Erythroderma: Epidemiology, Clinical Profile and Clinicopathological Correlation in 47 Patients

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ABSTRACT

Background: Erythroderma, or generalized exfoliative dermatitis, is a disease characterized by erythema and scaling of greater than 90% of the body's surface. There is paucity of Indian studies over the etiology, clinical profile and its histopathological correlation. **Aims and objectives:** To assess the demographic profile, clinical features and histopathological correlation in erythroderma patients. **Material and methods:** We registered all patients of erythroderma consecutively from January 2013 to December 2013. After a thorough history and clinical examination, a provisional clinical diagnosis was made. We performed biopsy from two representative sites of patient and it was sent for histopathological examination. The slides were examined by two pathologists and one dermatologist without any relevant clinical information. The clinical diagnosis was matched with the blinded microscopical diagnosis. **Results:** The mean age of onset was 54.1 years with a male-to-female ratio of 3.3:1. The most common causes were airborne contact dermatitis (53.2%) followed by psoriasis (21.2%), drug-induced erythroderma (12.7%), chronic actinic dermatitis (2.1%), atopic dermatitis (2.1%), endogenous dermatitis (2.1%), mycosis fungoides (2.1%), lichenoid dermatitis (2.1%) and idiopathic (2.1%). Histopathology was able to provide diagnosis in 32 (68%) patients. Out of these 32 patients, microscopical diagnosis was in accordance with clinical diagnosis in 28 patients. **Conclusion:** Most of the clinical features of erythroderma are overlapping. Specific and diagnostic features of disease are seen only in a few patients. Repeated evaluations, close follow-up and skin biopsy are recommended for a better clinical diagnosis and patient care.

Keywords: Erythroderma, generalized exfoliative dermatitis, erythema, biopsy, histopathological examination

Erythroderma or exfoliative dermatitis is an inflammatory disorder in which erythema and scaling occur in a generalized distribution involving more than 90% of the body surface. Because most patients are elderly and skin involvement is widespread, the disease implies an important risk to the life of the patient. The estimated annual incidence of erythroderma seems to be 1-2/1,00,000 patients. This disorder may represent a variety of cutaneous and systemic diseases, and therefore a thorough work-up is essential, which includes detailed history of triggering factors like drugs, occupation, sunlight exposure, pre-existing dermatoses, infections, malignancies, etc. It should be followed by a meticulous clinical examination for specific diagnostic clues to rule out its etiology. Histopathology can help in identifying the cause of erythroderma in up to 50% of cases, particularly by multiple skin biopsies.

Indian studies showed a higher prevalence of erythroderma than other studies. Sehgal and Srivastava recorded the incidence of erythroderma from the Indian subcontinent as 35/1,00,000 dermatologic outpatients. But, there are conflicting views over role of histopathology as some studies were unrewarding.

This study was performed to find out the causes of erythroderma in north-west part of India, to find out the epidemiological, clinical profile of these patients and histopathological correlation.

MATERIAL AND METHODS

The study was performed from January 2013 to December 2013. In this tenure, all cases of erythroderma attending skin outpatient department were included in the study. A thorough history which included duration, progression of disease, occupation,

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seasonal variation, precipitating factors, site of onset, other existing skin disease and other comorbidities like hypertension, atopy, etc. was taken from patient. It was followed by a thorough general physical and dermatological examination. Laboratory investigations such as complete hemogram, blood glucose, blood urea, serum creatinine, liver function tests, serum electrolytes and chest radiograph were performed. Abdominal ultrasound, peripheral smear, fine needle aspiration cytology (FNAC) of lymph nodes, CT scan, etc. were done only if required.

Four millimeter punch biopsy was performed in all patients from two representative sites. The slides were seen independently by two pathologists and dermatologist without relevant clinical information. Slides were examined by them independently for any specific diagnosis. The microscopical diagnosis was then correlated with clinical diagnosis.

