

Clinicopathological Correlation of Erythroderma Cases - A Study of 60 Cases.

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ABSTRACT

Background: Erythroderma or exfoliative dermatitis is an inflammatory disorder characterized by erythema and scaling in the body involving more than 90% of the body surface. Underlying etiologies which lead to erythroderma are commonly psoriasis (23%), spongiotic dermatitis (16%), drug hypersensitivity reactions (15%) and cutaneous T cell lymphoma (16%). **Aims:** The aim of our study was to find out the histopathologically erythroderma cases and to evaluate the clinicopathological correlation of such cases. **Methods:** Skin biopsies of 60 erythroderma cases were received in the department of Pathology. The samples were processed, stained and examined under light microscope. **Results:** Erythroderma was more common in males (60%) with male to female ratio 1.5:1. Mean age of incidence was 43.3 years. Majority of the cases were acute in onset (51.67%) with shortest duration of 5 days. Pre-existing dermatoses was responsible in 68.33% cases with maximum cases being psoriasis in 33.33% and eczema in 31.67%. Drug induced erythroderma was seen in 16.67% cases. Winter was the aggravating season in 48.14% patients especially in psoriasis. Systemic features such as fever, tachycardia, etc were reported in 76.67% cases. Scales were seen in 83.33% cases and nail changes in 68.33%. Out of 60 cases, 49 cases (81.67%) had positive clinicopathological correlation with best correlation seen in psoriatic erythroderma. P value is <0.001 with strong clinical significance. **Conclusion:** Erythroderma has many overlapping features which made the identification of underlying disease quiet challenging sometimes. Therefore thorough clinical examination and patients' detailed history along with microscopic findings is essential to rule out all the differential diagnosis.

Keywords: Erythroderma, psoriasis, eczema, drugs, DRESS (Drug Reaction with Eosinophilia and Systemic Symptoms).

INTRODUCTION

Erythroderma is an inflammatory disorder characterized by pruritis, erythema and scaling in the body involving more than 90% of the body surface Hebra in 1868.^[1]

The mean age at diagnosis was 48.6 years with more male preponderance in a study conducted in Pakistan.^[2] Same was the case in India with men outnumbering women with 1.85:1 ratio and 46.2 years being the mean age at diagnosis in a study conducted.^[3] Erythroderma affects all kinds of people irrespective of their races.^[4]

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Underlying etiologies which lead to erythroderma are psoriasis (23%), spongiotic dermatitis (16%),

drug hypersensitivity reactions (15%) and cutaneous T cell lymphoma (16%).^[5-8] It is a potentially life threatening disease and can be even fatal in properly managed cases because of its metabolic burden and complications. Therefore a detailed outline of patient's history is essential to rule out any possible triggering events.^[9]

Clinically the onset is acute in 69% patients and present with intense itching, chills and photosensitivity. The salient cutaneous signs include nail changes (80%), mucosal involvement (36.6%), and alopecia (30%).^[1]

Diseases linked with erythroderma are:-

Dermatoses:

- Spongiotic dermatitis- atopic, seborrheic, contact and stasis dermatitis.
- Bullous- pemphigus foliaceus, paraneoplastic pemphigus, bullous pemphigoid and Hailey-Hailey
- Papulosquamous- psoriasis, generalized pustular psoriasis, pityriasis rubra pilaris and impetigo herpetiformis

- Photosensitive- chronic actinic dermatitis and actinic reticuloid
- Adverse drug- acute generalized exanthematous pustulosis and toxic epidermal necrolysis
- Others- pseudolymphoma, erythema gyratum repens, perforating folliculitis, radiation recall dermatitis and senile erythroderma with hyper-IgE

Systemic:

- Dermatomyositis
- Subacute cutaneous lupus
- Acute graft-versus host disease
- Post-operative transfusion induced
- Thyrotoxicosis
- Sarcoidosis
- Hypercalcitonemia
- Idiopathic hypereosinophilic syndrome
- Monoclonal gammopathy of undetermined significance
- Hemophagocytic histiocytosis, viral associated

Infections:

