Diagnostic Criteria for Atopic Dermatitis in Thai Children

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Atopic dermatitis (AD) is a common skin disease in Thai children. There is no clinical or laboratory gold standard for the diagnosis. It is generally based on the guideline proposed by Hanifin and Rajka. Many studies have shown that some criteria are probably not all that significant in making the diagnosis. This study was designed to evaluate the frequency and diagnostic significance of clinical features of AD in Thai children. The authors studied 108 patients with AD and 103 controls including patients with other skin diseases. The AD group consisted of 60 girls and 48 boys. The mean age was 60.3 $\pm$ 36.1 months. All previously proposed features were evaluated and the difference in frequency was tested with the chi-square test.

History of pruritus, rash on typical distribution, chronically relapsing course, duration more than 6 months, personal or family history of atopy, age of onset before 2 years, recurrent conjunctivitis, itch when sweating, intolerance to rough textile, food and milk intolerance, history of dry skin, seasonal variation, visible dermatitis, dermatitis of a typical distribution, xerosis, ichthyosis vulgaris, foot dermatitis, Dennie-Morgan infraorbital fold, orbital darkening, periorbital dermatitis, pityriasis alba, peri-auricular dermatitis, anterior neck fold, truncal dermatitis, perifollicular accentuation, white dermographism and diffuse scaling of scalp were all significantly more frequent in AD ($p < 0.05$).

A minimum set of diagnostic criteria for AD was derived by using multiple stepwise logistic regression technique. It consisted of history of itchy rash, history of flexural dermatitis, chronicity more than 6 months, and visible xerosis, periorbital dermatitis and perifollicular accentuation.

Keywords : *Atopic dermatitis, Diagnostic criteria, Diagnosis*

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Atopic dermatitis (AD) is a common chronic dermatitis in children in many countries. There are different subgroups within the vast entity of AD. There is still no laboratory test or definite marker for establishing the diagnosis of AD. Clinical evaluation is the most important. The diagnosis is based on the presence or absence of clinical features. There are several sets of criteria used for diagnosis of AD such as by Hanifin and Rajka[1], U.K working group[2-4], and others[5-7], most of which were based on traditional clinical experience. The significance of certain minor criteria varied according to age group, ethnic and racial factors[7-10]. However, there are numerous features which are characteristic, but mostly nonspecific. Many investigators have evaluated the diagnostic significance of many clinical features in AD[11-23].

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This study was designed to assess the frequency and significance of the major and minor clinical features of AD in Thai children without laboratory investigations as proposed by Hanifin and Rajka and other studies, compared to the control group. The criteria for diagnosis of AD in Thai children were evaluated to improve the accuracy of diagnosis in this specific population.

Material and Method

Patients were selected from the Pediatric Dermatology Clinic at the Department of Pediatrics, Faculty of Medicine Siriraj Hospital. Diagnosis of AD with all degrees of severity was established according to Hanifin and Rajka. Control subjects matched to age and sex were randomly selected from the same clinic. Information was gathered both by history taking and physical examination. All atopic basic major and minor features described in previous studies except labora-

tory investigations and complicated physical examination were studied in both groups. To achieve a good inter-observer agreement, the clinical examination was performed by two dermatologists simultaneously. The features studies were subjectively evaluated as present or absent.

The following histories were obtained from the history alone; pruritus, flexural lichenification or linearity in older children, rash affected face or extensor surface in infants, chronically relapsing course, duration, personal and family history of atopy, age of onset, history of tendency toward cutaneous infections (bacteria, HSV, warts), history of tendency toward hand and foot dermatitis, recurrent conjunctivitis, itch when sweating, intolerance to wool or rough textiles, intolerance to lipid solvent and topical treatment/cream, food, milk, and drug intolerance, intolerance to metal (nickle sulfate)[11,23], history of dry skin, pronounced insect bite reaction[23], history of breast feeding, seasonal variation[23], smoking[24], pets and furry toys in the house, course influenced by environmental, emotional factors, infection and house dust[8].

Thirty-three features were examined including visible dermatitis, dermatitis on typical distribution, xerosis, ichthyosis vulgaris, palmar and plantar hyperlinearity, hand and foot dermatitis, conjunctivitis, Dennie-Morgan infraorbital fold[18], orbital darkening, periorbital dermatitis, cheilitis, facial pallor or erythema, pityriasis alba, periauricular dermatitis, infra-auricular fissure[16], anterior neck fold, truncal dermatitis, extensor dermatitis, nipple eczema, perifollicular accentuation, white dermographism, diffuse scaling of scalp[16], fine hair[2], Hertoghe's sign, insect bite reaction[23], dyshidrosis, nummular eczema, low hairline[20], geographic tongue and peeling of proximal nail fold.