RESULTS

Age of patients ranged from 14 to 86 years with median of 58 years and mean age of onset of 54.1 ± 17.8 years. Majority of patients belonged to age group of 51-60 years (Fig. 1). Male predominance was seen with male-to-female ratio of 3.3:1. The total duration of erythroderma in patients ranged from 10 days to 20 years with median of 2 years and mean of 4.1 ± 5.2 years. Exacerbation of disease ranged from 7 to 120 days with a mean of 43.3 ± 25.3 days. Majority of male patients were farmers (55.5%) followed by laborers (22.2%) and students (6.3%). Majority of female patients were housemakers (72.7%) (Table 1).

Most common aggravating factor was seasonal exacerbation seen in about 26 patients (55.3%) with summer exacerbation in 17 patients (36.1%). Seasons had no effects on disease in 21 patients (44.7%). History of atopy was present in 11 (23.4%) patients. Other aggravating factors were sunlight and dust, which were seen in 11 (23.4%) patients each. Drugs were responsible in 4 (8.5%) patients. History of pre-existing skin disease was present in 30 patients (63.8%). Other comorbidities, like hypertension was present in 17 patients (36.1%), diabetes in 4 patients (8.5%) and tuberculosis in 4 patients (8.5%). In 17 patients of hypertension, nine were already on antihypertensive medicine but 8 patients were diagnosed with hypertension for the first time. The site of onset of erythroderma was scalp and face in 20 patients (42.6%), extremities in 18 patients (38.3%), and trunk and abdomen in 8 patients (17.0%). Most common clinical finding was pruritus (100%) followed by lymphadenopathy (70.2%), edema (57.4%), nail changes (55.3%), fever (38.2%), palmoplantar keratoderma (21.2%), weight loss (14.9%) and loss of appetite (10.6%) (Table 2). Severe pruritus causing disturbance in sleep was present in 29 (61.7%) patients. Inguinal lymphadenopathy was present in 33 (70.2%) patients and axillary lymphadenopathy in one patient. Most common nail change was Beau's line followed by shiny nails, yellowish discoloration of nails, subungual hyperkeratosis, pitting and onycholysis. In 3 (6.3%) patients, 20 nail dystrophy was present. Pitting edema of the distal extremities was present in 21 (44.7%) patients. Generalized edema of pitting type was present in 4 (8.5%) patients. Histopathology was able to provide specific histopathological diagnosis e.g., psoriasis, dermatitis in 32 (68%) patients. Out of these 32 patients, clinical correlation occurred in 28 (87%) patients. Overall, in 28 (60%) patients, clinical diagnosis matched with histopathological diagnosis. Table 3 summarizes the clinicopathological correlation. Nonspecific biopsy was seen in 15 (32%) patients. Histopathology was most accurate in diagnosing drug reaction (100%), followed by mycosis fungoides (100%) and psoriasis (70%) (Fig. 2). The specific findings of biopsies are depicted in Table 4. The most common causes were airborne

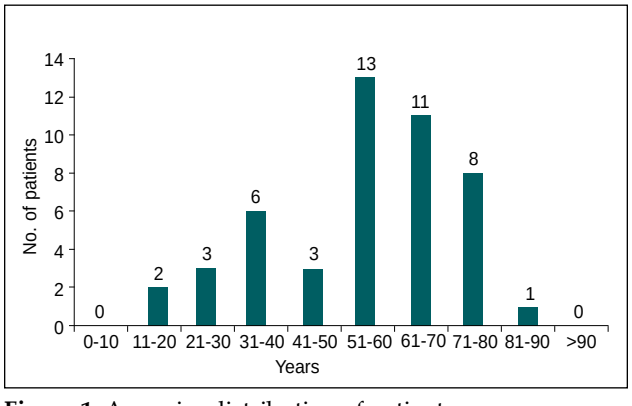

Figure 1. Age-wise distribution of patients.

