ABSTRACT: BACKGROUND: Erythroderma, characterized by generalized erythema and scaling involving more than 90% of the body surface area, poses a significant risk of morbidity and mortality. Thorough clinical and laboratory investigations may not detect the underlying causes many a times. Herein lays the importance of histopathology. OBJECTIVES: a) To study the aetiology of erythroderma b) To evaluate the clinicopathological profile of erythroderma. METHODOLOGY: during a 1 year study period from June 2013 to May 2014, 52 patients with erythroderma were evaluated to study the aetiology and demographic profile in Silchar Medical College and Hospital. RESULTS: The male female ratio was 4.2:1. The largest number of cases was found in the 6th decade of life. Preexisting dermatoses comprised of 57.69% cases, drugs comprised of 13.46% cases, malignancy was found to be the cause in 1.92% cases, while 26.92% cases were idiopathic. Psoriasis amongst the preexisting dermatoses, was the most common cause (25%). CONCLUSION: All 52 cases were subjected to histopathology. Histopathology helped in correlating & confirming the aetiology of erythroderma in 38 cases (73.07%) and did not help in 14 cases (26.92%). KEYWORDS: Erythroderma, histopathology, preexisting dermatoses.

INTRODUCTION: Erythroderma, first described by Von Hebra in 1868, is an inflammatory condition of the skin characterized by generalized erythema and scaling involving more than 90% of the body surface area.1 Erythroderma is the final common pathway for a number of acute and chronic cutaneous inflammatory diseases.2 The erythrodermic state is of great concern because it poses significant risk of morbidity and mortality, in addition to the risks inherent to the underlying disease and its therapy.3 So early diagnosis and proper management is a challenging task for the clinicians. Here lies the importance of trying to find out the aetiology, with special emphasis on histopathology, allowing early and appropriate intervention in each case.

OBJECTIVES:
1. To study the aetiology of erythroderma.
2. To evaluate the clinicopathological profile of erythroderma.

MATERIALS AND METHODS: The study has been conducted in the department of Dermatology, Silchar Medical College & Hospital, Silchar, Assam over a period of one year extending from 1st June 2013 to 31st May 2014 after approval from the institutional ethical committee and after obtaining informed consent from the patients.

All patients attending the Department of Dermatology, Silchar Medical College & Hospital during the study period with erythema and scaling involving more than 90% of the body surface area irrespective of the age and sex were enrolled. The involvement of the body surface area was calculated by using the ‘Rule of Nine of Wallace’. Detailed history & thorough clinical examination

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followed by laboratory investigations, histopathological examination and some special investigations whenever necessary were done. Repeated biopsies were done in those cases in which despite strong clinical suspicion, clinico histopathological correlation were not found.

RESULTS AND OBSERVATION: During the study period of 1 year, 52 patients of erythroderma were evaluated thoroughly to study the aetiology and the clinicopathological profile of erythroderma.

The total patients attending Dermatology opd during the 1 year period was 24,896.

The incidence of erythroderma was found to be 0.20%. Out of the 52 cases of erythroderma, 42 patients (81%) were male and 10 patients (19%) were female. Male outnumbered female with a ratio of 4.2: 1.

| Age Group in Years | Male | Female | Total | Percentage |
|-------------------|------|--------|-------|------------|
| 0- 10             | 03   | 01     | 04    | 7.69%      |
| 11--20            | 00   | 00     | 00    | 00%        |
| 21--30            | 03   | 01     | 04    | 7.69%      |
| 31--40            | 08   | 01     | 09    | 17.30%     |
| 41--50            | 05   | 00     | 05    | 9.61%      |
| 51--60            | 07   | 05     | 12    | 23.07%     |
| 61--70            | 10   | 01     | 11    | 21.15%     |
| 71-80             | 03   | 00     | 03    | 5.76%      |
| Above 80          | 03   | 01     | 04    | 7.69%      |
| **Total**         | **42** | **10** | **52** | **100%** |

Table 1: Age distribution with sex distribution

From the above table it is observed that the mean age at diagnosis is 50.99±21.61 (S.D) years. The youngest patient was 2 months old, while the oldest patient was 85 years old. The condition was seen in all age group. Peak incidence was found in 6th decade (23.07%).

