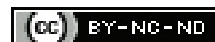


Estimating the Frequency of Hanifin and Rajka's Minor Criteria among Paediatric Atopic Cases at a Tertiary Care Hospital in Western Tamil Nadu, India- A Cross-sectional Study

K GOPALAKRISHNAN¹, S SIVANANDAM², SOWMYA S AITHAL³, VINUPRIYA SAKKARAVARTHI⁴, R PRABHU VIKASH⁵, K RAJENDRAN⁶, S JEEVITHAN⁷



ABSTRACT

Introduction: Atopic Dermatitis (AD) is a common relapsing inflammatory disorder, among the paediatric population clinically, characterised by pruritus and recurring eczematous skin lesions and a host of other cutaneous changes. Diagnosis is done on the basis of clinical findings with the usage of Hanifin and Rajka's criteria which includes 4 major and 23 minor criteria. Geographical, climatic factors and other population factors have been reported to influence the occurrence of minor criteria.

Aim: To estimate the frequency of Minor criteria among paediatric atopic dermatitis in Western Tamil Nadu, India.

Materials and Methods: This cross-sectional observational study was done by including 110 atopic children attending Paediatric and Dermatology Outpatient Departments (OPD) of KMCH IHSR, Coimbatore, Western Tamil Nadu, India, between March 2022 to August 2022. The clinical and ophthalmological findings were documented. Categorical variables were presented as frequency

and percentages, Continuous variables were presented as Mean±Standard deviation. The data was entered in excel and was analysed using Statistical Package For Social Sciences (SPSS) version 27.

Results: Among the total study population of 110, 53 (48.2%) were males and the rest 57 (51.8%) were females. The mean age was 24.73±5.18 years with a range of 2-15 years. Early age of onset was seen in 73.6% of study population. Hyperlinear palms were found in 70% of the study patients. 68.2% had Dennie Morgan infraorbital fold, 64.5% had xerosis, 61% had pityriasis alba and 60% had a family history of atopy.

Conclusion: Certain minor manifestations of AD like xerosis, ichthyosis, hyperlinear palms, and perifollicular accentuation were more common in the present study. Western Tamil Nadu having a tropical semi-arid climate tempered by higher altitude could explain the differences noted in the frequency of certain minor criteria.

Keywords: Hyperlinear palms, Ichthyosis, Keratosis pilaris

INTRODUCTION

Atopic dermatitis is a common allergic skin disorder affecting children. Its relapsing nature and the associated pruritus can result in significant distress to the affected child. AD is frequently associated with a personal or family history of asthma and allergic rhino conjunctivitis [1]. It can cause a variety of skin changes whose occurrence varies depending upon the geographic area of residence, age of onset, and other factors. The diagnosis is usually done with the use of criteria proposed by Hanifin and Rajka which has four major and 23 minor criteria out of which three from each category are necessary [2]. A systematic review done on the diagnostic criteria available for AD worldwide reported that Hanifin and Rajka diagnostic criteria's sensitivity and specificity ranged from 87.9-96.0% and from 77.6-93.8%, respectively, the U.K. diagnostic criteria showed sensitivity and specificity ranging from 10-100% and 89.3%-99.1%, respectively, the Schultz-Larsen criteria showed sensitivity from 88-94.4% and specificity from 77.6-95.9%, the Kang and Tian criteria and reported 95.5% sensitivity and 100% specificity [3]. A comparative study found that Hanifin and Rajka's criteria had a statistical advantage in comparison to the UK working party's criteria in diagnosing [4]. An Indian study found that certain minor criteria shows high sensitivity and specificity for AD diagnosis including xerosis, ichthyosis, palmar hyperlinearity, tendency of cutaneous infections, Dennie-Morgan infraorbital fold, pityriasis

alba, and perifollicular accentuation whereas, few other criteria were either very rare or non specific for AD. They further suggested that many of the minor criteria of Hanifin and Rajka may not hold much significance as far as Indian patients were concerned and a larger, multicentric nationwide study may be needed for the creation of a trimmed and improved version of Hanifin and Rajka criteria [5].

