35.3	91.7	72.6
Composite of 3 criteria					
A and B and C	47.5	92.0	39.5	77.8	74.8
A and B and D	50.8	98.0	48.8	93.8	77.2
A and C and D	37.3	98.0	35.3	91.7	72.6
B and C and D	30.5	99.0	29.5	94.7	70.7
Composite of 4 criteria					
A and B and C and D	30.5	99.0	29.5	94.7	70.7
Composite criteria					
A plus 1 or more	91.5	66.0	57.5	61.4	93.0*
B plus 1 or more	84.7	65.0	49.7	58.8	87.8
C plus 1 or more	54.2	85.0	39.2	68.1	75.9
D plus 1 or more	61.0	93.0	54.0	83.7	80.2
A plus 2 or more	74.6	90.0	64.6	81.5	85.7
B plus 2 or more	67.8	91.0	58.8	81.6	82.7
C plus 2 or more	54.2	91.0	45.2	78.0	71.1
D plus 2 or more	57.6	97.0	54.6	91.9	79.5
A and B plus 1 or more	67.8	91.0	58.8	81.6	82.7
A and C plus 1 or more	54.2	91.0	45.2	78.0	77.1
A and D plus 1 or more	57.6	97.0	54.6	91.9	79.5
B and C plus 1 or more	47.5	92.0	39.5	77.8	74.8
B and D plus 1 or more	50.8	98.0	48.8	93.8	77.2
C and D plus 1 or more	37.3	98.0	35.3	91.7	72.6

A = History of flexural dermatitis; B = Duration > 6 months; C = Visible flexural dermatitis; D = Visible dry skin.

In order to establish diagnostic criteria that can be used in population-based and clinical studies in the Thai population, criteria comprising one major criterion (a history of flexural dermatitis) plus two or more of the three remaining minor criteria (duration > 6 months, visible flexural dermatitis and visible dry skin) were most effective. These composite criteria can distinctly differentiate between patients with atopic dermatitis and patients with other inflammatory skin diseases.

DISCUSSION

Atopic dermatitis is a common skin disorder in Thai children. The prevalence of atopic dermatitis in Thai children is about 6-13%.[17,18] A diagnosis of atopic dermatitis is difficult because of a lack of ob-

jective laboratory findings. Many reports have evaluated the diagnostic significance of atopic criteria. De, *et al*.[19] reported that Hanifin and Rajka's criteria were more sensitive (96%) but less specific (93.8%) than the U.K. Working Party diagnostic criteria (86% and 95.8%, respectively). However, Johnke *et al*.[20] proposed that an agreement between different criteria for diagnosing atopic dermatitis was acceptable, but mild cases constituted a diagnostic problem. In general, major criteria should be sensitive enough to identify a majority of cases and minor criteria should then be used to exclude other skin diseases.

Wisuthsarewong *et al*.[21] proposed that the most useful diagnostic criteria for Thai children consisted of a history of itchy rash, a history of flexural dermatitis, chronicity for more than 6 months, visible xerosis, periorbital dermatitis, and perifollicular accentuation. In our study, we documented that the most sensitive criterion is a history of flexural dermatitis and the most specific criterion is visible dry skin followed by visible flexural dermatitis. These criteria have a satisfactory sensitivity and specificity for diagnosing atopic dermatitis in Thai people older than 13 years.

Our data confirm that a patient must have a history of flexural dermatitis plus two or more of the following: duration longer than 6 months, visible flexural dermatitis, or visible dry skin. These criteria can be used to diagnose Thai patients with atopic dermatitis who are older than 13 years-old in population-based studies. However, our study was limited by the small sample size. Further studies need to expand on this research examining larger samples and community settings to confirm the results of our study.

