

Clinico-etiological and histopathological correlation in erythroderma: In a tertiary care hospital of Eastern Odisha



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ABSTRACT

Background: Erythroderma, or “exfoliative dermatitis,” is a generalized inflammatory disorder of the skin manifesting with erythema and scaling affecting more than 90% of the skin surface. Primary erythroderma develops in normal skin, and etiological factors include drug reaction, lymphomas, and hematological malignancies, which may be idiopathic. **Aims and Objectives:** The present study is to evaluate the clinico-etiological and histopathological correlations in erythroderma. **Materials and Methods:** This prospective observational study was done in the Department of Dermatology, S.C.B. Medical College, Cuttack, from 2021 to 2022. Erythema and scaling involving more than 90% of the body surface area were calculated by Wallace’s rule of nine. A detailed demographic profile and history were recorded with a thorough clinical examination for each patient, involving type of scales, sizes of scales, color of scales, associated lichenification or fissuring, pedal edema, examination of the scalp for scales, hair loss, examination of the nails and mucosa, and associated arthritis. **Results:** The most common disease was psoriasis (16), Idiopathic (7), followed by atopic and drug-induced dermatitis 6 patients each. Seborrheic dermatitis showed 3 cases, followed by contact dermatitis, Reiter’s disease, Pemphigus foliaceus, Ichthyosis (congenital), Dermatomyositis, and malignancy-induced 2 cases each, whereas contact dermatitis and Dermatophyte infection were found to be one patient each. **Conclusion:** Though some of the etiology remains unknown, repeated investigations and continued follow-up are necessary to determine long-term complications. The role of alternative medicines and the injudicious use of steroids by quacks or untrained practitioners should be discouraged, and proper awareness should be given to patients with erythroderma.

Key words: Exfoliative dermatitis; Lichenification; Psoriasis and Reiter’s disease

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INTRODUCTION

Erythroderma, also known as “exfoliative dermatitis,” is a generalized inflammatory skin manifestation with erythema and scaling affecting more than 90% of the skin surface of the human body.¹ Primary erythroderma develops in normal skin, and etiological factors are drug reactions, lymphomas, and hematological malignancies, which may be idiopathic (25%).² While secondary erythroderma arises from pre-existing dermatoses such as eczema, psoriasis, pityriasis rubra pilaris (PRP), and

lichen planus.³ Erythroderma is a morphological reaction pattern of skin with a number of underlying causes, which include pre-existing dermatological disorders like psoriasis, contact dermatitis, atopic dermatitis, and systemic skin manifestations including drug reactions and malignancy. Even a thorough clinical examination and investigations may not detect the underlying causes many times.⁴ The disease is usually associated with underlying cutaneous, systemic disorder, or drug intake, and rarely, it may be idiopathic. Erythroderma affects the skin as well as other systems of the body, giving rise to hemodynamic

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disturbances, biochemical derangement, fever, tachycardia, hypoalbuminemia, and pedal edema, in addition to various cutaneous changes.⁵

Treatment addresses the underlying etiology, symptomatic relief, and potential systemic complications.⁶ Though it is a rare disease, the mortality rates are low, and morbidity related to it is considerably high, as it is often a chronic disease with debilitating signs and symptoms such as intense pruritis and scaling. Thus, it is important to find the etiology with a special emphasis on histopathology, allowing early and appropriate intervention for each case.⁷

As most of the earlier studies were from Western countries and other parts of India, the present study of 58 cases of erythroderma was carried out to study the etiology, clinical features, course, evolution, associated systemic derangement, and histopathological correlation in this region.

Aims and objectives

The aim of the study is to determine the clinico-etiological and histopathological correlation in erythroderma.

MATERIALS AND METHODS

Subjects

It was a prospective observational study conducted among individuals attending the outpatient department (OPD) and inpatient department of the Department of Dermatology, S.C.B. Medical College, during the period March 2021 to September 2022.