Also, the prevalence of these clinical features may vary depending on geographical region, climate, genetic makeup, and socio-economic background [6,7]. Western Tamil Nadu has a semi-arid tropical climate but a higher altitude than the mean sea level results in a cooler and drier climate throughout most parts of the year, while the rest of the state has a hotter and more humid climate [8]. This could have an influence on the skin manifestations in atopy. The aim of this study was to evaluate the frequency of occurrence of minor skin lesions and other epidemiological factors noted in atopic children in Western Tamil Nadu and compare it with similar studies.

MATERIALS AND METHODS

A cross-sectional study was conducted at the Department of Paediatrics at Kovai Medical Centre and Hospital Ltd. Coimbatore, western, Tamil Nadu, India. Duration of the study was six months from March 2022 to August 2022. Permission to conduct the study was obtained from Institutional Research Committee and Institutional Ethics Committee (43/IHEC/2021). The data of individual study

participants collected was compiled into a master excel sheet, from which the frequency of each minor criteria and the total number of it present in each individual was calculated.

Sample size calculation: According to Parthasarathy N et al., the common minor criteria observed in Karnataka and its prevalence are as follows [Table/Fig-1] [6].

Minor criteria	Percentage
Xerosis	67.2
Hyperlinear palms/Early age of onset	67.8
Dennie Morgan infra orbital fold	71.8
Pityriasis Alba	57.5
Perifollicular accentuation	47.7

[Table/Fig-1]: Common minor criteria by Parthasarathy N et al., [6].

Substituting these values in the below mentioned formula, the sample size was calculated [Table/Fig-2].

$$n = Z_{1-\alpha/2}^2 (1-P)/\epsilon^2 P$$

As a rule of thumb, the highest sample must be considered as the study sample. We took 110 samples as adequate sample size.

Single proportion-relative precision					
Expected proportion	0.672	0.678	0.718	0.575	0.477
Relative precision (%)	20	20	20	20	20
Desired confidence level (1-alpha) %	95	95	95	95	95
Required sample size	47	46	38	71	105

[Table/Fig-2]: Sample size calculation.

Inclusion criteria: All pediatric AD cases diagnosed using the major criteria of Hanifin and Rajka [2] attending Paediatric/Dermatology Outpatient at KMCH IHSR were included.

Exclusion criteria: All children who were on oral and topical steroids in the past two months and those children whose parents did not consent for the study were excluded.

Operational Definitions

Operational definitions of the historical and clinical criteria used in this study were taken from a study published by Parthasarathy N et al., as mentioned below [6]. After taking informed consent from the parent/attender, a thorough history including current age, age of onset (early age of onset was considered when onset of symptoms of atopy was before the age of 5 years), family history of atopy, a tendency towards cutaneous infections (defined as presence of at least two episodes of folliculitis/furunculosis/impetiginisation or diagnosed herpes simplex infection in the past 1 year) and non-specific hand and foot dermatitis (described as presence of itchy lesions on one or both hands/feet with erythema and papules/vesicles or scaling, with or without oozing, crusting, fissures, or lichenification), history of recurrent conjunctivitis, itch when sweating, intolerance to wool, food hypersensitivity and influence of environmental factors were recorded in a proforma.

Study Procedure

A dermatological examination was done to identify the presence of all the minor criteria of Hanifin and Rajka which require clinical examination. It included xerosis, ichthyosis, palmar hyperlinearity (defined by the presence of more than 5 prominent lines longer than 1 cm running across the palm), keratosis pilaris, nipple eczema, cheilitis, Dennie-Morgan infraorbital fold (defined as present when

at least one infraorbital crease running laterally crosses the pupillary midline), orbital darkening, facial pallor or erythema (facial erythema was defined as erythema over cheeks without papules/scaling and facial pallor as skin pallor over face which is often accentuated perinasally and/or periorally), pityriasis alba, anterior neck folds (defined as prominent horizontal skin crease(s) on anterior aspect of neck, when head is upright), perifollicular accentuation (defined as dermatitis enhanced around hair follicles in ≥ 2 areas with a diameter > 5 cm), and white dermographism. An ophthalmological screening was done for keratoconus and anterior subcapsular cataract.