- Bacterial- tuberculosis and congenital syphilis
- Viral- hepatitis C, HIV and HHV 6
- Fungal- dermatophyte, histoplasmosis and congenital cutaneous candidiasis
- Parasite- Norwegian scabies, toxoplasmosis and leishmaniasis
- Toxin- mediated infections- Staphylococcal scalded-skin syndrome and toxic shock syndrome

Malignancy:

- Solid tumours
- Lymphoproliferative- cutaneous T-cell lymphoma, Sezary syndrome, any type of leukemia or lymphoma, hypereosinophilic syndrome, mastocytosis, histiocytosis, Rosai-Dorfmann syndrome, etc

Congenital:

- Immunodeficiency, metabolic, Ichthyosis, etc.^[6]

Drugs causing exfoliative dermatitis:

- Antibiotics- cefoxitin, isoniazid, penicillin, streptomycin, sulfonamides, vancomycin, etc
- Antivirals- interferon α , indinavir, zidovudine, etc
- Antilepromatous- dapsone and clofazimine
- Antifungals- nystatin, terbinafine, etc
- Antiepileptics- carbamazepine, phenytoin, phenobarbital, etc
- Anti-inflammatory- aspirin, nystatin, piroxicam, celecoxib, etc
- Cardiac drugs- quinidine, captopril, diltiazem, nifedipine etc
- Chemotherapy- cisplatin, imatinib, vinca alkaloids, doxorubicin, etc
- Diabetic- sulfonylureas and chlorpropamide
- Psychiatric- barbiturates, phenothiazine, imipramine, etc

- Other- antimalarials, allopurinol, gold, BCG immunization, homeopathic medicines, codeine, arsenicals, furosemide, etc.^[6]

Aim of study

- To evaluate out the histopathological findings in skin biopsy samples of 60 erythroderma cases.
- To find out the clinicopathological correlation of erythroderma cases.

MATERIALS AND METHODS

The present study comprised of 60 cases of erythroderma biopsy of which were received in the department of Pathology, Government Medical College, Patiala.

In every case, a detailed clinical history was taken. Complete physical and systemic examination was done to search for any associated disease. The tissues are processed for paraffin sections and stained with hematoxylin and eosin. Special stains, whenever needed were done.

RESULTS**Age distribution:**

About half of the cases (53.33%) were above 40 years of age. Maximum incidence was observed in 6th decade (33.33%). Mean age of incidence was 43.3 years.

Sex distribution:

60% males and 40% females and male to female ratio was 1.5:1. See [Table 1]

Residence and sex distribution:

61.67% patients reported from rural areas with 70.27% males and 29.73% females. Whereas, 38.33% people reported from urban areas where 43.48% were males and 56.52% were females. See [Table 2]

Total duration of erythroderma:

Thirty one cases (51.67%) were acute in onset with 23 cases (38.33%) reported within 1 month of duration. Duration was usually shorter in drug induced erythroderma cases. Shortest duration was of 5 days and longest duration was of 10 years.

Etiological factors:

Pre-existing dermatoses were responsible for exfoliation in 68.33% cases- eczema in 31.67%, psoriasis in 33.33% and pityriasis rubra pilaris and ichthyosis vulgaris in 1.67% cases each. Drug induced erythroderma were reported in 16.67% cases. In 15% cases cause could not be determined even after extensive investigations. See pie [Chart 1]

Causes of erythroderma and sex distribution:

Pre-existing dermatoses were responsible for exfoliation in 68.33% cases (eczema in 31.67%, psoriasis in 33.33% and pityriasis rubra pilaris and ichthyosis vulgaris in 1.67% cases each). Drug induced erythroderma were reported in 16.67% cases.

Drugs implicated in drug induced erythroderma:

Majority of patients had oral carbamazepine as most common drug with 36.36% cases. An HIV positive patient developed Stevens Johnson syndrome after taking ceftriaxone. A known case of chronic myeloid leukemia developed erythroderma after taking imatinib. Another patient developed DRESS with erythroderma after taking ceftriaxone and sulfasalazine.

Contact history and history of allergy/ asthma in erythroderma:

Contact history with lead paints had highest prevalence (44.44%) followed by cement exposure (22.22%). 52.94% patients had either history of allergy or asthma along with atopic dermatitis that eventually developed exfoliative dermatitis.