Inclusion criteria

All new cases of erythroderma of both sexes and of all age groups who attended the OPD of the Department of Dermatology were included for this study.

Exclusion criteria

Patients not willing for investigation and follow up were excluded from the study.

Study design

The erythroderma cases were clinically evaluated with a detailed history and a complete physical examination.

Erythema and scaling involving more than 90% of the body surface area were calculated by Wallace's rule of nine. A detailed demographic profile and history were recorded with a thorough clinical examination for each patient, involving type of scales, sizes of scales, color of scales, associated lichenification or fissuring, pedal edema, examination of the scalp for scales, hair loss, examination of the nails and mucosa, and associated arthritis.

Peripheral blood was analyzed for hemoglobin percentage, total and differential leucocyte count, erythrocyte sedimentation rate (ESR), peripheral smear study, and platelet count.

Biochemical tests were done for blood sugar, blood urea, serum creatinine, serum electrolyte, serum calcium and uric acid, and total proteins with an albumin-globulin ratio.

Ethical approval

The present study was approved by the Ethics Committee of the S.C.B. Medical College Cuttack vide IEC No. 861 dated June 11, 2021, as per the principles of the Helsinki Declaration.

Statistical analysis

All the findings were recorded, evaluated, and compared with other studies. Statistical analysis will be done using the Statistical Package for the Social Sciences (SPSS) (version 24; SPSS Inc., Chicago, IL, USA). The results were calculated for mean (standard deviation), frequency, and proportion. The $P < 0.05$ level was chosen as a level of significance in all statistical tests in the study.

RESULTS

Erythroderma was diagnosed in 58 patients within 1½ years in the present study. The incidence of erythroderma during the period was 0.033% among 58 out of 173,523 patients attending the Dermatology OPD.

The age of the patients ranged from 1 year to 78 years, with an average age of 49.12 years. The maximum number of patients belonged to the age group of 60–69 years. Among 58 patients, 44 were male (75.9%) and 14 were female (24.1%), the male-to-female ratio being 3.1:1, showing a male predominance (Table 1).

The majority 47/58 (81%) of patients had insidious onset of erythroderma, 11/58 (19%) of patients had sudden onset. Scaling and redness were presented in 58 (100%) cases. The most common complaints were recorded as itching in 54 (93.1%), chills 54 (93.1%), malaise 48 (82.7%), and 23 (39.7%) had fever. Only 9 (15.5%) in this study had oliguria. Two patients complained of loose stools suggestive of dermatogenic enteropathy.

The most common aggravating factor was winter season 20 (34.48%), followed by intake of allopathic drugs 10 (17.24%), Ayurvedic medication 9 (15.51%), summer season 8 (13.8%), contact with parthenium, cement, and homeopathic medication 1 (1.7%) each.

Low hemoglobin was seen in 26 patients (44.8%). Leukocytosis was observed in 23 patients (39.7%).

Eosinophilia was found in 22 patients (37.9%). Raised ESR was seen in 31 cases (53.4%). Hypoproteinemia was seen in 36 patients (62.1%). High blood sodium levels were seen in 7 patients (12.1%), low sodium levels in 6 patients (10.3%), and decreased potassium levels in 8 patients (13.8%).

Low albumin was detected in 35 cases (60.3%), low globulin level in 4 patients, and high globulin level in 3 patients. An altered albumin-to-globulin ratio (A: G ration) was observed in 36 patients (62.1%). Four patients (6.9%) had high serum creatinine, and five patients (8.6%) had increased serum bilirubin. Seven patients (12.06%) had altered liver function tests. Out of five patients who were drug-induced, one had dermatomyositis and one had psoriasis.

The most common disease was psoriasis (16), idiopathic (7), followed by atopic and drug-induced dermatitis (6 patients each). Seborrheic dermatitis showed 3 cases, followed by contact dermatitis, Reiter’s disease, Pemphigus foliaceus, ichthyosis (congenital), dermatomyositis and malignancy-induced 2 cases each, whereas contact dermatitis and dermatophyte infection were found to be one patient each (Table 2, Figures 1 and 2).