Criteria which were not studied included immediate skin test reactivity, serum IgE level, keratoconus, and anterior subcapsular cataract. These criteria are important for research purposes but not for practical purposes.

Statistical analysis

For each parameter, the difference in frequency between AD patients and controls was tested by the chi-square test. The level of significance chosen was $p < 0.05$. The p value from the Fisher Exact test was calculated when expected count was less than 5. Multiple logistic regression was applied to find out the minimum set of diagnostic criteriafor AD.

A minimum set of diagnostic criteria for AD was derived by using multiple stepwise logistic regression technique.

Results

There were 108 children in the AD group consisting of 60 girls, and 48 boys. The control group comprised 103 patients with 44 girls and 59 boys with various skin diseases such as seborrheic dermatitis, nummular eczema, insect bite reaction, hand and foot eczema, dyshidrosis, contact dermatitis, scabies, impetigo, psoriasis, lichen striatus, and other miscellaneous skin diseases. The mean age of patients with AD was 60.3 ± 36.1 months and of control was 57.0 ± 39.2 months. The minimum age of the AD group was 2 months and maximum age was 11 years. There was no significant difference in sex, and age between patients with AD and control ($p = 0.08$ and $p = 0.53$).

The frequencies of all features evaluated and the p value are shown in Table 1. Of all the features evaluated, history of pruritus, rash on typical distribution, chronically relapsing course, duration more than 6 months, personal and family history of atopy, age of onset before 2 years, recurrent conjunctivitis, itch when sweating, intolerance to rough textiles, food and milk intolerance, history of dry skin, seasonal

Table 1. The frequencies of all criteria evaluated and the p value

History	AD (%)	Control (%)	p-value
1. Pruritis	99.1	78.6	0.001
2. Typical distribution	99.1	29.1	0.001
3. Chronically relapsing course	100.0	57.3	0.001
4. Personal history of atopy	39.8	21.4	0.006
5. Family history of atopy	66.7	44.7	0.002
6. Age of onset before 2 yr	65.7	39.2	0.001
7. Tendency toward cutaneous infections	19.4	18.4	0.993
8. Tendency toward hand dermatitis	28.7	23.3	0.461
9. Tendency toward foot dermatitis	23.1	22.3	1.000
10. Recurrent conjunctivitis	12.0	2.9	0.025
11. Itch when sweating	77.8	35.9	0.001
12. Intolerance to wool or rough textile	24.1	4.9	0.001
13. Intolerance to lipid solvent	13.9	5.8	0.084
14. Intolerance to topical treatment-cream	7.9	4.9	0.628
15. Food intolerance	36.1	9.7	0.001
16. Milk intolerance	8.3	1.0	0.019
17. Drug intolerance	8.3	5.8	0.659
18. Intolerance to metal	19.4	10.7	0.114
19. History of dry skin	88.0	39.8	0.001
20. Pronounce insect bite reaction	41.7	46.6	0.560
21. Breast feeding during the first 6 m	93.5	88.3	0.284
22. Seasonal variation	75.0	26.2	0.001
23. Course influenced by emotional factors	1.9	3.9	0.437
24. Course influenced by infections	6.5	1.9	0.171
25. Smoking in the house	50.0	53.4	0.722
26. Pets in the house	36.1	38.8	0.790
27. Furry toy in the house	42.6	43.7	0.983
28. Course influenced by house dust	29.6	20.4	0.165

Additional History	AD (%)	Control (%)	p-value
1. Itchy rash	100.0	81.6	0.001
2. Itchy rash come and go > 6 m	93.5	41.7	0.001
3. Itchy rash come and go on the skin crease > 6 m	92.6	1.0	0.001
Physical examination	**AD (%)**	**Control (%)**	**p-value**
1. visible dermatitis	100.0	95.1	0.026
2. dermatitis on typical distribution	100.0	80.6	0.001
3. xerosis	60.2	13.6	0.001
4. ichthyosis vulgaris	24.1	7.8	0.002
5. palmar hyperlinearity	49.1	42.7	0.431
6. plantar hyperlinearity	33.3	28.2	0.506
7. hand dermatitis	36.1	45.6	0.205
8. foot dermatitis	25.9	42.7	0.015
9. conjunctivitis	7.4	2.9	0.247
10. Dennie Morgan infraorbital fold	21.3	9.7	0.033
11. orbital darkening	50.0	34.0	0.027
12. periorbital dermatitis	48.1	6.8	0.001
13. cheilitis	8.3	3.9	0.290
14. facial pallor / facial erythema	4.6	4.9	1.000
15. pityriasis alba / hypopigmented patch	28.7	15.5	0.033
16. peri-auricular dermatitis	38.9	21.4	0.009
17. infra-auricular fissure	10.2	8.7	0.920
18. anterior neck fold	72.2	44.7	0.001
19. truncal dermatitis	74.1	45.6	0.001
20. extensor dermatitis	77.8	74.8	0.723
21. nipple eczema	4.6	5.8	0.936
22. perifollicular accentuation	47.2	3.9	0.001
23. keratosis pilaris	9.3	2.9	0.103
24. white dermographism	18.5	1.0	0.001
25. diffuse scaling of scalp	23.1	10.7	0.026
26. fine hair	9.3	8.7	1.000
27. Hertoghe's sign	0.9	0.0	1.000
28. insect bite reaction	25.9	29.1	0.714
29. dyshidrosis	2.8	4.9	0.490
30. nummular eczema	8.3	8.7	1.000
31. low hairline	69.4	68. 9	1.000
32. geographic tongue	5.6	6.8	0.930
33. peeling skin at proximal nailfold	38.9	36.9	0.875