Seasonal changes:

Winter presented as the aggravating reason in 48.14% patients especially in most of the cases associated with psoriasis. Spring season influenced in 25.93% cases predominantly in atopic dermatitis associated erythroderma.

Clinical features:

Fever, chills and tachycardia were seen in 76.67% cases with 19 patients of psoriasis, 10 of eczema, 9 of drug reactions and 10 of undetermined causes.

Scales were present in 83.33% cases which included 100% scales in psoriatic erythroderma. Mucosal changes were evident in 25% cases.

Nail changes which included ridging of nails, beau's lines, dystrophy and discoloration were observed in 68.33% cases. All the patients of psoriasis presented with nail changes.

Hair loss/ alopecia were observed in 13.33% patients.

Lymphadenopathy was seen in 50% cases.

Discharge was present in 45% cases.

Clinicopathological correlation:

Out of 60 cases, 49 cases (81.67%) had positive Clinicopathological correlation. Best Clinicopathological correlation was established with psoriatic erythroderma. The typical picture of psoriasis along with relevant history provided ample amount of help to the clinician to diagnose such cases easily. P value was 0.000 (<0.001) i.e. strong clinical significance when all the 4 main types of erythroderma were considered. See bar [Chart 1-4].

Table 1: Age and Sex Distribution.

Age group in years	Males	Females	Total	Incidence (%)
0-10	-	1	1	1.67%
11-20	3	-	3	5.0%
21-30	2	4	6	10.0%
31-40	8	10	18	30.0%
41-50	15	5	20	33.33%
>50	8	4	12	20.0%
Total	36	24	60	100.0%

Table 2: Residence and Sex Distribution.

Residence	Males	Females	Total	Percentage (%)
Rural	26	11	37	61.67%
Urban	10	13	23	38.33%
Total	36	24	60	100.0%

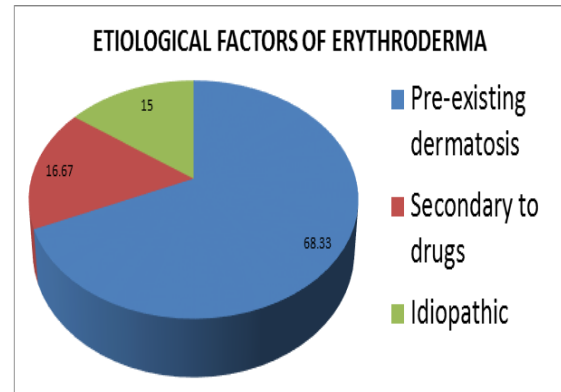


Figure 1: Etiological factors of Erythroderma.

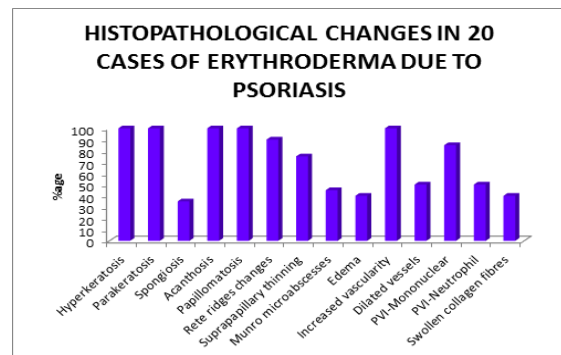


Figure 2: Histopathological changes due to psoriasis.

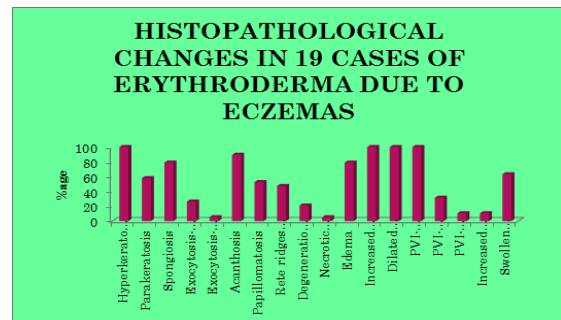


Figure 3: Histopathological changes due to Eczema.

