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Diagnostic Criteria for Atopic Dermatitis

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Abstract

Atopic dermatitis is a disease of various names and presentations. There is no definitive diagnostic test for atopic dermatitis. The diagnosis depends on a set of clinical features. Ever since Hanifin and Rajka first proposed a set of diagnostic criteria for atoipc dermatitis in 1980, various other criteria have been suggested from different geographic locations. In this article, we have described the need for uniform diagnostic criteria, various criteria proposed, their validation studies, and the cause of wide variation in the results of the validation studies.

Key words: dermatitis, atopic dermatitis, diagnostic criteria

Introduction:

Atopic dermatitis is a chronic or chronically relapsing hypersensitive manifestation of the skin with itching as a predominant feature. There is a wide range of other associated features that are seen in a proportion of patients.

Recent years have seen a gradual increase in the prevalence of atopic dermatitis (AD) which can be ascribed to environmental changes consequent to rapid development allover the world. The current cumulative prevalence is 5-17% (1,2) by the age of 7 years and in adults, it is 2-10% (3). In a 12-month study of prevalence of symptoms of asthma, allergic rhinoconjuctivitis and atopic eczema in the International Study of Asthma and Allergies in Childhood (ISSAC), the prevalence of atopic eczema in 56 countries was found to vary

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between 3-20.5% (4). Overall, AD has almost equal sex distribution, though in children males are more commonly affected while females are commonly affected among adults. Indian data on epidemiology of AD is meager. As part of ISAAC study, more than 37000 children from India were studied at 14 different centers. All centres except Kottayam (Kerala) reported a 12 month period prevalence between 2.4% and 6% while Kottayam reported a prevalence of >9% (4). It is commonly believed that AD is less prevalent in India, though personal experience of the authors is that the prevalence of AD is increasing in India due to modernization and westernization of Indian lifestyle. In a study in North India in hospital setting, it was found that mean age at onset and mean duration of the disease were 4.2 months and 3.3 months, respectively, in the infantile group. The corresponding figures were 4.1 years and 1.9 years in the childhood group. Patients from urban areas significantly outnumbered those from rural background (5).

What is the need for diagnostic criteria for diagnosis of AD?

Atopic dermatitis is a difficult disease to define. AD has a wide spectrum of manifestations in terms of clinical presentation, severity and distribution. Until 1980, the diagnosis of AD depended upon clinical judgment of the treating physician and there was significant inter-personal variation. What appeared to be AD to one physician need not have appeared to be the same to another physician. Multiple studies conducted previously showed widely variable prevalence rate in different types of population. Most probable cause of such discrepancy is lack of disease definition. There is no diagnostic test as yet which can confirm a clinical diagnosis of AD. Establishment of diagnostic guidelines for atopic dermatitis stems from the need for clear delineation of study populations in investigative studies. Until a distinctive diagnostic test becomes available, it is important to apply uniform criteria in diagnosing atopic dermatitis.

What are the diagnostic criteria for atopic dermatitis?

Hanifin and Rajka's criteria (6) (Table-1)

In 1980, Hanifin and Rajka formulated a minimum set of criteria based upon their clinical experience which they divided into basic and minor features. To satisfy as a case of AD, one should have a minimum of 3 basic and minor features each. Diagnostic features were based upon patient history, clinical

Table 1: Hanifin and Rajka's criteria

Basic features:

- Pruritus
- Typical morphology and distribution
- Flexural lichenification or linearity in adults
- Facial and extensor involvement in infants and children
- Chronic or chronically relapsing dermatitis
- Personal or family history of atopy (asthma, allergic rhinitis, atopic dermatitis)

Minor features:

- Xerosis
- Ichthyosis/palmar hyperlinearity/ keratosis pilaris
- Immediate (type 1) skin test reactivity
- Elevated serum IgE
- Early age of onset
- Tendency towards cutaneous infection (specially Staph. aureus and Herpes simplex)/ impaired cell mediated immunity
- Tendency towards non-specific hand and foot dermatitis
- Nipple eczema
- Cheilitis
- Recurrent conjunctivitis
- Dennie-Morgan infraorbital fold
- Keratoconus
- Anterior sub-capsular cataract
- Orbital darkening
- Facial pallor/facial erythema
- Pityriasis alba
- Anterior neck folds
- Itch when sweating
- Intolerance to wools and lipid solvents
- Perifollicular accentuation
- Food intolerance
- Course influenced by environmental/ emotional factors
- White dermographism/delayed blanch

findings, skin tests and laboratory findings. However, there are shortcomings in the Hanifin and Rajka's criteria. Studies have failed to establish specificity of many of the minor features (7-11) and researchers have even questioned the validity of the basic features (12). Slight adjustment in the definition/ interpretation of the minor features may lead to wide variability in their understanding. Features such as periorbital pigmentation, infra-orbital