variation, visible dermatitis, dermatitis of a typical distribution, xerosis, ichthyosis vulgaris, foot dermatitis, Dennie-Morgan infraorbital fold, orbital darkening, periorbital dermatitis, pityriasis alba, peri-auricular dermatitis, anterior neck fold, truncal dermatitis, perifollicular accentuation, white dermographism and diffuse scaling of scalp were statistically significantly more frequent in AD ($p < 0.05$). The prevalence of several minor features has been found worthless because they did not differ significantly between AD patients and controls.

All patients with AD had visible dermatitis on the typical distribution at the time of examination. The mean duration of AD patients in the present study was 36.2 ± 26.9 months and 77.8% of them had the disease longer than one year. Onset of the eruption was 31.5%, 65.7% and 88.9% before the age of 6 months, 2 years and 5 years, respectively. The disease was aggravated in summer in 51.9%, winter in 15.7% and both seasons in 6.5%. Among the patients who had a personal history of atopic disease (39.8%), 34.3% had allergic rhinitis, 11.1% had asthma, 0.9% had allergic conjunctivitis and 7.4% had both asthma and allergic rhinitis. Family history of allergic rhinitis was also more frequent than other atopic diseases. Periorbital dermatitis was found with periorbital darkening in 15.7% and both of them were found with Dennie-Morgan infraorbital fold in 11.1% of AD patients. Perifollicular accentuation was commonly found on the back, chest, abdomen and arm. Irritation from textiles was obtained in about 24.1%. Almost one third of AD reported food intolerance. Most of the patients in both groups were breast-fed during the first 6 months. History of the reaction to drugs and milk was minimal.

Using multiple stepwise logistic regression technique, the minimum set of diagnostic criteria for atopic dermatitis was derived. The most useful diagnostic criteria consisted of history of itchy rash, history of flexural dermatitis, chronicity more than 6 months, visible xerosis, periorbital dermatitis and perifollicular accentuation.

Discussion

AD is a common skin disorder. Prevalence of AD in Thai children in the general population is about 13.4% and 6-9% in the Pediatric Dermatology Clinic [25,26]. To make the diagnosis of AD with confidence, one has to depend on the history and clinical pictures. It is relatively easy for an experienced dermatologist to recognize classic atopic individuals just from their appearance. The diagnostic problem for AD especially in presumably AD individuals without typical manifestation, patients with AD during remission or modified by some treatment or infancy with the early stage of disease may pose a problem to non-dermatologists who lack familiarity with cutaneous disease. Diagnostic guidelines can be of special value in this situation but there is no uniform diagnostic criteria for AD. Hanifin and Rajka developed a list of criteria to help in diagnosing AD[1]. Many criteria have no precise definition. Some are very infrequent and some are non-specific. The list has gained almost universal acceptance and provides some uniformity in the diagnosis of AD. Many investigators evaluated the diagnostic significance of these clinical features and found a large variation[11-23]. The previously proposed criteria were validated in various age groups and population settings[27-30]. The variation could be partly because of differences in age, genetic background, environmental factors of the population and the method studied[7-10].

Previous data on the prevalence of stigmata in AD in Thai children is scarce. The prevalence of most stigmata evaluated in the present study was significantly higher in the patients with AD compared with controls. The 3 major criteria including pruritus, typical distribution and chronic relapsing course proposed by Hanifin and Rajka are very common and very helpful in differentiating AD from other dermatologic diseases. Although the prevalence of extensor dermatitis in Thai AD is high, it is also common in quite a number of presumably non-atopic individuals. Extensor dermatitis in this study which average age of the subjects was about 5 years old is of little value to differentiate AD in childhood from other dermatoses. History of dry skin in the last year was more frequent than the presence of xerotic skin. It may be due to the intermittent clinical course from season to season at the time of examination. Many features fluctuate and are influenced by previous treatment. Dry skin disappears with the passage of time. Therefore, the evaluation of some signs should rely on clinical examination and history or on history alone. Perifollicular accentuation was as common as in the study of other Asian populations such as Koreans and Chinese[10,13]. In agreement with earlier studies, the group with early age of onset predominates[13,16,22]. Emotional factors seem not to be the important aggravating factor of AD in children as in adults. Some aggravating factors such as smoking[24] and pets in the house which are helpful in Western countries are of little value in distinguishing the disorder in Thailand because of the good ventilation in Thai houses. A history of a particular seasonal variation was given in 75% which is nearly the same as the study done in Sweden[23]. Although several typical findings have been found worthless because of their high frequency in controls, they may be required for firm diagnosis in AD patients with less typical features or those who are unable to give sufficient information. Some may serve for isolating special subgroups within the disease entity.