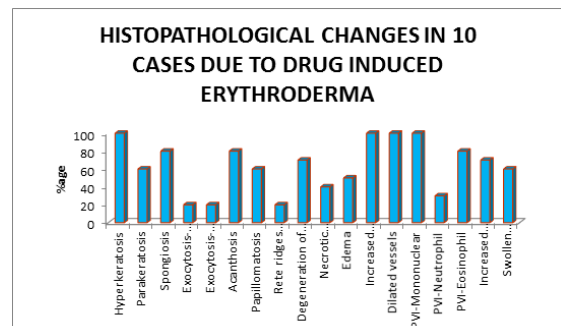


Figure 4: Histopathological changes due to drug induced Erythroderma.

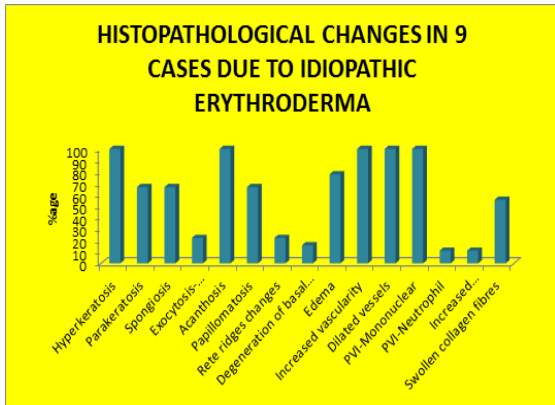


Figure 5: Histopathological changes due to Idiopathic Erythroderma.

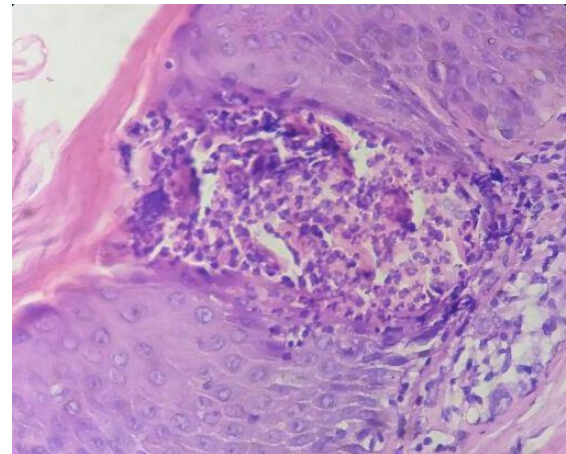


Figure 3: Microphotograph of Munro microabscess. It is a subcorneal pustule with neutrophilic collections, usually seen in psoriasis as shown with the red arrow. (H&E 400X).



Figure 1: Patient of psoriatic erythroderma presenting with generalized erythema, silvery scales and exudates. Nail discoloration and pitting is evident here.

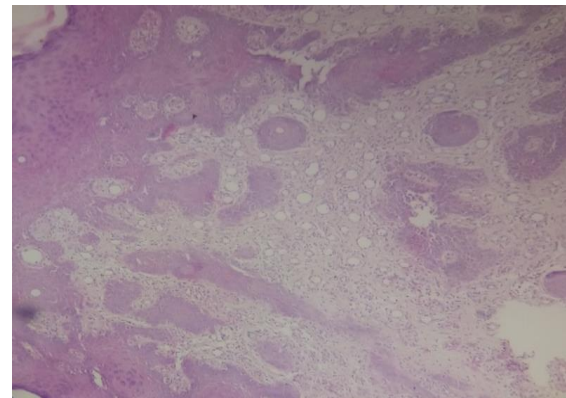


Figure 4: Microphotograph shows histopathological features of eczema induced erythroderma. Epidermis shows irregular papillomatous acanthosis. Underneath dermis is loose showing increased dilated capillaries and intense mononuclear inflammatory cells. (H&E 100X).