Table 1. Occupational Profile of Patients

Occupation	No. of males	No. of females
Farmer	20	-
Laborer	8	-
Student	3	2
Housemaker	-	8
Carpenter	1	-
Sarpanch	1	-
Service	2	1
Army officer	1	-

Table 2. Clinical Profile of Patients

Symptom/disease	Airborne contact dermatitis (n = 25)	Psoriasis (n = 10)	Drug-induced erythroderma (n = 6)	Mycosis fungoides (n = 1)	Other (n = 5)
Pruritus	25	10	6	1	5
Fever	7	8	3	0	0
Loss of appetite	3	1	0	1	0
Weight loss	4	1	0	1	1
Edema	15	6	3	0	3
Lymphadenopathy	18	9	3	1	2
Nail changes	15	9	0	0	2
Palmoplantar keratoderma	4	6	0	0	0
Hypertension	14 6 ND	1 ND	1		1ND
Diabetes	3	0	0	0	1

ND: Newly diagnosed case.

Table 3. Clinicopathological Correlation

Clinical diagnosis	Histopathological diagnosis	Clinicopathological correlation
Airborne contact dermatitis (n= 25)	Dermatitis (n = 10) Psoriasis (n = 3) Nonspecific (n = 12)	40%
Psoriasis (n = 10)	Psoriasis (n = 7) Dermatitis (n = 1) Nonspecific (n = 2)	70%
Drug-induced erythroderma (n = 6)	Drug-induced (n = 6)	100%
Chronic actinic dermatitis (n = 1)	Dermatitis (n = 1)	100%
Endogenous dermatitis (n = 1)	Dermatitis (n = 1)	100%
Atopic dermatitis (n = 1)	Dermatitis (n = 1)	100%
Mycosis fungoides (n = 1)	Mycosis fungoides (n = 1)	100%
Lichenoid dermatitis (n = 1)	Lichenoid dermatitis (n = 1)	100%
Idiopathic (n = 1)	Nonspecific (n = 1)	-

contact dermatitis (53.2%) followed by psoriasis (21.2%), drug-induced erythroderma (12.7%), chronic actinic dermatitis (2.1%), atopic dermatitis (2.1%), endogenous dermatitis (2.1%), mycosis fungoides (2.1%), lichenoid dermatitis (2.1%) and idiopathic (2.1%) (Fig. 3).

DISCUSSION

The approach to patients with erythroderma depends on their previous dermatologic background. Patients with pre-existing dermatoses are easy to diagnose. Otherwise, erythroderma remains a diagnostic challenge, especially in those patients without history of dermatologic diseases and who deny having recently taken any medications.

In our study, age of patients ranged from 14 to 86 years with mean age of onset of 54.1 ± 17.8 years. This is in accordance with various previous studies. In this series, men outnumbered women in a ratio of 3.3:1. Similar findings were seen in other studies. In a study by Hulmani et al, male-to-female ratio was quite high at 14:1. As men are commonly involved than women

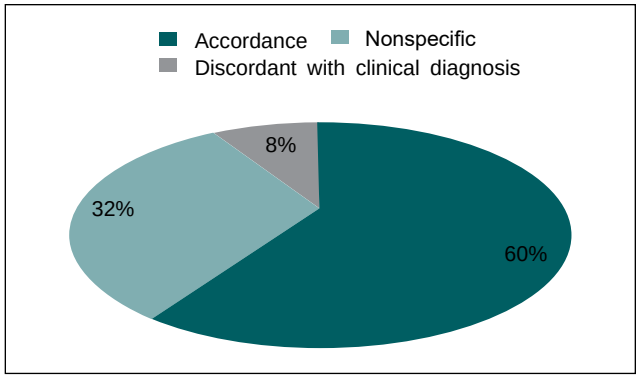

Figure 2. Clinical and histopathological diagnosis.

