

## CLINICOPATHOLOGICAL CORRELATION IN ERYTHRODERMA

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### Abstract

**Background:** Erythroderma, or generalized exfoliative dermatitis, is a disease characterized by erythema and scaling involving more than 90% of the body's surface. Diagnosing erythroderma is easy but finding its cause is difficult. There is a 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 2014. 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 three independent observers without any relevant clinical information. The clinical diagnosis was matched with the blinded microscopical diagnosis.

**Results:** A total of 66 patients were enrolled in this study. The mean age of the study group was 53.7±16.56 years (Range: 14 to 86 years) with male outnumbering female in a ratio of 3.4:1. Most common cause of erythroderma noted in the study was eczema of various types (53.03%), followed by psoriasis (30.30%), drug induced (12.12%), lymphoma (1.515%), mycosis fungoides (1.515%) and idiopathic (1.515%). Clinico-pathological correlation occurred in about 67% (range: 63.6% to 68.2%) of patients (k value 0.495 to 0.572).

**Conclusion:** Most of the clinical features of erythroderma are overlapping. Specific and diagnostic features of diseases are seen only in a few patients. Clinico-pathological correlation should be done for better diagnosis of patient. Repeated evaluations, close follow-up and multiple skin biopsies are recommended for a better clinical diagnosis and patient care.

**Key words:** erythroderma, clinicopathological correlation, histopathology

### Introduction

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.<sup>1</sup> Because most patients are elderly and skin involvement is widespread, the disease implies an important risk to the life of the patient.<sup>2</sup> Hasan and Jansen estimated the annual incidence of erythroderma to be 1 to 2 per 100,000 patients.<sup>3</sup> This disorder may represent a variety of cutaneous and systemic diseases, and therefore a thorough workup is essential which include 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.<sup>4</sup>

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 per 100,000 dermatologic outpatients. But there are conflicting views over role of histopathology as some studies were unrewarding.<sup>5</sup>

The 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 conducted from January 2013 to December 2014. All cases of erythroderma attending skin outpatient department were included in the study. A thorough history followed by a meticulous general, physical and dermatological examination was to form a clinical diagnosis. Laboratory investigations including complete hemogram, blood glucose, blood urea, serum creatinine, liver function test, serum electrolytes and chest radiograph were done in all cases. Other relevant investigations including abdominal ultrasound, peripheral blood smear, fine needle aspiration cytology (FNAC) of lymph nodes and CT scan were done wherever needed. A four millimeter skin punch biopsy was performed in all patients from two representative sites. The slides were independently analysed by three different observers without relevant clinical information. Histopathological diagnosis was correlated with clinical diagnosis to make final diagnosis.

Clinical Features	Psoriasis	Eczema	Drug Induced	Lymphoma	Mycosis Fungoides	Idiopathic	Total	P Value
Itching	20	35	7	1	1	1	65	0.214
Fever	10	6	4	1	0	0	21	0.059
Shivering	12	10	4	1	0	0	27	0.151
Arthralgia	7	2	0	0	0	0	9	0.047
Edema	9	20	3	1	0	1	34	0.575
Lymphadenopathy	14	22	3	1	1	0	41	0.409
Palmoplantar Keratoderma	10	5	0	0	0	0	15	0.023
Nail Changes	17	20	1	0	0	0	38	0.005
Pallor	7	10	2	1	0	0	20	0.72

**TABLE 1:** Clinical Profile of Patients

### Results:

A total of 66 patients were enrolled in this study. The mean age of the study group was 53.7±16.56 in years (range : 14 to 86 Years). Males outnumbered females in a ratio of 3.4:1. The total duration of disease ranged from 10 days to 20 years with an average duration of 3.9 years. The exacerbation of disease was from 7 days to 1 year with a mean of 1.9 months. Majority of male patients were involved in outdoor activities and were farmers (39.4%) and laborers (16.67%). Majority of female patients were housewives (80%).

Most common aggravating factor was seasonal variation. Seasonal exacerbation was present in about 51.51% of patients. Winter exacerbation was present in 40% of psoriasis patients and 2.8% of eczema patients. Summer exacerbation was present in 54.2% of eczema patients and 25% of psoriasis patients. History of atopy was present in 19 patients. Drugs were responsible in 8 patients.

