Validation of the Diagnostic Criteria for Atopic Dermatitis

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Objective: To validate the accuracy of newly proposed diagnostic criteria for atopic dermatitis (AD).

Design: Double-blind, cross-sectional study comparing the achievement of new criteria with the diagnosis of a dermatologist.

Setting: A private, general dermatology, outpatient clinic.

Patients: A sample of 416 consecutive patients attending the clinic within 2 months (146 males and 270 females), consisting of 60 patients with AD and 356 control patients with other skin diseases.

Main Outcome Measures: Sensitivity, specificity, and positive and negative predictive values of proposed criteria in the diagnosis of AD.

Results: Sensitivity, specificity, and positive and negative predictive values of proposed diagnostic criteria for AD were 10.0% (95% confidence interval [CI], 4.1%-21.2%), 98.3% (95% CI, 96.2%-99.3%), 50.0% (95% CI, 22.3%-77.7%), and 86.6% (95% CI, 82.8%-89.7%), respectively.

Conclusions: These diagnostic criteria for AD are highly specific and are suitable for clinical trials. However, they may not achieve enough sensitivity to be useful for large, population-based epidemiological studies or for routine clinical practice, at least in Iran.

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A TOPIC DERMATITIS (AD) is a common skin disorder, especially in children. Recently, a new set of criteria for its diagnosis has been suggested. Based on these criteria, to be considered a patient with AD an individual must have an itchy skin condition (or parental report of scratching or rubbing in a child) plus 3 or more of the following: (1) a history of flexural involvement (including cheeks in children younger than 10 years); (2) a personal history of asthma or hay fever (or a history of atopic disease in a first-degree relative of children younger than 4 years); (3) a history of generalized dry skin in the past year; (4) visible flexural eczema (including the cheeks and forehead and outer limbs in children younger than 4 years); and (5) onset of rash at younger than 2 years (not used if child is younger than 4 years). These criteria showed a sensitivity of 69% and a specificity of 96% in a sample of dermatology outpatients of all ages. Sensitivity referred to the proportion of true positives correctly diagnosed, and specificity denoted the proportion of true negatives correctly excluded. In other words, the criteria made a correct diagnosis of AD in 69% of patients with AD and ruled out a diagnosis of AD in 96% of patients with other skin diseases. The sensitivity and specificity of these criteria were 85% and 96%, respectively, in a sample of 114 consecutive children attending outpatient pediatric dermatology clinics.

This study was designed to validate these criteria in another population with a different ethnic background, different environmental factors, and a different health care system. Any forthcoming diagnostic criteria should be evaluated in other independent samples.

RESULTS

Four hundred sixteen consecutive patients attending the clinic were evaluated in this study, 60 of whom were diagnosed as having AD by the dermatologist, and 356 of whom had other skin diseases. Age and sex distributions of the patients are shown in Table 1. Mean ± SD age of patients with AD was 22.4 ± 14.7 years, and of controls was 28.5 ± 13.0 years. There were no significant differences in sex, level of education, or social class between patients with AD and controls.

Diagnoses of 356 controls included inflammatory dermatoses such as psoriasis, acne, and lichen planus (31.3%); other forms of dermatitis (14.2%); scalp and hair inflammation (4.8%); urticaria (2.8%); and other dermatoses (22.6%).
PATIENTS AND METHODS

A cross-sectional study was designed with consecutive patients attending the private office of a senior dermatologist (M.N.K.) within 2 months. Using the exact questionnaire proposed for determining 1-year prevalence of AD,3 3 forms of questionnaires were prepared for the 3 age groups: younger than 4 years, 4 to 10 years, and older than 10 years.

After a brief explanation and consent obtained, the patients were observed consecutively, first by an observer who completed the questionnaires and then by the senior dermatologist. For patients younger than 10 years, the questions were asked of their parents. The observer, a fifth-year medical student (A.N.F.), was unaware of the goal of the study and of the diagnosis made by the senior dermatologist. He was specifically trained to record the signs of visible flexural dermatitis according to the protocol suggested by Williams et al.6 The senior dermatologist decided whether the patient had AD (whether currently active) in his clinical opinion (criterion standard of the study). He completed a diagnosis sheet for each patient consisting of the chief complaints of the patient, the diagnosis, and whether the patient had AD. No attempts were made to define AD for the dermatologist, who was not aware of the data collected by the observer for any patient.

Using a microcomputer, the completed questionnaires with their corresponding diagnosis sheets were double entered into Epi-Info (version 6; Centers for Disease Control and Prevention, Atlanta, Ga). All statistical analyses were carried out by Stata (version 4; World Health Organization, Geneva, Switzerland). The sensitivity, specificity, and predictive values of various combinations of the criteria were calculated.7

Table 2. Frequency of the 6 Proposed Diagnostic Criteria for Atopic Dermatitis in Patients and Controls

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Patients With Atopic Dermatitis</th>
<th>Controls</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Itch</td>
<td>42 (70.0)</td>
<td>128 (36.0)</td>
<td></td>
</tr>
<tr>
<td>History of involvement of skin creases</td>
<td>20 (33.3)</td>
<td>40 (11.2)</td>
<td></td>
</tr>
<tr>
<td>History of asthma or hay fever</td>
<td>11 (18.3)</td>
<td>51 (14.3)</td>
<td></td>
</tr>
<tr>
<td>History of general dry skin</td>
<td>24 (40.0)</td>
<td>35 (9.8)</td>
<td></td>
</tr>
<tr>
<td>Visible flexural eczema</td>
<td>8 (13.3)</td>
<td>9 (2.5)</td>
<td></td>
</tr>
<tr>
<td>Onset at age &lt;2 y</td>
<td>3 (5.0)</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