STATISTICAL ANALYSIS

The data was entered in excel and was analysed using SPSS version 27. Categorical variables were presented as frequency and percentages, Continuous variables were presented as Mean \pm Standard deviation. Data was tabulated using Microsoft excel.

RESULTS

Among the total study population of 110, 53 (48.2%) were males and the rest 57 (51.8%) were females. The mean age was 24.73 \pm 5.18 years with a range of 2-15 years. 81 (73.6%) had early age of onset. 71 (65%) had symptoms less than one year. The frequency of minor criteria in the study population is presented in [Table/Fig-3].

Particulars	Absent		Present	
	N	%	N	%
Xerosis	39	35.5	71	64.5
Ichthyosis	97	88.2	13	11.8
Hyperlinear palms	33	30.0	77	70.0
Keratosis pilaris	101	91.8	9	8.2
Early age of onset	29	26.4	81	73.6
Tendency for cutaneous infection	105	95.5	5	4.5
Tendency to non specific hand/foot dermatitis	104	94.5	6	5.5
Nipple eczema	107	97.3	3	2.7
Cheilitis	103	93.6	7	6.4
Recurrent conjunctivitis	103	93.6	7	6.4
Dennie morgan infraorbital fold	35	31.8	75	68.2
Orbital darkening	96	87.3	14	12.7
Facial pallor	80	72.7	30	27.3
Facial erythema	103	93.6	7	6.4
Pityriasis alba	43	39.1	67	60.9
Anterior neck folds	102	92.7	8	7.3
Itch when sweating	104	94.5	6	5.5
Intolerance to wool and lipid solvents	106	96.4	4	3.6
Perifollicular accentuation	52	47.3	58	52.7
Food hypersensitivity	99	90.0	11	10.0
Course influenced by environmental factors	83	75.5	27	24.5
White dermographism	108	98.2	2	1.8
Serum IgE level elevated	102	92.7	8	7.3

[Table/Fig-3]: Frequency of minor criteria in the study population.

Hyperlinear palms were found in 77 (70%) of the study population. 75 (68.2%) had Dennie Morgan infraorbital fold, 70 (64.5%) had xerosis, and 67 (61%) had pityriasis alba 66 (60%) had a family history of atopy, and 58 (52.7%) had perifollicular accentuation. 30 (27.3%) had facial pallor. 27 (24.5%) had their course influenced by environmental factors. 14 (12.7%) had orbital darkening. 13 (12%) had ichthyosis.

Food hypersensitivity, keratosis pilaris anterior neck folds, cheilitis, recurrent conjunctivitis, facial erythema, the tendency to non specific hand/foot dermatitis, itch when sweating, tendency for cutaneous infection, intolerance to wool and lipid solvents, nipple eczema, white dermographism were found in less than ten percent of the study population [Table/Fig-3]. Serum IgE was done only among 29 study populations and 8 (27.6%) among them were positive. Family history of atopy was present in about 60% (n=66) in the present study.

[Table/Fig-4] shows the frequency/percentage distribution of total number of minor criteria present in an individual participant.

Total number of minor criteria number present in an individual participant	Frequency	Percentage
2	2	1.82
3	4	3.64
4	21	19.09
5	29	26.36
6	36	32.73
7	11	10.00
8	6	5.45
10	1	0.91
Total	110	100

[Table/Fig-4]: Frequency/Percentage distribution of total number of minor criteria present in individual participants.

Clinical images showing Xerosis in the Leg, Pityriasis alba in the Right cheek, Ichthyosis in the Leg, Keratosis pilaris in the posterior aspect of forearm and Foot eczema in the sole [Table/Fig-5-9].



[Table/Fig-5]: Xerosis in the Leg. **[Table/Fig-6]:** Pityriasis alba in the Right cheek. (Images from left to right)



[Table/Fig-7]: Ichthyosis in the Leg. **[Table/Fig-8]:** Keratosis pilaris in the posterior aspect of forearm. (Images from left to right)



[Table/Fig-9]: Foot eczema in the sole.