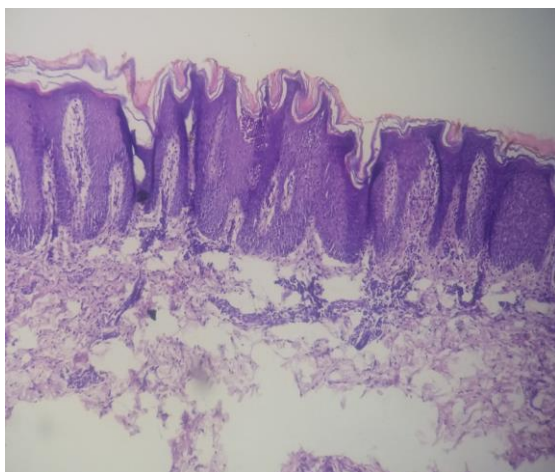


Figure 2: Microphotograph of skin biopsy with features of pustular psoriatic erythroderma. Epidermis show hyperkeratosis, spongiosis, regular acanthosis with broad rete ridges and intraepidermal munro microabscesses. Also seen exocytosis of polymorphs and lymphocytes. Underneath dermis show dense inflammatory infiltrates. (H&E 40X).

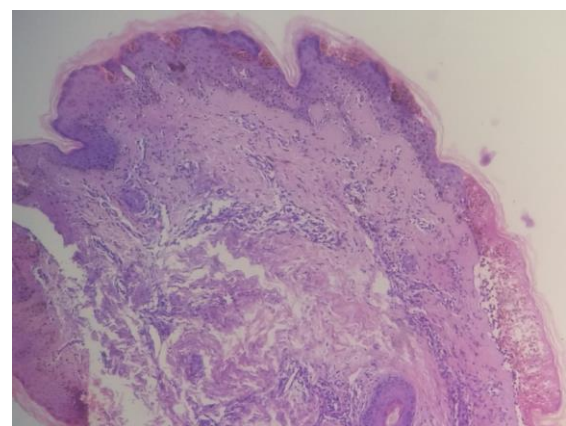


Figure 5: Microphotograph of skin biopsy with features of Stevens Johnson Syndrome. Epidermis show focal hyperkeratosis, mild acanthosis and spongiosis, subepidermal separation with eosinophilic necrosis and focal basal degeneration. Dermis shows mild edema and perivascular dense inflammatory infiltrates of eosinophils and mononuclear cells. (H&E 100X).

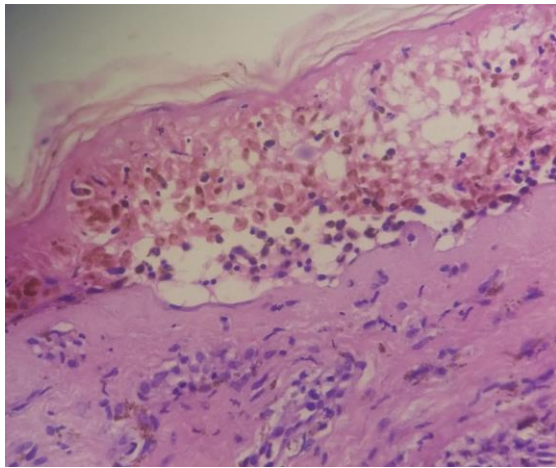


Figure 6: Microphotograph shows subepidermal separation with eosinophilic necrosis as indicated with red arrow. There is seen extravasation of RBCs within the blister. (H&E 400X).

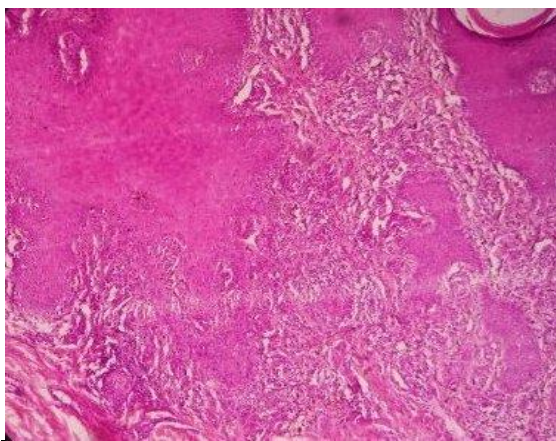


Figure 7: Microphotograph shows imatinib induced drug reaction in a known case of chronic myeloid leukemia. The dermis shows dense inflammatory infiltrate of mononuclear cells and increased melanophages along with basal layer degeneration at many places. (H&E100X).

DISCUSSION

This work has been undertaken to study the clinical and histopathological aspects in 60 cases of erythroderma seen, examined and treated in the department of Dermatology and Venereology. The patients were then diagnosed clinically and diagnosis was confirmed histopathologically in the department of Pathology. The results of the study were compiled, evaluated, analysed and compared with those reported in the literature.