DISCUSSION

In the present study, the average incidence of erythroderma in patients with skin diseases was 0.033% attending OPD.⁶ The maximum number of patients with erythroderma was

Table 1: Age/sex distribution of erythroderma in the study population

Patient’s age	Number of cases (n=58)	Percentage	Male	Female
1–9	4	6.9	4	00
10–19	1	1.72	1	00
20–29	4	6.9	4	00
30–39	7	12.07	4	3
40–49	9	15.52	7	2
50–59	10	17.24	6	4
60–69	17	29.31	14	3
70–78	6	10.34	4	2
Total	58	100 (%)	44 (75.9%)	14 (24.1%)

Table 2: Comparison of clinical, histopathological and final diagnosis of erythroderma (n=58)

Etiology	Clinical diagnosis	Histopathological diagnosis	Male	Female
Psoriasis	16	Psoriasis	14	17
		Nonspecific	1	
		Spongiotic dermatitis	1	
Seborrheic dermatitis	3	Eczema of various types		
		Psoriasis	1	3
		Spongiotic dermatitis	1	
Contact dermatitis	2	Endogenous dermatitis	1	
		Nonspecific	1	3
Stasis dermatitis	1	Endogenous dermatitis	1	1
Atopic dermatitis	6	Endogenous dermatitis	3	5
		Spongiotic dermatitis	1	
		Nonspecific	2	
Pityriasis rubra pilaris	6	Nonspecific	1	6
		Pityriasis rubra pilaris	5	
Reiter’s disease	2	Nonspecific	1	1
		Reiter’s	1	
Pemphigus foliaceus	2	Pemphigus foliaceus	2	2
Ichthyosis (congenital)	2	Nonspecific	1	1
		Pityriasis rubra pilaris	1	
Dermatophyte infection	1	Nonspecific	1	1
Dermatomyositis	2	Nonspecific	2	1
Drug induced	6	Drug induced	5	6
		Nonspecific	1	
Malignancy induced	2	Endogenous dermatitis	1	1
		Spongiotic dermatitis	1	
Idiopathic	7	Endogenous dermatitis	1	10
		Nonspecific	5	
		Psoriasis	1	
Total	58	58		58



Figure 1: Exfoliative eruptions and stasis dermatitis



Figure 2: Psoriatic erythroderma

seen in the age group 60–69 years (29.31%), followed by 50–59 years (17.24%), and 40–49 years (15.52%). This is in concurrence with other studies, where the maximum incidence was in the 41–61-year-old age group.⁸ The average age of the patient in this study was 49.12 years, which is similar to earlier studies.⁹

This study showed a male predominance with a male-to-female ratio of 3.1:1, which is in agreement with previous studies, i.e., male-to-female ratio ranging from 2:1 to 4:1. The reason for male dominance could be the habit of alcohol intake and predominant outdoor work by male patients, which are known to exacerbate psoriasis and eczemas, respectively.¹⁰

Scaling and erythema were seen in all patients; in most cases, it was erythema that began first, followed by scaling over a period of 4–5 days. In acute cases, scales were large and easily detachable, and in chronic cases, they were smaller. In our study, we did not measure total proteins loss through scaling, Kanthraj *et al.*¹¹ showed that daily protein

loss increased by 25–30% in psoriatic erythroderma and 10–15% in non-psoriatic erythroderma. Previous studies have shown that generalized erythema and scaling are the most common findings, seen in up to 100% of cases.¹²

The symptoms Irrespective of etiology, the clinical features of erythroderma were almost identical. It was difficult to differentiate between various causes of erythroderma once the erythroderma diagnosis was established. The commonest symptoms were generalized scaling 58 (100%), redness 58 (100%), chills 54 (93.1%), malaise 48 (82.7%), and itching 54 (93.1%). Fever was present in 23 (39.7%) cases, and 9 (15.5%) had oliguria. Two patients had dermatogenic enteropathy. These findings were similar to previous studies.¹³

