A Cross-Sectional Study Comparing Application of Hanifin and Rajka Criteria in Indian Pediatric Atopic Dermatitis Patients to that of Other Countries

Abstract

Background: Hanifin and Rajka criteria are considered to be the gold standard for atopic dermatitis diagnosis. However, the exhaustive nature limits its use in clinical settings. Objective: To determine the frequency of Hanifin and Rajka criteria commonly found in Indian pediatric atopic dermatitis patients and variation from the findings of other studies. Material and Methods: An observational, descriptive study with a sample size of 52 pediatric atopic dermatitis patients. Patients were divided into infantile, childhood, and adolescent. Results: Overall, xerosis, early age of onset, Dennie–Morgan fold, aggravation because of environmental factors, palmar hyper-linearity, ichthyosis vulgaris, keratosis pilaris, pityriasis alba, and orbital darkening were found in more than 50% of patients. Dennie–Morgan fold was more commonly found in Indian pediatric atopic dermatitis patients. Peri-follicular accentuation was less prevalent in Indian patients as compared to other Asian studies. None of the parents reported food intolerance, which was seen in studies from other countries. Limitations: A small sample size and ophthalmological evaluation was not performed in all patients. Conclusion: The frequency of different Hanifin and Rajka minor criteria varies widely among different study populations. Hence, the criteria specifically applicable to the Indian population need to be derived for ease of diagnosis.

Keywords: Aggravating factors, atopic dermatitis, clinical features, diagnostic criteria, Hanifin and Rajka criteria, India, minor criteria, pediatric dermatology

Introduction

Since 1980, Hanifin and Rajka criteria are used for the diagnosis of atopic dermatitis. However, many modifications have been developed, such as the United Kingdom working party criteria, Japanese Dermatological Association criteria, and Korean Dermatological Association criteria. However, the Hanifin and Rajka criteria continue to be the most widely used criteria.

Although it has the highest sensitivity and specificity, the exhaustive nature of minor criteria limits its use in clinical settings. Hence, the use is mostly limited to epidemiological based studies. At the same time, the minor criteria satisfied depend upon the age, ethnicity, course, and disease duration. In Indian patients, Sharma *et al.*^[2] found that the presence of itch, history of flexural involvement, history of dry skin, family history of atopy, personal history

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of diagnosed asthma, and visible flexural dermatitis were diagnostic. However, no further studies were performed for validation.

This study aimed to determine the frequency of individual criteria seen in patients from a tertiary care center in western India and to compare the results with that of other Indian and foreign studies. This will help in establishing minor criteria which are relevant to Indian patients. In addition, it may help in developing a standard criteria for Indian patients.

Material and Methods

Newly diagnosed atopic dermatitis patients presenting to a tertiary care center in western Maharashtra were taken for study from September 2019 to August 2021. The study was initiated after approval from the institutional ethics committee. These children were diagnosed as AD by a senior

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dermatologist with the help of Hanifin and Rajka diagnostic criteria. Any patient with a confounding disease such as dermatophyte infection or seborrheic dermatitis or patients who were previously treated were excluded from the study. Hence, a sample size of 52 patients was taken after proper consent from parents and assent from children older than 8 years. Among the criteria, 4 major and 21 minor criteria were taken into consideration. Invasive criteria such as serum IgE levels and immediate Type I hyper-sensitivity were excluded. The criteria were considered positive based on the definition by Böhme et al.[3] Parents/guardians were counselled for ophthalmological evaluation to screen for keratoconus and anterior subcapsular cataract. At the same time, they were enquired about aggravating factors, if any present. In regard to food items, parents were asked to recall any association between any of the food item and aggravation of disease. Also, they were specifically asked for any aggravation with wheat, milk, soy, fish, eggs, and peanut.

Compilation of data and statistical analysis was performed using SPSS version 25. Collected data was coded, and these were entered in Microsoft Excel. The results are presented in tabular and graphical format. Various rates, ratios, and percentages, along with standard deviation, were derived. Along with these, different associations were studied using the Chi-square test.

Results

Age

Based on the age, the patients were divided into 1. Infantile phase (<2 years), 2. Childhood phase (2–12 years), and 3. Adolescent phase (>12 years). The majority of the patients belonged to the childhood phase (50%), followed by the infantile group (38.5%). 11.5% of patients were in the adolescent group.