History of preexisting skin disease was present in 30 patients (62.1 %). Other co-morbidities like hypertension were present in 26 patients (39.3%), diabetes in 4 patients (6.06%), and tuberculosis in 4 patients (6.06%). The site of onset of erythroderma was scalp and face in 28 patients (42.4%), extremities in 27 patients (40.9%), and trunk & abdomen in 11 patients (16.67%).

Most common clinical features were itching (98.48%), fever (31.8%), shivering (40.9%), arthralgia (13.63%), lymphadenopathy (62.1%), edema (51.5%), palmoplantar keratoderma (22.7%) and nail changes (57.8%) [Table1]. The clinical finding in psoriasis, dermatitis and drug induced erythroderma have been described in detail in Table 2. Most common nail change was beau's line followed by shiny nails, yellowish discoloration of nails, subungual hyperkeratosis, pitting, and onycholysis. In 3 patients, twenty nail dystrophy was present. Investigations revealed anemia in 33.3%, increased ESR in 37.9%, abnormal TLC in 18.1%, abnormal LFT in 15.2%, hypoalbuminaemia in 34.8% and abnormal RFT in 9.09% of cases.

Clinico-pathological correlation occurred in about 67% (range:

63.6% to 68.2%) of patients with a kappa score ranging from 0.495 to 0.572. It was of moderate agreement. In psoriatic erythroderma patients, we were able to elicit microabscess, dilated blood vessel and suprapapillary thinning in 60%, 80% and 65% cases respectively. Presence of mitotic cells was also specific for psoriasis but it was present in only 20% of cases. The biopsies of drug induced erythroderma patients had necrotic keratinocyte, basal cell vacuolization and eosinophils in infiltrate in 62.5%, 75% and 87.5% of patients respectively. Spongiosis was present in 62.8% of patients of eczema. But it was also present in 50 % of drug induced erythroderma patients and 10% of psoriasis patients. [Table 3] In five patients, clinical findings mismatched histopathological findings. In these patients, clinical findings suggested the diagnosis of eczema but it came out psoriasis histopathologically. [Table 4]

Most common cause of erythroderma in this study was eczema of various types (53.03%), followed by psoriasis (30.30%), drug induced (12.12%), lymphoma (1.515%), mycosis fungoides (1.515%) and idiopathic (1.515%). [Figure 1]

### Discussion

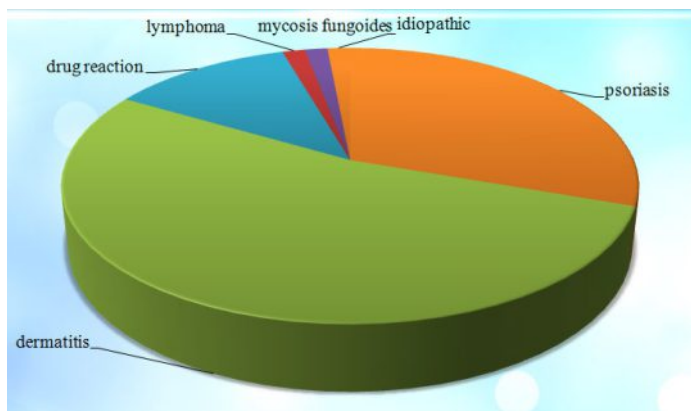
The approach to patients with erythroderma depends on their previous dermatologic background. Patient with a preexisting dermatoses are easy to diagnose. Otherwise, erythroderma remains a diagnostic challenge, especially in those patients without history of dermatologic diseases and who deny having recently taken any medications.<sup>6</sup>

In this study, the mean age of diagnosis was 53.7±16.56 years (range: 14 to 86 Years) with men outnumbering women in a ratio of 3.4:1. This is in accordance with various previous studies.<sup>3,6,7</sup> However, in a recent study by Hulmani et al, male to female ratio of 14:1 was noted.<sup>8</sup>

In our study, most common cause of erythroderma was air borne contact dermatitis compared to Hulmani et al where most common etiology was psoriasis.<sup>8</sup> The different etiologies of erythroderma found in various studies has been summarized in Table 5.