Allopathic drugs were the most common offending factor in 10 (17.24%) of cases, while 9 (15.51%) were ayurvedic drugs and homeopathic medications. 1 (1.7%) induced erythroderma in the study population. The drugs implicated were diclofenac, phenytoin, dapsone, sulfasalazine, amoxicillin, and prednisolone. In three cases, the intake of steroids in patients with psoriasis aggravated the condition.¹³

Treatment with ayurvedic medications aggravated the condition in 9 (15.51%) of patients, out of which 6 had psoriasis, one each of atopic dermatitis, PRP, and stasis dermatitis. Injudicious use and irritation leading to koebnerization, would have aggravated psoriasis, leading to erythroderma in these patients. Homeopathic medication was implicated as a factor in one patient. An allergic contact dermatitis to parthenium in one patient and to cement in another patient was seen. These findings were in concurrence with studies conducted by Hulmani *et al.*¹⁴

The most common aggravating factor was winter season 20 (34.48%). Out of the 20 patients who had winter aggravation of the condition, 10 were of psoriasis, 3 of each were of atopic dermatitis and PRP, 2 were of seborrheic dermatitis, and one patient was each of idiopathic and Reiter's disease. Summer aggravation was seen in 8 (13.8%) of patients (Table 3).¹⁵

Hemoglobin was low in 26 (44.8%) of cases, which is in agreement with the study by Bandyopadhyay *et al.*,¹⁶ (48% cases), and leukocytosis was observed in 39.7% of cases, which was consistent with previous studies.^{13,17}

Eosinophilia was seen in 22 (37.9%) cases, followed by increased ESR in 53.4% of cases, which is in concurrence with previous studies.¹⁸ High blood sugar was observed in 16 patients, of whom 13 were known diabetic patients on treatment.¹⁸

Table 3: Frequency of symptoms and aggravating factors related to erythroderma in the study population

Symptoms	No. of cases n = 58	Percentage
Itching	54	93.1
Scaling	58	100
Redness	58	100
Fever	23	39.7
Chills	54	93.1
Malaise	48	82.7
Oliguria	9	15.5
Joint pain	10	17.2
Weakness	53	91.4
Diarrhoea	2	3.4
Weight loss	5	8.6
Aggravating factors	No. of cases	Percentage
Ayurvedic medication	9	15.51
Drugs	10	17.24
Homeopathic medication	1	1.7
Cement	1	1.7
Summer	8	13.8
Winter	20	34.48
Parthenium	1	1.7

Hypoproteinemia with an altered albumin-to-globulin ratio was demonstrated in 36 (62.1%) of cases in this study, which was in concurrence with the earlier studies.¹⁹ Hypoproteinemia could be due to protein loss through scaling, chronic malnutrition, or dilution due to hypervolemia.¹⁹

Elevated levels of blood urea and serum creatinine were seen in 4 (6.9%) of patients who were also known diabetics; preexisting diabetes could be the cause of this finding. There were elevated lactate dehydrogenase (LDH), serum glutamic oxaloacetic transaminase, serum glutamate pyruvate transaminase, and serum bilirubin suggestive of hepatic impairment (Table 4).²⁰

Clinical diagnosis of psoriasis was found in 16 patients, of which histopathological correlation was found in 14 patients. In one patient, features were suggestive of nonspecific findings and in another patient, it was suggestive of spongiotic dermatitis.²¹

Seborrheic dermatitis was clinically diagnosed in 3 patients, of which histopathologically, psoriasis, spongiotic dermatitis, endogenous dermatitis, and non-specific were diagnosed in one patient each. A clinical diagnosis of atopic dermatitis was made in 6 patients, out of which a histopathological correlation was made in 5 patients, and one was reported as non-specific. PRP was observed in 6 patients, out of which a histopathological correlation of PRP was made in 5 patients; one was reported as non-specific. Two patients were found to have Reiter's disease clinically, but one patient was histopathologically correlated,