folds, and hyperlinear palms are probably dependent on age, sex, race and ethnicity of population (8-10). Some features may be more prevalent in hospital settings with more clinical severity leading to florid manifestation of many basic features like anterior neck folds and hyperlinear palms. However, these features may be less frequent in community setting where mild or moderately severe cases are predominantly seen. Many of the criteria have no precise definition [e.g. pityriasis alba (13)], some occur very infrequently [e.g. keratoconus (14)], and others are non-specific [e.g. white dermographism (15)]. The criteria contain invasive tests, which makes it relatively unsuitable for routine clinical practice and studies with small children. Until recently, these criteria were not validated against physician's diagnosis or tested for repeatability (16,17).

To satisfy a diagnosis of AD, one should have at least 3 basic and 3 minor features

These criteria suggested by Hanifin and Rajka continue to be valuable in hospital based setting due to high sensitivity. Lengthy and complex evaluation and lack of simplicity made them unsuitable for epidemiological purposes in community settings.

U.K. Working Party's diagnostic criteria (18) (Table 2)

To overcome the shortcomings of Hanifin and Rajka's criteria, Williams et al. conducted a study in 1994 to develop a definition that is sensitive, specific, reproducible, non-invasive, and applicable to a range of ethnic groups

Table 2: U.K. Working Party's diagnostic criteria

1.	Presence of an itchy skin condition within last 12 months
2.	History of flexural dermatitis (including cheeks in children below 10 years)
3.	Onset below the age of 2 years (only if child is over 4 years old)
4.	Personal history of asthma or hay fever (or history of atopic diseases in a first-degree relative in children under 10 years of age)
5.	History of generally dry skin in last year
6.	Visible flexural dermatitis (or eczema involving the cheeks or extensors in children below 4 years of age)

and which are easy to perform in population based and clinical studies. The U.K. Working Party's criteria have shortcomings too, namely, according to the authors themselves, it may not be applicable in infants and in communities where prevalence of AD is low as compared to other itchy dermatoses.

To satisfy a diagnosis of AD, one should have criterion 1 plus at least 3 of the other features

Different studies in distant parts of world in patients with varied ethnicity, language and culture [U.K. (19, 20), Romania (21), China (22), Iran (23), India (24), Denmark (25), Australia (26), Italy (27), Ethiopia (28), and South Africa (29)] have validated this criterion in hospital and community settings. The results of these validations studies have been widely variable; excellent [e.g. in China (22)] to poor [e.g. in Iran and South Africa (23,29)] (Table 3).

Diepgen et al. derived a scoring system of useful diagnostic features of atopic dermatitis (30). They showed that some features, such as personal or family history of atopy, which are considered as major features in Hanifin and Rajka's criteria, are not as useful as some previously designated minor features such as xerosis. They also showed that a raised total serum IgE is neither particularly sensitive nor specific for AD (30). Using this scoring system, they demonstrated good separation between cases and controls. Their criteria has drawbacks too. The scoring system was tested on same data set from which the criteria were derived, as opposed to an independent sample. Moreover, their scoring system refers to discrimination of hospital based AD cases from community controls who don't have AD, and as such has not been subjected to more stringent test of discriminating AD cases from subjects with other forms of dermatitis or dermatoses.

In an Indian study, Sharma (31) derived a minimum set of criteria which include presence of itch, history of flexural dermatitis, history of dry skin, family history of atopy, personal history of diagnosed asthma and visible flexural dermatitis. The criteria were derived from 34 potentially useful clinical features including the evaluation of photo-sensitivity.

In a validation study by the authors (24), it was derived that dermatitis in classical distribution, its chronic/ relapsing nature, dry skin and infra-orbital folds had high relative values. So, these features may be helpful in discriminating cases of atopic dermatitis from controls.

Table 3: Major validation studies and their results

Criteria	Author	Hospital or community based	Sensitivity	Specificity	PPV	NPV
U.K. diagnostic criteria	Williams et al. (1994)	Hospital	69%	96%	78%	93%
	Williams et al. (1994)	Hospital	85%	96%	92%	92%
	Williams et al. (1994)	Hospital	88%	93%	94%	87%
	Firooz et al. (1999)	Hospital	10%	98%	29%	87%
	Gu et al. (2001)	Hospital	95%	97%	97%	96%
	De et al. (2006)	Hospital	86%	96%	98%	77%
	Williams et al. (1996)	Community	69%	93%	47%	97%
	Popescu et al. (1998)	Community	79%	97%	80%	97%
	Chalmers et al. (2006)	Community	44%	98%	18%	99%
	Olsen et al. (2001)	Community	90%	97%	97%	91%
	Fleming et al. (2001)	Community	100%	93%	92%	100%
	Girolomoni et al. (2003)	Community	78%	99%	86%	98%
	Hamada et al. (2005)	Community	59%	95%	45%	97%
	Saeki et al. (2007)	Community	72%	89%	45%	96%
Hanifin & Rajka's criteria	Williams et al. (1994)	Hospital	93%	78%	83%	90%
	De et al. (2006)	Hospital	96%	94%	97%	92%