Table 4. Histopathological Findings

Psoriasis (n = 10)	
Hyperkeratosis	7
Parakeratosis	10
Munro microabscess	7
Granular layer absent	8
Acanthosis	7
Suprapapillary thinning	6
Dilated blood vessel	6
Perivascular lymphocytic infiltrate	9
Infiltrate having neutrophils	3
Drug-induced (n = 6)	
Hyperkeratosis	5
Parakeratosis	4
Necrotic keratinocyte	3
Basal cell vacuolization	5
Melanin incontinence	4
Lichenoid infiltrate	3
Perivascular lymhocytic infiltrate	5
Eosinophils in infiltrate	3
Dermatitis (n = 29)	
Hyperkeratosis	25
Parakeratosis	25
Acanthosis	24
Spongiosis	11
Perivascular lymphocytic infiltrate	27
Eosinophils in infiltrate	8

in outdoor activities, male-to-female ratio is quite high in this study.

Most common aggravating factor was seasonal variation seen in 26 patients. Summer exacerbation was seen in 17 patients. Dust and sunlight aggravated the condition in 11 patients each. This is in contrast to another study where winter season was aggravating

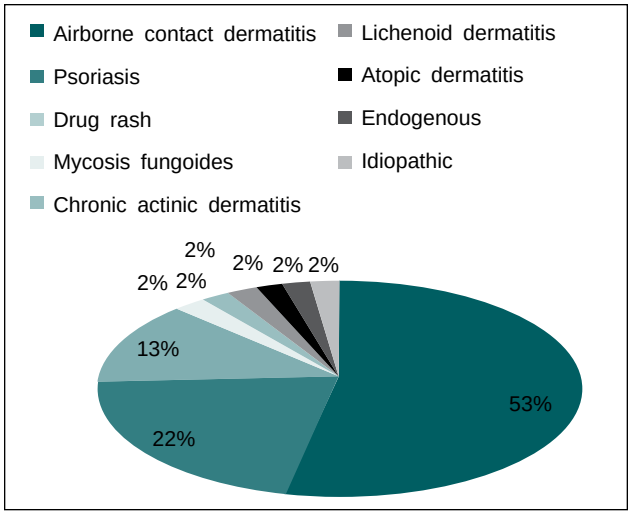

Figure 3. Etiology of erythroderma.

factor seen in 30% patients. In our study, most common cause of erythroderma was airborne contact dermatitis compared to Hulmani et al where most common etiology was psoriasis. This might be the cause of winter exacerbation in their study. Most of the clinical findings were in accordance with other studies. Lymphadenopathy was seen in 70% of our patients and was quite high. Some studies showed it as 19-33%. Others showed it to be around 55%. Nail changes were seen in 55% of patients. Nail changes were Beau's lines, shining in the nails, subungual hyperkeratosis, pitting, yellowish discoloration and onychodystrophy. Similar findings were present in other studies.

Histopathology was successful in determining the specific cause of erythroderma in 32 (68%) of the patients. So, overall clinicopathological correlation occurred in 60% of patients. As in our study, relevant clinical information wasn't provided to the pathologist but still they were able to match the clinical diagnosis in 28 (60%) patients. The percentage might push up higher with relevant clinical information. In a study by Rym et al, histopathological correlation was found in 74% of patients; in a study by Bandopadhyay et al, there was correlation in 52% of cases. Most common histopathological finding in our study was perivascular lymphocytic infiltrate.

The findings are comparable with slight differences from a study by Walsh et al. Comparison of our etiologic diagnosis with the previous studies is compiled in Table 5. In our case series, most common clinical diagnosis was airborne contact dermatitis. It is quite different from other studies where it constituted a minority group.