Table 4: Laboratory parameter in the study population

Variable	Frequency	Percentage
Anaemia	26	44.8
Leukocytosis	23	39.7
Neutrophilia	20	34.5
Lymphocytosis	2	3.4
Eosinophilia	22	37.9
High ESR	31	53.4
Low S. Protein	36	62.1
High sodium	07	12.1
Low S. Potassium	8	13.8
Variable	Outcome	Frequency (%)
S. Albumin	Low	35 (60.3)
S. Globulin	Low	4 (6.9)
	High	3 (5.2)
A: G ratio	Low	36 (62.1)
Blood urea	High	4 (6.9)
S. Creatinine	High	4 (6.9)
S. Bilirubin	High	5 (8.6)
SGOT	High	7 (12.06)
SGPT	High	7 (12.06)

S.: Serum, ESR: Erythrocyte sedimentation rate, SGOT: Serum glutamic oxaloacetic transaminase, SGPT: Serum glutamate pyruvate transaminase

and another patient, not correlated, was finally considered as idiopathic.²²

Likewise, clinically, one patient with dermatophyte infection did not correlate with histopathological findings, but in the final diagnosis, it was considered a dermatophyte infection as per history, evolution of the disease, and the presence of characteristic lesions all over the body. Two patients were diagnosed as cases of dermatomyositis clinically; none of them correlated histopathologically. Finally, one patient was considered a case of dermatomyositis on the basis of history, evolution of the disease, examination findings, and lab investigations like high LDH, high alanine aminotransferase/aspartate transaminase level, and significant specific investigations. Another patient was considered Idiopathic. Two patients with pemphigus foliaceus and one with stasis dermatitis correlated both clinically and histopathologically.²³

The second group, which consisted of drug-induced erythroderma, had 6 (10.35%) patients. Clinically, drug-induced erythroderma was found in six patients, of whom histopathological correlation was given in five patients and one as non-specific. But as that patient had a seizure disorder for which he was taking phenytoin, it was finally considered as a case of drug-induced erythroderma. Hence, in the final diagnosis, six patients were referred to as having drug-induced erythroderma.²⁴

The third group consisted of malignancy-associated erythroderma (1 patient, 1.72%). In the case of malignancy-

induced erythroderma, histopathological findings were one with endogenous dermatitis and one with spongiotic dermatitis.

The last group was idiopathic, which comprised 10 (17.24%) patients with no specific history, associated factor, or specific histology. In 7 patients, clinically, we could not attribute any etiology; out of these 7 cases, a histopathological impression of endogenous dermatitis was given in one and psoriasis was found in one patient. But in five patients, it was a nonspecific finding, considering them to have idiopathic erythroderma. Hence, in the total final diagnosis, 10 cases were diagnosed with idiopathic erythroderma (Table 2).²⁵

Limitations of the study

Diagnosis of Erythroderma is quite difficult. It requires multiple skin biopsies for confirmation, which is the major limitation of the present study. Others include the social taboos for late reporting of cases.

CONCLUSION

Erythroderma, although a very disturbing disorder, does not pose a significant risk to the patient's life. Morbidity, not mortality, is the matter of concern in erythroderma. Even though in some cases the etiology remains unknown, continued follow-up and repeated investigations are necessary for these patients, and also to know the long-term complications of the disease and rule out malignancy.

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Author's Contributions:

DKS- Definition of intellectual contents, literature survey, implementation of study protocol, data collection and data analysis; **PCS-** Prepared first draft of Manuscript and submission of manuscript, concept design, clinical protocol, manuscript revision; **JM-** Design of study, statistical analysis and interpretation, Review of manuscript and preparation of figures; **DNM-** Final revision of manuscript coordination and manuscript Submission.

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