The youngest patient was 1 month old, whereas the oldest patient was 14 years old. The mean age of patients was 4.5 years \pm 4.2 years, and the median age was 3.3 years.

Age of onset

Most of the patients in our study had onset between 6 and 12 months (25%). 46.2% and 55.8% of patients had onset of eruption before 1 year and 2 years, respectively. However, 80.8% of patients had onset of eruption before 5 years. Hence, 19.2% had disease onset after 5 years in our study. The mean age of onset was 3.3 ± 3.7 years.

Distribution

Most of the patients in our study had involvement of cheeks (42.3%), followed by the extensor aspect of legs and arms (38.5%). Flexural involvement was seen in the form of popliteal fossa (34.6%), cubital fossa (28.8%), flexural aspect of hands and feet (17.3%), posterior thigh (15.4%), axilla (7.7%), and inguinal (3.8%). Truncal distribution

was seen on the back (13.5%), abdomen (11.5%), and chest (11.5%).

Major criteria

Pruritus was the most common criteria seen in 94.2% patients. 92.3% had a typical morphology and distribution along with chronic or chronically relapsing dermatitis. However, 55.8% of patients had a personal/family history of atopy.

Minor criteria

The minor criteria seen in more than half of the patients [Table 1] were xerosis in (86.5%), an early age of onset (80.8%), Dennie Morgan fold (76.9%), aggravation because of emotional/environmental factors (67.3%), palmar hyper-linearity, ichthyosis vulgaris, keratosis pilaris (61.5%), pityriasis alba (55.8%), and orbital darkening (51.9%). Less than 5% manifested recurrent conjunctivitis (3.8%) and nipple dermatitis (1.9%). Parents of 29 patients consented for ophthalmological examination (7 patients from infantile, 17 patients from childhood, and 5 patients from the adolescent age group). Only one patient was diagnosed as a keratoconus suspect (3.5%). None of the patients had cataract and food intolerance in study population.

In the infantile age group [Table 3], xerosis was seen in almost all patients (95%). Criteria seen in more than one-fourth of the patients were Dennie–Morgan fold (80%), aggravation because of emotional/environmental factors (75%), pityriasis alba (55%), palmar hyper-linearity, ichthyosis vulgaris and keratosis pilaris (40%), white dermographism (35%), and tendency toward cutaneous infection (30%). Also, along with cataract and food intolerance, none of the patients had nipple dermatitis and keratoconus.

In the childhood age group [Table 4], xerosis (80.77%), Dennie–Morgan fold (80.77%), an early age of onset (80.77%), Palmar hyper-linearity, ichthyosis vulgaris and keratosis pilaris (76.92%), orbital darkening (73.08%), pityriasis alba (57.69%), aggravation because of emotional/environmental factors (53.85%), and peri-follicular accentuation (30.77%) were seen in more than one-fourth patients.

In the adolescent age group [Table 5], all patients had orbital darkening and aggravation because of emotional/environmental factors. However, xerosis was seen in 83.3%, and palmar hyper-linearity, ichthyosis vulgaris, and keratosis pilaris in 66.7%, Dennie–Morgan fold in 50%, pityriasis alba in 50%, and cheilitis in 33.33%. None of the patients exhibited nipple dermatitis, keratoconus, cataract, tendency toward cutaneous infections, recurrent conjunctivitis, non-specific hand and foot dermatitis, facial pallor, itch because of sweating, food intolerance, and white dermographism.

Table 1: Minor criteria seen in the present and other Indian studies				
Minor Criteria	Present Study	Parthasarathy et al.[4]	Nagaraja <i>et al.</i> ^[5]	Kanwar et al.[6]
Xerosis	86.5	67.2	76	80
Early age of onset	80.8	67.8	73	74
Dennie-Morgan infra-orbital fold	76.9	71.8	63	82
Palmar Hyper-linearity/Keratosis Pilaris/Ichthyosis	61.5	67.8/4/11.5	23/33/4	54/46/-
Course influenced by environmental factors	67.3			26
Winters	57.7	8	29	Not performed
Summers	1.9	0	15	Not performed
Pityriasis alba	55.8	57.5	34	78
Orbital darkening	51.9	6.9	12	32
Peri-follicular accentuation	19.2	47.7	39	22
Tendency for cutaneous infections	19.2	2.9	36	62
Intolerance to wool/lipid solvents	17.3	2.3	41	28
White dermographism	15.4	0	40	12
Cheilitis	15.4	7.5	3	6
Anterior neck folds	9.6	6.3	6	12
Tendency to non-specific hand or foot dermatitis	9.6	4.6	12	42
Facial Pallor/Erythema	7.7	21.3	26	14
Itch when sweating	7.7	8	35	66
Recurrent conjunctivitis	3.8	0	14	4
Nipple eczema	1.9	0	1	8
Food intolerance	0	0	0	0