REFERENCES

1. Laughter D, Istvan JA, Tofte SJ, Hanifin JM. The prevalence of atopic dermatitis in Oregon school children. J Am Acad Dermatol 2000; 43: 649-55.
2. Wordemann M, Polman K, Diaz RJ, *et al.* The challenge of diagnosis atopic diseases: outcomes in Cuban children depend on definition and methodology. Allergy 2006; 61: 1125-31.
3. Fukiwake N, Furusyo N, Kubo N, Takeoka H, Toyoda K, Morita K. Incidence of atopic dermatitis in nursery school children- a follow- up study from 2001 to 2004, Kyushu University Ishigaki Atopic Dermatitis Study (KIDS). Eur J Dermatol 2006; 16: 146-9.
4. Vichayanond P, Jirapohgsananuruk O, Tuchinda M, Visitsunthorn N. Prevalence of asthma, rhinitis and eczema in children from the Bangkok area using the ISAAC questionnaires. J Med Assoc Thai 1998; 81: 175-84.
5. Vichayanond P, Sunthornchart S, Singhirannusorn V, Ruangrat S, Kaewsomboon S, Visitsunthorn N. Prevalence of asthma, allergic rhinitis and eczema among university students in Bangkok. Respir Med 2002; 96: 34-8.
6. Williams HC. Is the prevalence of atopic dermatitis increasing? Clin Exp Dermatol 1992; 17: 385-91.
7. Mohammedamin RS, van der Wouden JC, Koning S, *et al.* Increasing incidence of skin disorder in children? A comparison between 1987 and 2001. BMC Dermatol 2006; 6: 4.
8. Hanifin JM, Rajka G. Diagnostic features of atopic dermatitis. Acta Derm Venereol (Stockh) 1980; (Suppl.1); 92: 44-7.
9. Williams HC, Burney PGJ, Hay RJ, *et al.* The U.K. Working Party's Diagnostic Criteria for Atopic Dermatitis I: Derivation of a minimum set of discriminators for atopic dermatitis. Br J Dermatol 1994; 131: 383-96.
10. Sladden MJ, Dure-Smith B, Berth-Jones J, *et al.* Ethnic differences in the pattern of skin disease seen in a dermatology department - atopic dermatitis is more common among Asian referrals in Leicestershire. Clin Exp Dermatol 1991; 16: 348-9.
11. Jaafar RB, Pettit JHS. Atopic eczema in a multiracial country (Malaysia). Clin Exp Dermatol 1993; 18: 496-9.
12. Schultz Larsen F, Holm NV, Henningsen K. Atopic dermatitis: A genetic-epidemiologic study in a population-based twin sample. J Am Acad Dermatol 1986; 15: 487-94.
13. Cork MJ, Robinson DA, Vasilopoulos Y, *et al.* New perspectives on epidermal barrier dysfunction in atopic dermatitis: gene-environment interactions. J Allergy Clin Immunol 2006; 118: 3-21.
14. Bowker NC, Cross KW, Fairburn EA, Wall M. Sociological implication of an epidemiological study of eczema in the City of Bermingham. Br J Dermatol 1976; 95: 137-44.
15. Wanitphakdeedecha R, Sivayathorn A. Diagnostic Criteria for Atopic Dermatitis in Adult Thai Population. Indian J Dermatol 2007; 52: 83-8.
16. Williams HC, Burney PGJ, Pembroke AC, Hay RJ. The U.K. Working Party's Diagnostic Criteria for Atopic Dermatitis III: Independent hospital validation. Br J Dermatol 1994; 131: 406-16.
17. Chutsirimongkol S. Prevalence of allergy in school-children. Thai J Pediatr 1996; 35: 188-98.
18. Wisuthsarewong W, Viravan S. Analysis of skin disease in referral pediatric dermatology clinic in Thailand. J Med Assoc Thai 2000; 83: 999-1004.
19. De D, Kanwar AJ, Handa S. Comparative efficacy of Hanifin and Rajka's criteria and the UK working party's diagnostic criteria in diagnosis of atopic dermatitis in a hospital setting in North India. J Eur Acad Dermatol Venerol 2006; 20: 853-9.
20. Johnke H, Vach W, Norberq LA, Bindslev-Jensen C, Host A, Anderson KE. A comparison between criteria for diagnosing atopic eczema in infants. Br J Dermatol 2005; 153: 352-8.
21. Wisuthsarewong W, Viravan S. Diagnostic criteria for atopic dermatitis in Thai children. J Med Assoc Thai 2004; 87: 1496-50.