DISCUSSION

The chronic itching and scratching associated with AD can be a source of concern and social embarrassment for the affected child and parents. Since, there is no diagnostic laboratory gold standard marker for atopic dermatitis, diagnosis depends on specific clinical manifestations of the disease [2]. In the present study, 73.6% of the study population had an early age of onset. Early age of onset reported in a majority of their study population by Nagaraja et al., and Bohme et al., [9,10]. About 60% had a family history of atopy in the present study. The highest number of minor criteria noted in an individual participant was 10 (n=1) and the lowest was 2 (n=2). Majority of the study participants [86 (78.18%)] had between 4-6 minor criteria present. This was in line with the established diagnostic criteria of having 3 or more minor criteria in the diagnosis of AD.

A study done by Nagaraja et al., at Chandigarh, India evaluated the occurrence of minor criteria of Hanifin and Rajka in children up to 12 years of age and divided the study population into several age-related subgroups [9]. They reported variable significance of the minor features among different age groups and also found that two new additional features such as diffuse scaling of scalp and infra-auricular fissuring to be significantly associated. They concluded by suggesting the modification of criteria by deletion of some minor features and addition of newer ones.

Kanwar AJ et al., and Dhar S and Kanwar AJ have published two papers evaluating the epidemiological factors of AD and evaluation of its minor cutaneous features [11,12]. They found that nipple eczema, chielitis and conjunctivitis were not significantly associated in AD. In addition, they also suggested the term Atopic facies

with facial pallor or erythema, orbital darkening, Dennie-Morgan infraorbital folds, conjunctivitis, keratoconus, anterior subcapsular cataracts, infraauricular fissure, pityriasis alba, xerosis along with diffuse scaling of the scalp and anterior neck folds as its features. These studies quoted above were done in Northern India where both summer and winter seasons are known to have extremes of temperature and humidity.

Parthasarathy N et al., estimated the frequency of minor criteria among atopic children in Southern India [6]. They found that keratoconus, anterior subcapsular cataract, nipple eczema, recurrent conjunctivitis, food hypersensitivity, white dermographism were not observed in their study population. They also suggested that Lichen spinulosus be considered as a significant marker of AD. This study was done in North Karnataka, India a geographic region of Deccan plateau with an elevation ranging from 300 to 730 metres above mean sea level. It has a subtropical climate with hotter and less humid summers and dry winters [5]. A study done by Sehgal VN et al., on the minor features concluded that AD is a distinct entity frequently displaying varying demographic and clinical connotation [13]. The comparison of the above studies with the results of the present study is shown in the [Table/Fig-10] [4-6,9,13].

Mevorah B et al., suggested that the presence of Hyperlinear palms and Dennie Morgan infraorbital fold were of less significance in their study patients, the present study showed the presence of hyperlinearity in 70% and Dennie-Morgan infraorbital fold in 68.2% of the study population [14]. 64.5% had xerosis, 61% of patients

had pityriasis alba and 52.7% had perifollicular accentuation, these features were also seen in higher frequency in the study by Parthasarathy N et al., i.e., 67.2%, 57.5% and 47.7% respectively [6]. 27.3% had facial pallor, which is produced by vasoconstriction. 24.5% had course influenced by environmental factors with winter exacerbation, which can be explained by the dry cold climate in western Tamil Nadu. Similar values were found in another study by Kanwar AJ et al., [11]. 12.7% had orbital darkening i.e., circumscribed darkness around orbits. About 12% had ichthyosis characterised by small polygonal scales, especially on the extensor surfaces of the legs. Nagaraja et al., found ichthyosis, anterior neck folds, and food intolerance to be non specific and did not find any keratoconus or anterior subcapsular cataract in their patients [9]. Similar findings were observed in the present study.

Nipple eczema, cheilitis, and conjunctivitis were less commonly found in the present study similar to other studies [9,14,15]. Kanwar AJ et al., found intolerance to wool in 28% of the children in their study, but, in this study showed presence in only 3.4% of cases. It may be explained by the relatively less use of woollen clothes in this population [11]. Serum IgE was done only among 29 study populations and 8 (27.6%) among them were positive. Also, total serum IgE level may not be a specific criterion according to the study done by Hamada M et al., [16].