Table 5. Comparison of Different Etiology of Erythroderma in Various Studies

Study causes	Pal et al[10]	Rym et al[11]	Bandopadhyay et al[9]	Sudho et al[12]	Chaudhary et al[13]	Hulmani et al[8]	Our study
Psoriasis	37.8	51.25	33.33	32	40	33.33	21.2
Eczema	12.2	7.5	4	12	20	20	57.4*
Ichthyosis	7.8	0	1.33	0	0	0	0
Pityriasis rubra pilaris	2.2	5.25	1.33	0	0	3.33	0
Scabies	2.2	1.25	3.33	0	0	0	0
Pemphigus foliaceus	5.6	6.25	5.33	4	0	0	0
Lichen planus	0	1.25	0	0	0	0	0
Atopic dermatitis	0	0	13.33	8	6.66	6.6	2.1
Other dermatoses	6.6	3.75	0	8	0	0	2.1
Drug reaction	5.5	11.25	12	24	10	16.6	12.7
Malignancy	5.5	8.75	2.67	4	6.66	3.3	2.1
Idiopathic	14.6	7.5	21.33	08	16.6	16.6	2.1

SUGGESTED READING

1. Vasconcellos C, Domingues PP, Aoki V, Miyake RK, Sauaia N, Martins JE. Erythroderma: analysis of 247 cases. Rev Saude Publica. 1995;29(3):177-82.
2. Botella-Estrada R, Sanmartin O, Oliver V, Febrer I, Aliaga A. Erythroderma. A clinicopathological study of 56 cases. Arch Dermatol. 1994;130(12):1503-7.
3. Hasan T, Jansen CT. Erythroderma: a follow-up of fifty cases. J Am Acad Dermatol. 1983;8(6):836-40.
4. Walsh NM, Prokopetz R, Tron VA, Sawyer DM, Watters AK, Murray S, et al. Histopathology in erythroderma: review of a series of cases by multiple observers. J Cutan Pathol. 1994;21(5):419-23.
5. Sehgal VN, Srivastava G. Exfoliative dermatitis. A prospective study of 80 patients. Dermatologica. 1986;173(6):278-84.
6. Li J, Zheng JU. Erythroderma: a clinical and prognostic study. Dermatology. 2012;225(2):154-62.
7. Sehgal VN, Srivastava G, Sardana K. Erythroderma/ exfoliative dermatitis: a synopsis. Int J Dermatol. 2004;43(1):39-47.
8. Hulmani M, Nandakishore B, Bhat MR, Sukumar D, Martis J, Kamath G, et al. Clinico-etiological study of 30 erythroderma cases from tertiary center in South India. Indian Dermatol Online J. 2014;5(1):25-9.
9. Bandopadhyay D, Chowdhury SN, Roy AK. Seventy five cases of exfoliative dermatitis. Ind J Dermatol. 1999;44(2):55-7.
10. Pal S, Haroon TS. Erythroderma: a clinico-etiologic study of 90 cases. Int J Dermatol. 1998;37(2):104-7.
11. Rym BM, Mourad M, Bechir Z, Dalenda E, Faika C, Iadh AM, et al. Erythroderma in adults: a report of 80 cases. Int J Dermatol. 2005;44(9):731-5.
12. Sudho R, Hussain SB, Bellraj E, Frederick M, Mahalaxmi V, Sobhana S, et al. Clinicopathological study of exfoliative dermatitis. Indian J Dermatol Venereol Leprol. 2003;69(1):30-1.
13. Chaudhary A, Gupte PD. Erythroderma: a study of incidence and aetiopathogenesis. Indian J Dermatol Venereol Leprol. 1997;63(1):38-9.

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Hyperthermia

- Extraordinarily high fever (>41.5°C). Observed in patients with severe infections, most commonly occurs in patients with central nervous system hemorrhages.
- Most patients with elevated body temperature have fever; but, there are a few conditions in which an elevated temperature represents hyperthermia: Heat stroke syndrome, certain metabolic diseases and the effects of pharmacologic agents that interfere with thermoregulation. It is important to differentiate between fever and hyperthermia.
- Hyperthermia can be rapidly fatal, and its management differs from that of fever.

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