PPV- positive predictive value
NPV- negative predictive value
(Adapted from Brenninkmeijer et al. Br J Dermatol 2008;158:754-765)

There are other diagnostic criteria too which are developed to cater to the need of individual country (Table 4). As of today, Hanifin and Rajka's criteria and U.K. Working Party's diagnostic criteria are most commonly used in clinical practice.

Validation studies of the commonly used criteria

U.K. Working Party's diagnostic criteria have most commonly been validated while Hanifin and Rajka's criteria have been validated only in 2 studies. The former criteria have been validated in both hospital and community based settings while the later has been validated in the community setting only. As summarized earlier, the validation studies yielded widely variable results.

Causes of wide variation in results of validation studies of U.K Working Party's diagnostic criteria

Various reasons have been speculated for wide variation in results of U.K Working Party's diagnostic criteria validation studies (32). The manifestation of AD varies with age.

Table 4: Diagnostic criteria used in AD

Hanifin and Rajka's criteria (6)
U.K. Working Party's criteria (18)
Kang and Tian diagnostic criteria (33)
Schultz-Larsen criteria (34)
Japanese Dermatology Association criteria (35)
Diepgen's criteria (30)
Millennium diagnostic criteria (36)
International Study of Asthma and Allergies in Childhood criteria (37)

(Adapted from Brenninkmeijer et al. Br J Dermatol 2008;158:754-765) (32)

Different studies have recruited patients with widely variable age groups leading to inconsistent study results. The study population also varied widely in terms of culture, skin type, and rural-urban as well as rich-poor social class gradient. In general, the clinical diagnosis by an experienced physician is considered to be gold-standard. This again is an area of weakness unless a group of qualified dermatologists consider a case to be of AD because there might be wide variation in perception of what constitutes AD to an individual

physician. Scabies is very common itchy dermatosis in children and its manifestation mimics AD. In areas of high prevalence of scabies, false positive results were high. Moreover, positive predictive value of a study depends on the prevalence of the disease in the study population. In study population where prevalence of AD was low, the criteria did not perform satisfactorily as far as PPV is concerned. There may be many socio-cultural issues also, which can influence the results. In the study by Chalmers et al (29) in Xhosa- speaking African population, 30% patients who were deemed to have active disease by the dermatologist did not answer positively to questions related to itch while AD is considered to be uniformly associated with itch. There might have been a problem in understanding questions related to itch or it might have been considered commonplace by the respondent and thus unimportant. Moreover, it might not have bothered the patient enough or due to competing hardship, they did not report itch to the investigators. Though 81% of their study population had visible flexural eczema, 69% did not report positively when enquired about history of visible flexural eczema. To use a criteria in a community setting, the questionnaire in an alien language is translated in local language and then it is back-translated so as to assess whether any meaning is lost in the process of the translation. Back translation is an acceptable means of assessing accuracy of translation, but it is often possible to pick up only gross errors rather than subtle changes in the concept being conveyed.

The Hanifin and Rajka's criteria have been validated twice in the hospital setting where it was conducted solely by dermatologists, thus circumventing most of the drawbacks of U.K Working Party's diagnostic criteria (19, 24). The results of these validation studies were comparable. As more severe cases of AD present to hospital with more florid clinical features, sensitivity of these validation studies could have been high.

Where do we stand?

In a disease like AD where there is widespread variation in respect to epidemiology, clinical manifestations, severity of disease and interpretation of what constitutes a case of AD, and where there is no diagnostic test to confirm the clinical diagnosis, a diagnostic criteria is needed for uniform interpretation of study results. Hanifin and Rajka's criteria and U.K. Working Party's diagnostic criteria are most commonly used criteria for diagnosis of AD. Both have been validated in either community based setting or hospital setting or both as has

been discussed earlier. Both of the criteria have pros and cons. However, according to the present evidence, Hanifin and Rajka's criteria continue to be gold-standard in hospital based setting for experimental studies. U.K. Working Party's criteria are useful in community based setting or epidemiological studies. Both the criteria need further and extensive validation in different geographical locations with varied socio-cultural background.

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