Overall, this study's findings correlated with the study done by Parthasarathy N et al., which was based in South India, particularly in the occurrence of xerosis, ichthyosis, hyperlinear palms, and

Parameters	Kanwar AJ et al., [4] (Chandigarh, India, 1991) (n=50)	Nagaraja et al., [9] (Chandigarh, India, 1996) (n=100)	Sehgal VN et al., [13] (New Delhi, India, 2010-2011) (n=100)	Parthasarathy N et al., [6] (Bijapur, Karnataka, 2019) (n=174)	Dutta A et al., [5] (West Bengal, India, 2018-2020) (n=100)	Present study (Coimbatore, Western Tamil Nadu, 2022) n=110)
Xerosis	80	76	80	67.2	71	64.5
Ichthyosis	-	4	50	11.5	19	11.8
Hyperlinear palms	54	23		67.8	56	70.0
Keratosis pilaris	46	33	50	4	2	8.2
Early age of onset	74	73		67.8	83	73.6
Tendency for cutaneous infection	62	36	66	2.9	37	4.5
Tendency to non specific hand/foot dermatitis	42	12	80	4.6	20	5.5
Nipple eczema	8	1	20	0	6	2.7
Cheilitis	6	3	58	7.5	9	6.4
Recurrent conjunctivitis	4	14	25	0	0	6.4
Dennie morgan infraorbital fold	82	63	-	71.8	52	68.2
Orbital darkening	32	12	58	6.9	3	12.7
Facial pallor	14	26	-	21.3	11	27.3
Facial erythema	-	56	-	9.8	4	6.4
Pityriasis alba	78	34	20	57.5	54	60.9
Anterior neck folds	12	6	68	6.3	22	7.3
Itch when sweating	66	35	70	8	7	5.5
Intolerance to wool and lipid solvents	28	41	68	2.3	0	3.6
Perifollicular accentuation	22	39	-	47.7	37	52.7
Food hypersensitivity	-	-	72	-	0	10.0
Course influenced by environmental factors	26	44	66	8	30	24.5

[Table/Fig-10]: Comparison of frequency of minor criteria in percentage with other Indian studies [4-6,9,13]. Values given are in percentages for population studied

perifollicular accentuation [6]. Whereas, the studies done in Northern part of India correlated within them with respect to occurrence of keratosis pilaris, tendency to hand and foot dermatitis, itch when sweating and white dermographism [4,9,13]. Geographical, climatic, dietary and other as yet unidentified factors could have resulted in the above observation.

Limitation(s)

The sample drawn in this study is hospital-based and may not truly represent the prevalence of the minor clinical features of the population.

CONCLUSION(S)

Among the minor cutaneous manifestations of AD, some features like xerosis, ichthyosis, hyperlinear palms, and perifollicular accentuation are reportedly more common in the present study. Studies done in different regions of the country have demonstrated wide variation in these cutaneous manifestations. A larger multicentric study could throw more light in the variation of minor cutaneous features with respect to geographic and climatic conditions.

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PARTICULARS OF CONTRIBUTORS:

1. Associate Professor, Department of Dermatology, KMCH IHSR, Coimbatore, Tamil Nadu, India.
2. Associate Professor, Department of Paediatrics, KMCH IHSR, Coimbatore, Tamil Nadu, India.
3. Assistant Professor, Department of Dermatology, KMCH IHSR, Coimbatore, Tamil Nadu, India.
4. Assistant Professor, Department of Dermatology, KMCH IHSR, Coimbatore, Tamil Nadu, India.
5. Assistant Professor, Department of Paediatrics, KMCH IHSR, Coimbatore, Tamil Nadu, India.
6. Professor, Department of Paediatrics, KMCH IHSR, Coimbatore, Tamil Nadu, India.
7. Professor, Department of Community Medicine, KMCH IHSR, Coimbatore, Tamil Nadu, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:

K Gopalakrishnan,
Associate Professor, Department of Dermatology, KMCH IHSR, 99, Avinash Road,
Coimbatore, Tamil Nadu, India.
E-mail: gopukris83@gmail.com

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