The UK working party developed a new set of diagnostic criteria for AD which were claimed to be sensitive, highly specific, repeatable, noninvasive, applicable, and easily used in epidemiological and clinical studies[2-4,27]. The authors suggest criteria which are different from the study in the UK. The achievement of any diagnostic criteria depends on the frequency of the signs and symptoms in the population studied. Therefore, the differences in age group, genetic background of the patients, cultural and environmental factors in Thailand might be responsible for this difference.

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การวินิจฉัยโรคผื่นภูมิแพ้ทางผิวหนังในเด็กไทย

วาณี วิสุทธิ์เสรีวงศ์, สุจิตรา วีรวรรณ

โรคผื่นภูมิแพ้ทางผิวหนังเป็นโรคผิวหนังที่พบได้บ่อยในเด็กไทย ปัจจุบันการวินิจฉัยส่วนใหญ่อาศัยประวัติและอาการแสดงที่ตรวจพบในผู้ป่วยเป็นสิ่งที่ช่วยยืนยันการวินิจฉัย การศึกษานี้ทำเพื่อดูความถี่ของประวัติและอาการแสดงต่าง ๆ ที่ใช้ในการวินิจฉัยโรคผื่นภูมิแพ้ทางผิวหนังในเด็กไทยว่าพบบ่อยมากน้อยเพียงใด

การศึกษานี้ศึกษาผู้ป่วยเด็กโรคผื่นภูมิแพ้ทางผิวหนังจำนวน 108 คน เป็นเด็กผู้หญิง 60 คน เด็กผู้ชาย 48 คน อายุเฉลี่ย 60.3 $\pm$ 36.1 เดือน เปรียบเทียบกับผู้ป่วยเด็กโรคผิวหนังอื่น ๆ 103 คน

ผลการศึกษาพบว่าประวัติอาการคัน ผื่นผิวหนังในตำแหน่งที่พบเฉพาะของโรคนี้ อาการโรคเป็นเรื้อรังระยะเวลาที่เป็นโรคมานานกว่า 6 เดือน ผื่นเริ่มเกิดก่อนผู้ป่วยอายุ 2 ปี ตาอักเสบเรื้อรัง อาการคันเมื่อมีเหงื่อ อาการระคายเคืองเมื่อใส่เสื้อผ้าเนื้อหยาบ มีประวัติแพ้อาหารหรือนม ประวัติการมีผิวแห้ง อาการผื่นเปลี่ยนแปลงตามฤดูกาล การตรวจร่างกายพบผื่นแพ้ซึ่งอยู่ตามตำแหน่งที่เฉพาะของโรค ผิวแห้ง ผื่นที่เท้า ร่องใต้ดวงตา รอยดำคล้ำรอบดวงตา ผื่นรอบดวงตา กลากน้ำนม ผื่นรอบใบหู รอยพับเป็นเส้นบริเวณลำคอ ผื่นบริเวณลำตัว ตุ่มนูนรอบรูขุมขน รอยขาวหลังถูกขีดที่ผิวหนัง สะเก็ดบนหนังศีรษะเป็นประวัติและอาการแสดงที่ตรวจพบในผู้ป่วยโรคผื่นภูมิแพ้ทางผิวหนังได้บ่อยกว่าโรคผิวหนังชนิดอื่นโดยมีความแตกต่างอย่างมีนัยสำคัญทางสถิติ ($p < 0.05$)

ผลของการคำนวณทางสถิติหาหลักการในการวินิจฉัยโรคผื่นภูมิแพ้ทางผิวหนัง พบว่าสิ่งที่มีประโยชน์ช่วยในการวินิจฉัยโรคอย่างมากคือประวัติผื่นที่มีอาการคัน ประวัติผื่นตามบริเวณซอกพับของร่างกาย ประวัติโรคที่มีอาการเรื้อรังมานานมากกว่า 6 เดือน การตรวจพบผิวหนังแห้ง ผื่นรอบดวงตา และตุ่มนูนรอบรูขุมขน