Table 3: Comparing the Mean Age of Disease Onset.

Author and year of study	Mean age of disease onset
Jowkar F et al (2006) ^[2]	48.6 years
Torres-Camacho et al (2009) ^[10]	44 years
Khaled et al (2010) ^[11]	55.13 years
Hulmani M et al (2014) ^[12]	52.3 years
Cesar A et al (2016) ^[13]	54.4 years
Present study	43.3 years

Erythroderma is evident in more than 40 years of age patients. In the present study, the mean age of incidence was 43.3 years which is comparable with the others.

Table 4: Comparing Male: Female Ratio.

Author and year of study	Male: female ratio
Akhyani et al (2005) ^[3]	1.85:1
Jowkar F et al (2006) ^[2]	1.9:1
Kalsy J et al (2013) ^[14]	2.5:1
Choon SE et al (2014) ^[15]	2:1
Cesar A et al (2016) ^[13]	1.5:1
Present study	1.5:1

In all the previous studies men had outnumbered women. In the present series, the male: female ratio was 1.5:1 (36 males and 24 females). The general preponderance of males over females could be explained by the fact that

- Men are the main bread earners of the family and report early to treatment.
- Also most of the patients in this study out of 60 cases 37 patients were residing in rural areas (61.67%) so they take treatment from quacks which prove harmful.
- Men are also more exposed to environmental pollution, industrial hazards, worldly tensions and anxieties.

Table 5: Comparing Causes of Erythroderma.

Author and year of study	Pre-existing dermatoses (%)	Drug induced (%)	Malignancies (%)	Idiopathic (%)	Total patients
Pal et al (1998) ^[1]	74.4%	5.5%	5.5%	14.6%	90
Akhyani et al (2005) ^[3]	57.9%	21.6%	10.3%	7.2%	97
Khaleed et al (2010) ^[11]	43.9%	21.9%	4.87%	25.6%	82
Hulmani M et al (2014) ^[12]	63.5%	16.6%	3.3%	16.6%	30
Cesar A et al (2016) ^[13]	65%	18.4%	11.7%	3.9%	103
Present study	68.33%	16.67%	0%	15.0%	60

Pre-existing dermatoses contributed to predominant predisposing factor for erythroderma in all the studies. Usually in every study, psoriasis was the major dermatoses that had maximum cases. In the present study, psoriatic erythroderma constituted 20 cases out of 41 cases of pre-existing dermatoses. In

Indian subcontinent increased incidence of psoriasis may be related to the genetic make-up and frequent inter-regional marriages. In drug induced erythroderma oral carbamazepine was the most common drug followed by oral ceftriaxone. In 1 case the patient was HIV positive and he developed Stevens Johnson Syndrome after taking oral ceftriaxone.

Table 6: Comparing Clinico-Pathological Correlation.

Author and year of study	Positive clinico-pathological correlation
Jowkar F et al (2006) ^[2]	66.4%
Khaled et al (2010) ^[10]	77%
Hulmani M et al (2014) ^[11]	73.3%
Present study	81.67%

Skin biopsy proved in most of the studies an important diagnostic approach in investigating erythroderma cases. In this present study clinicopathological correlation has been established in maximum cases as compared to the previous studies because:-

- All the cases were biopsied within the next of hospital admission.
- Before performing the biopsy no treatment was given to the patient so that typical histopathological picture is altered.
- New lesions were always preferred in choosing the biopsy site.
- Detailed history and physical examination helped the pathologist to rule out the various differential diagnoses in every case.
- Patients' were convinced enough to give correct relevant history that turned out to be beneficial for the pathologist.

The best Clinicopathological correlation was established with psoriasis in this present study.

CONCLUSION

Erythroderma has many overlapping features which makes the identification of underlying disease quiet challenging at times. Therefore thorough clinical examination and patients' detailed history along with microscopic findings is essential to rule out all the differential diagnosis.

In this study, rural and urban areas were separately analysed in which rural areas had more male preponderance whereas in urban areas females were more affected. This has provided an information regarding sex ratio distribution which shows increased incidence of erythroderma in urban females whereas overall males dominate the ratio.

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