Minor Criteria	Present Study	Bangladesh	Thai	
		Wahab et al.[7]	Wisuthsarewong et al.[8	
Xerosis	86.5	43.8	60.2	
Early age of onset	80.8	31	65.7	
Dennie-Morgan infra-orbital fold	76.9	39.5	21.3	
Palmar Hyper-linearity/Ichthyosis/Keratosis Pilaris	61.5	24.8/34.3/14.8	49.1/24.1/9.3	
Course influenced by environmental/emotional factors	67.3	66.7	75/1.9	
Pityriasis alba	55.8	14.3	28.7	
Orbital darkening	51.9	Not mentioned	50	
Peri-follicular accentuation	19.2	Not mentioned	47.2	
Tendency for cutaneous infections	19.2	80	19.4	
Intolerance to wool/lipid solvents	17.3	50/6.7	24.1/13.9	
White dermographism	15.4	Not mentioned	18.5	
Cheilitis	15.4	10.5	8.3	
Anterior neck folds	9.6	Not mentioned	72.2	
Tendency to non-specific hand/foot dermatitis	9.6	9/7.6	28.7/23.1	
Facial Pallor/Erythema	7.7	ND/1.9	4.6	
Itch when sweating	7.7	26.7	77.8	
Recurrent conjunctivitis	3.8	Not mentioned	12	
Nipple eczema	1.9	Not mentioned	4.6	
Food intolerance	0	19	36.1	

Aggravating factors

Environmental factors were the most common aggravating factors with winter (57.7%) being the most common aggravating factor in most patients, seasonal changes (5.8%), summers (1.9%), and rains (1.9%). Woolen clothes were responsible for aggravation in 7.7% patients. Other precipitating factors were jewellery (5.8%),

sweating (3.8%), change in water hardness (1.9%), and change in soap (1.9%).

Discussion

The mean age was 4.5 (\pm 4.2) years, which was similar to the result of Parthasarathy *et al.*^[4] and Nagaraja *et al.*^[5] among the Indian studies. Moreover, the mean age in Wisuthsarewong *et al.*^[8] was similar to that of

Table 3: Minor criteria seen in the infantile population in the present and other country studies

Minor criteria	Current	Sweden	China
	Study	Böhme et al.[3]	Shi et al.[9]
Xerosis	95	100	75.0
Dennie-Morgan folds	80	3	1.1
Aggravation because	75/0	87/3	Not done
of environmental/ emotional factors			
Pityriasis alba	55	6	0.3
Palmar Hyper-linearity,	40	4/0/4	9.3/1.8/0.8
Ichthyosis Vulgaris,			
Keratosis Pilaris			
White dermographism	35	3/0	4.3
Tendency toward cutaneous infections	30	1	Not performed
Wool/lipid intolerance	20	6/15	Not performed
Facial pallor/erythema	15	1/54	Not performed
Orbital darkening	10	0	0.5
Non-Specific hand and	10	28/03	29.2
foot dermatitis			
Cheilitis	5	1	22
Recurrent conjunctivitis	5	1	Not performed
Anterior neck folds	5	1	3
Itch because of sweating	5	34	Not performed
Peri-follicular	5	1	46.5
accentuation			
Nipple dermatitis	0	2	9.9
Food intolerance	0	39/11	Not performed

Table 4: Minor criteria seen in the childhood population in the present and other country studies

Minor Criteria	Present	South Korea	China	
	Study	Lee <i>et al</i> .[10]	Shi et al.[9]	
Xerosis	80.8	71	86.7	
Nipple dermatitis	3.9	2	2.2	
Palmar Hyper-linearity,	76.9	31/17/19	25.3/5.2/4.3	
Ichthyosis Vulgaris,				
Keratosis Pilaris				
Cheilitis	19.2	48	32.4	
Dennie-Morgan folds	80.8	52	9.6	
Facial pallor	3.9	23	Not performed	
Pityriasis alba	57.7	64.6	5.9	
Anterior neck folds	11.5	44	20.1	
Peri-follicular accentuation	30.8	73	83	
White dermographism	3.9	35	8.6	

Indian studies. In the study by Shi *et al.*,^[9] the mean age of patients was 3.60 (\pm 6.91) years. However, the study population included adult patients also.