S.No.	Points	PSORIASIS	DERMATITIS	DRUG
1	Age group	Any	Predominantly Elderly age group(5- 7 decade)	Any
2	Seasonal Exacerbation	winter	Summer and spring	No
3	Preexisting disease	May	May	No
4	History of drug	No	No	Yes
5	Disease onset	Insidious	Mostly chronic	Acute
6	Site of onset	Predominantly extensors and scalp	Exposed surfaces Involvement of eyelids, other folds(ABCD)	Sometimes cephalo-caudal
7	Scaling	Thick, large, silvery	Fine	Fine
8	Erythema	Red, fiery red	Fading red	Red/ fading red
9	Nose sign	Absent	Seen	Absent
10	Oozing, cracking, fissuring, excoriation	Absent	Present	Absent
11	Vesiculation	Absent	May be	May be
12	Pustulation	May be	Generally Absent except (Secondary infection)	May be
13	Skin	Dry erythematous	Glossy skin with lichenification	Dry erythema
14	Itching	Mild	Severe	Mild
15	Palmoplantar keratoderma	May be (in some studies it is common)	Common	Absent
16	Fever	May be	Gen. Absent	May be
17	Shivering	++	++	+
18	Edema	+	+	++
19	Arthralgia	++	Gen. absent	++
20	Lymphadenopathy	++	+	++
21	Nails	++	-	-
	Pitting	++	-	-
	Beau's lines	-	++	-
	Onycholysis	++	May be	Absent
	Shinning in nails	-	++	-
	Subungual hyperkeratosis	++	+	-

**TABLE 2 :** Differences in clinical profile of erythroderma patients



**Figure 1:** Etiology of erythroderma

Lymphadenopathy was seen in 62.1% of our cases. Previous studies have reported its prevalence varying from 19% to 55%.<sup>6, 8-10</sup> Nail changes were seen in 57.8% of patients. Nail changes were beau's lines, shinning in the nails, subungual hyperkeratosis, pitting, yellowish discoloration and onychodystrophy. Similar findings were present in other studies.<sup>8, 10</sup>

Clinico-pathological correlation occurred in about 67% (range: 63.6% to 68.2%) of patients. In a similar study by Zip et al,<sup>4</sup> each set of pathological diagnoses was compared with the final discharge diagnoses, a positive correlation of 86% was observed in the nonblinded (original) diagnostic group as opposed to 66% in the blinded group. The results of blinded group were in accordance to our study which is also a blinded study. In another study by Vasconcellos et al,<sup>1</sup> one or more skin biopsies along with clinical findings were diagnostic or suggestive of the underlying disease in 63.6% of the cases. Khaled et al<sup>14</sup> reported positive clinico-histological correlation in 77%, Jun Li et al<sup>6</sup> in 55.56% and Rym et al<sup>11</sup> in 74% of patients.

The histopathology of erythroderma differs depending on the underlying diagnosis. In our study, in psoriasis patients the findings observed were munromicroabscess (60%), dilated blood vessel (80%), suprapapillary thinning (65%) and mitotic cells (20%). In similar study by Zip et al,<sup>4</sup> biopsies of psoriatic erythroderma patients revealed suprapapillary thinning, dilated blood vessel and munromicroabscess in 69%, 81% and 69% of patients respectively.

The biopsies of drug induced erythroderma patients had necrotic keratinocyte, basal cell vacuolization and eosinophils in