Frequencies of the 6 diagnostic criteria in patients with AD and controls are shown in Table 2. Sensitivity and specificity of various combinations of these criteria are shown in Table 3. The suggested combination of pruritus and 3 minor criteria showed a sensitivity of only 10.0% (95% confidence interval [CI], 4.1%-21.2%), although it achieved a specificity of 98.3% (95% CI, 96.2%-99.3%). Positive predictive value of this set of criteria was 50.0% (95% CI, 22.3%-77.7%), and its negative predictive value was 86.6% (95% CI, 82.8%-89.7%).

Sensitivity and specificity of these criteria were 12.5% and 100%, respectively, in patients aged 10 years and younger, although the number of such patients in this study was small (16 patients with AD and 17 controls). Even in the 16 patients considered by the dermatologist to have active AD and who showed active inflammatory skin lesions, only 6 were diagnosed as having AD by these criteria (sensitivity, 37.5%).

Of 6 patients falsely diagnosed as having AD by these criteria, 3 had psoriasis, 1 had generalized skin xerosis, 1 had acne, and 1 had lichen planus.

Mean time for completing the questionnaires was 1.98 minutes (range, 1.00-5.00 minutes). Only a few patients needed some explanation regarding flexural distribution, signs of asthma or hay fever, and skin xerosis. Also, some patients (or their parents) had difficulty recalling the age at onset or history of asthma or hay fever.

Atopic dermatitis is a common skin disorder. Prevalence of AD in children varies from 1.7%8 to 23.0%.9 Such large variation could be partly because of differences in age, genetic background, and environmental factors of the population studied.10 However, another important factor was the absence of uniform diagnostic criteria for AD in these studies. Although the major and minor diagnostic criteria suggested by Hanifin provided some uniformity in the diagnosis of AD in hospital-based studies, they are not suitable for population-based studies or for general clinical practice.14 Also, these criteria have never been validated against the diagnosis of a physician.

These limitations encouraged a group of dermatologists (the U.K. Working Party) to develop a new set of diagnostic criteria for AD,1-3 which were claimed to be sensitive, highly specific, repeatable, noninvasive, applicable, and easily used in epidemiological and clinical studies.
The main goal of this study was to validate the sensitivity and specificity of these criteria in patients attending a general dermatology outpatient clinic. The specificity of the criteria in this study was comparable with that of the original study (98.3%).\(^3\) Six patients were falsely diagnosed as having AD: 3 had psoriasis, 1 had xerosis, 1 had acne, and 1 had lichen planus. In other words, 5 patients had skin disorders resembling AD.

Sensitivity of the criteria was only 10.0% in this sample of patients; in those 10 years and younger, sensitivity was 12.5%. Furthermore, these criteria achieved a poor diagnosis of AD in patients with active inflammatory lesions—only 6 (38%) of 16 patients with active AD. Ten of 54 patients with false-negative results had active AD, and the rest attended the clinic for other skin conditions (eg, hair loss and acne).

There were no significant differences between patients with false-negative results and those with true-positive results regarding sex, ethnic group, or level of education. Also, patients with either false-negative or true-positive results showed no differences in the frequency of any of the 6 criteria (data not shown).

The low sensitivity achieved by these criteria in this study could be explained in several ways:

1. Sample differences. The relative proportions of AD and other skin diseases in this sample of patients are similar to those in the original study.\(^3\) Also, mean patient age was comparable with that study. The achievement of any diagnostic criteria depends on the relative frequency of the signs and symptoms in the population studied. Therefore, the differences in genetic background of the patients and in environmental factors (including geographic, nutritional, and cultural factors) might be responsible for the low occurrence or different manifestations of some of these criteria in this sample of patients.

2. Setting differences. The original validation study\(^3\) was done in a hospital-based outpatient clinic. Patients attending this clinic might have more severe manifestation of the disease than those attending a private outpatient clinic. Moreover, the past medical records of patients were not available in the private clinic, and many patients (or their parents) had difficulty recalling the age at onset or history of asthma or hay fever. This problem was reflected in the low occurrence of criteria “onset at younger than 2 years” in patients with AD (3 of 60).

3. Bias. The original validation study was done by the same U.K. Working Party members who were involved in the development of the criteria. This might have introduced an unwanted bias in their diagnosis of AD. On the other hand, the diagnosis made by a single senior dermatologist (M.N.K.) was the criterion standard. Overdiagnosis of AD by the dermatologist may have also produced a bias.

In conclusion, the diagnostic criteria proposed by the U.K. Working Party for the diagnosis of AD seem to be highly specific, which makes them useful for clinical trials. However, they may not achieve the claimed high sensitivity in other communities with different genetic backgrounds, environmental factors, and health care systems than those in the United Kingdom. As such, these criteria may not be suitable for large, population-based epidemiological studies or for routine clinical practice, at least in communities where the past medical histories of patients are not available.

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### REFERENCES