A higher prevalence was seen in male as compared to female (1.5:1). This was similar to what was observed with most Indian studies such as Nagaraja *et al.*,^[5] Kanwar *et al.*,^[6] and Dhar *et al.*,^[11] However, in Parthasarathy *et al.*,^[4] there was almost equal distribution among both

genders. In the Thai study (Wisuthsarewong *et al.*^[8]), the ratio was 1:1.3, showing a female predominance.

Most of the patients in our study had onset between 6 and 12 months (25%). However, in the study performed by Dhar *et al.*,^[11] the maximum number of patients had onset between 3 and 6 months (34.52%). In Shi *et al.*,^[9] only 2.9% had disease onset after 5 years. However, 19.2% had disease onset after 5 years in our study. In addition, Shi *et al.*,^[9] included adult patients, which meant that a very small proportion of Chinese patients had adult-onset AD.

Like in most studies, atopic dermatitis in most minor patients manifested before 5 years. The mean age of onset was 3.3 ± 3.7 years, whereas for Dhar *et al.*,^[11] the mean age of onset was 4.2 months.

The most commonly satisfied major criteria was pruritus among all the studies (Indian and Thai studies). On the other hand, the personal/family history of atopy varied among different studies.^[8,9,11]

Overall, the three common criteria seen in Indian studies [Table 1] were xerosis, an early age of onset, and Dennie-Morgan fold.^[4,5,6] Although our study and Nagaraja et al.[5] reported xerosis to be the most common minor criteria, Parthasarathy et al.[4] and Kanwar et al.[6] reported Dennie-Morgan folds to be the most common minor criteria. A higher incidence of xerosis could be because of the dry climate in the study area. Aggravation because of environmental/emotional factors was higher in our study (67.3%) with maximum patients reporting winter aggravation (57.7%) and 1.9% of patients reporting summer aggravation. Such a high association with environmental factors was not reported in other Indian studies. Similar was the case with orbital darkening, which was higher in our patients as compared to other Indian studies. None of the patients in Indian studies, including the current study, had food intolerance.[4,5,6]

When these results were compared to studies performed in other countries [Table 2], a study performed by Wahab *et al.*^[7] on Bangladeshi children reported a tendency toward cutaneous infection to be the most common factor (80%), whereas Wisuthsarewong *et al.*^[8] found that the most common minor criteria in Thai AD patients was itch when sweating (77.8%). Also, food intolerance was found in 36.1% of Thai patients^[8] and 19.1% of Bangladeshi patients.^[7]

Although none of the Indian studies divided the patients into infantile, childhood, and adolescent groups based on age, a few studies from other countries have divided their study population, such as Shi *et al.*^[9] (China) and Lee *et al.*^[10] (South Korea). Only the data from the same age group were taken into consideration for comparison. Böhme *et al.*^[3] (Sweden) applied Hanifin and Rajka criteria in patients <2 years of age (infantile).

The average of minor criteria satisfied in the infantile group was 5.9 ± 1.4 , that satisfied in the childhood group was 6.3 ± 2 , and that satisfied in the adolescent group was 5.3 ± 1.2 . However, the difference between them was not statistically significant (p > 0.05).

For the infantile age group [Table 3], xerosis was mostly found in high frequency in other studies as well.[3,9] Early age of onset was not taken into consideration as the criteria were satisfied by any patient who develops AD before the age of 5 years. Dennie-Morgan fold and pityriasis alba, which were significant in the present study, were not found to be significant in both Swedish and Chinese studies. Furthermore, white dermographism and the tendency toward cutaneous infection were observed in one-fourth of patients, whereas other studies did not have such involvement. Like all the Indian studies, the current study did not have any patients with food intolerance. However, Böhme et al.[3] found that 39% of patients had skin reactions from ingested food, whereas 11% developed skin reactions from food contact. Moreover, peri-follicular accentuation was present in 47% of patients in the study performed by Shi et al.[9] but in only 5% in the current study. Similar was the case with anterior neck fold, which was found in 22% of infants in Shi et al.; [9] however, only 5% of patients had this criteria in the present study.