Histopathological Findings	Drug Induced	Psoriasis	Eczema
	%	%	%
Hyperkeratosis	87.5	100	94.2
Parakeratosis	87.5	100	74.2
Munro's microabscess	0.0	60	0.0
<b>Granular layer</b>			
Normal	87.5	15.0	82.8
Hypergranulosis	12.5	5.0	11.4
Hypogranulosis/Absent	0.0	80.0	5.8
<b>Acanthosis</b>	62.5	100.0	94.2
Regular	0	65.0	8.5
Irregular	62.5	35.0	85.7
Mitotic cell	0.0	20.0	0.0
Spongiosis	50.0	10.0	62.8
Suprapapillary thinning	0.0	65.0	2.9
Necrotic keratinocyte	62.5	0.0	0.0
Basal cell vacuolisation	75	0.0	11.4
Exocytosis	0.0	10.0	22.8
Epidermotropism	0.0	0.05	2.9
Dilated blood vessels	0.0	80.0	0.0
<b>Infiltrate</b>			
Lymphohistiocytic	37.5	95.0	62.9
Lichenoid	37.5	0.0	0.0
Mixed	12.5	5.0	28.5
Mononuclear	12.5	0.0	8.6
Eosinophilic infiltrate	87.5	5.0	11.4
Melanin incontinence	75.0	10.0	8.6

**TABLE 3:** Histopathological findings

infiltrate in 62.5%, 75% and 87.5% of patients respectively. In study by Zip et al<sup>4</sup>, necrotic keratinocyte and eosinophils in infiltrate were present in 50% of cases each. Microscopically, eosinophils in infiltrate, necrotic keratinocyte and basal cell vacuolization were the most specific findings to diagnose a case of drug induced erythroderma. In previous studies, spongiosis was one of characteristic finding to diagnose a case of erythroderma due to eczema, present in 62.8% patients. But it was also present in 50% of drug induced erythroderma patients and 10% of psoriasis patients. Thus as spongiosis was not one of the specific findings to diagnose a case of erythroderma due to eczema we had to collaborate it with other findings for diagnosis. It is generally thought that oozing, cracking,

S. No.	Itching	Oozing	Lichenification	Seasonal exacerbation	H/O Atopy	Previous H/O	Palmoplantar involvement	Nail changes	Scaling	Histopathological Diagnosis	Clinical diagnosis
1.	Mild	+	-	-	-	-	-	Beau's line	Fine	Psoriasis	Dermatitis
2.	Severe	+	+	Summer	+	Eczema	-	Yellow discoloration	Fine	Psoriasis	Dermatitis
3.	Severe	+	-	Summer	-	-	-	-	Fine	Psoriasis	Dermatitis
4.	Mild	+	+	Summer	+	+	+	Beau's line	Fine	Psoriasis	Dermatitis
5.	Severe	+	+	-	-	Eczema	-	Beau's line	Fine	Psoriasis	Dermatitis

**TABLE 4:** clinical findings of patients with mismatched histopathological findings

fissuring, presence of beau's lines, nail discoloration are useful for diagnosing eczema in erythroderma patients, but in our study we found that these changes were also present in some patients of psoriasis. Thus these changes might help in diagnosis of eczema but they are not diagnostic and a biopsy should be done in all patients to confirm diagnosis even when sure clinically.

Comparison of our etiologic diagnosis with the previous studies is compiled in table 4. In our case series, most common final diagnosis was eczema. It is quite different from other studies where it constituted a minority group.

### Conclusion

Although clinical diagnosis is possible in most cases, histopathology is required to corroborate with clinical diagnosis and to avoid any misdiagnosis as clinical features might overlap, for example psoriasis versus eczema. Microscopical clues that might help in diagnosis are munromicroabscess, dilated blood vessel and suprapapillary thinning for psoriasis and necrotic keratinocyte, basal cell vacuolization and eosinophils for drug induced erythroderma patients. Erythroderma still remains a challenge and requires skills of the dermatologist.

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Study causes	Pal et al[10]	Rym et al[11]	Bandyopadhyay et al[9]	Sudha et al [12]	Chaudhary et al[13]	Hulmani et al[8]	Our study
Psoriasis	37.8	51.25	33.33	32	40	33.33	53.03
Eczema of various types	12.2	7.5	4	12	20	20	30.3
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	0
Other Dermatoses	6.6	3.75	0	8	0	0	0
Drug Reaction	5.5	11.25	12	24	10	16.6	12.1
Malignancy	5.5	8.75	2.67	4	6.66	3.3	1.5
Mycosis fungoides	0	0	0	0	0	0	1.5
Idiopathic	14.6	7.5	21.33	08	16.6	16.6	1.5

**TABLE 5:** Comparison of different etiology of erythroderma in various studies