For the childhood age group [Table 4], Dennie–Morgan fold was noticed more in the current study (80.8%) as compared to both studies performed by Lee *et al.*^[10] (52%) and Shi *et al.*^[9] (9.6%). In addition, pityriasis alba was observed more in South Korean patients (65%) as compared to Chinese patients, who showed minimal involvement (6%). Peri-follicular accentuation was a significant factor that involved more than 70% of patients in both the studies performed by Lee *et al.*^[10] (73%) and Shi *et al.*^[9] (83%). However, only 30.8% of patients had this criteria in our study.

Cheilitis was significant in Lee *et al.*^[10] (48%) and Shi *et al.*^[9] (32%) studies. However, only 19.2% of patients had

Table 5: Minor criteria seen in the adolescent population in the present and other country studies

Criteria	Present	China
	Study	Shi <i>et al.</i> [7]
Orbital darkening	100	8.3
Xerosis	83.3	87.5
Palmar Hyper-linearity, Ichthyosis	66.7	25/16.7/4.2
Vulgaris, Keratosis Pilaris		
Dennie-Morgan folds	50	12.5
Cheilitis	33.3	50
Pityriasis alba	50	8.3
Anterior neck folds	16.7	20.8
Peri-follicular accentuation	16.7	83.3
Non-Specific hand and foot dermatitis	0	25
White dermographism	0	29.2

this criteria in our study. Nipple dermatitis was minimally present in all the studies.

For the adolescent age group [Table 5], orbital darkening (100%) was the most common criteria in our study. Peri-follicular accentuation was more involved in Shi *et al.*^[9] (83.3%) than in our study (16.7%). However, Dennie–Morgan fold was observed more in our study (50%) than in Shi *et al.*^[9] (13%). White dermographism and non-specific hand/foot dermatitis were not seen in any of our patients; however, 29.2% and 25% of the patients had them in the Shi *et al.*^[9] study, respectively. Also, amongst the atypical criteria atopic dirty neck appearance [Figure 1] and juvenile plantar dermatoses [Figure 2] were each seen in one patient (1.9%) respectively.

In our study, white dermographism was statistically significantly more in the infantile group than in the childhood and adolescent groups (p < 0.0001). Palmar hyper-linearity, ichthyosis vulgaris, and keratosis pilaris (p < 0.05) and orbital darkening (p < 0.001) were significantly higher in the childhood and adolescent age groups than in the infantile group. Peri-follicular accentuation was more commonly found in the childhood age group; however, it was not statistically significant as P > 0.05.

Hence, it was established that the incidence of white dermographism declined with age. In contrast, the incidence of palmar hyper-linearity, ichthyosis vulgaris, keratosis pilaris and orbital darkening increased with age. Furthermore, Shi *et al.*^[9] reported seven criteria, that is, xerosis, palmar hyper-linearity, anterior neck fold, white dermographism, Dennie–Morgan fold, ichthyosis vulgaris, and keratosis pilaris, which gradually increased with age.

Limitation

Ophthalmological examination was not performed in all patients, and the small sample size was the major limitation of this study. In addition, the invasive minor criteria were



Figure 1: Atopic dirty neck appearance in an adolescent patient



Figure 2: Juvenile plantar dermatosis seen in an adolescent female

not studied. Also, the studies compared were performed in separate time frames by different observers.

Conclusion

The list of Hanifin and Rajka minor criteria seen commonly (>50% patients) in our study is as follows: Xerosis, early age of onset, Dennie–Morgan fold, aggravation because of emotional/environmental factors, palmar hyper-linearity/ichthyosis vulgaris/keratosis pilaris, pityriasis alba, and orbital darkening.

As compared to studies from other countries, Dennie–Morgan fold was more commonly found in Indian pediatric atopic dermatitis patients. Peri-follicular accentuation was less prevalant in Indian patients as compared to other Asian studies. None of the parents reported food intolerance in our study, which was seen in other studies.

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Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient (s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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