The maximum number of patients in our study was farmers (23.07%). Manual labourers and housewives were the second most common group (13.46%) each.

In majority of the patients i.e. 46.15% the time interval between disease onset and development of erythroderma was between 1-3 months. In 30.76% of the cases, it took more than 3 months for the development of erythroderma. In the rest of the cases, i.e. 23.07% of them erythroderma developed within 1 month.

Redness and scaling were the most common symptoms, in all the cases (100%). Pruritus was complained in 46 patients (88.46%). Chill and fever were present in 25 cases (48.07%) and 20 cases (38.46%) respectively. Oliguria was present in 8 cases (15.38%) while loose stool suggestive of dermatogenic enteropathy was not observed in any case. Fever was found in 20 cases (38.46%), whereas pedal oedema was seen in 16 cases (30.76%). 15 patients presented with lymphadenopathy (28.84%). 25% of the cases i.e., 13 cases were hypertensive. Hepatomegaly was found in 3 cases (5.76%) whereas no case with splenomegaly was found. Hypothermia with temperature less than 35°C was found in 1 case.

Erythema and scaling were present in all the patients. Nail changes were seen in 26 cases. Ridging of the nails was the most common finding (26.92%). Other nail changes observed are
discolouration (19.23%), pitting (15.38%), subungual hyperkeratosis (15.38%), shiny nails (7.6%), beau’s line (7.6%) and onychodystrophy (7.6%).

Palmoplantar involvement in the form of keratoderma, scaling, hyperkeratosis, erythema & fissuring was seen in 38.46% cases. Lichenification of the involved skin was seen in 15 patients (28.84%). Hair changes in the form of alopecia were seen 25% of the cases.

Mucosal changes were seen in 9 patients (17.30%) mostly in the drug induced erythroderma. The patients had erosions, fissuring and candidiasis.

Deck chair sign was seen in 8 patients (15.38%). Nose sign of erythroderma was seen in 6 patients with erythroderma (11.53%), while ectropion was observed in 7 patients (13.46%).

We recorded the initial site of involvement of the skin prior to becoming generalized and found the following results. In 13 cases (25%), the disease presented in a generalized manner from the very outset. In the rest of the patients, they gave history of the following sites of involvement initially. Head and neck was the initial site in 11 patients (21.15% patients), while there were 9 patients (17.30%) with involvement of trunk as the initial site. The extensor surfaces in 7 cases (13.46%), upper & lower limbs in 6 cases (11.53%), flexures in 5 cases (9.6%) and genitalia in 1 case (1.9%).

| Laboratory Parameters                        | No. of Patients | Percentage |
|---------------------------------------------|-----------------|------------|
| Anaemia                                     | 36              | 69.23%     |
| Increased erythrocyte sedimentation rate (ESR)| 33              | 63.46%     |
| Low serum protein                           | 18              | 34.61%     |
| Leucocytosis                                | 15              | 28.84%     |
| Eosinophilia                                | 12              | 23.07%     |
| Altered albumin: globulin ratio(A:G)        | 12              | 23.07%     |
| Elevated liver enzymes                      | 10              | 19.23%     |
| Lowered sodium                              | 10              | 19.23%     |
| Lowered potassium                           | 07              | 13.46%     |
| Raised serum creatinine                     | 06              | 11.53%     |

Table 2: Laboratory Findings

| Aetiology                                 | Provisional Clinical Diagnosis | Histopathological Diagnosis | Final Aetiology |
|-------------------------------------------|-------------------------------|----------------------------|-----------------|
| Psoriasis                                 | 12                            | Features of Psoriasis 12    | 13              |
| Seborrhoeic dermatitis                    | 08                            | Spongiotic dermatitis with neutrophil parakeratosi                | 03              |
|                                           |                               | Non specific                | 04              |
|                                           |                               | Feature of ichthysiform disease          | 01              |
| Air borne contact dermatitis              | 08                            | Spongiotic dermatitis        | 03              |
|                                           |                               | Non specific                | 05              |
Psoriasis: Clinically psoriatic erythroderma was diagnosed in 12 patients. On histopathology, these 12 patients showed features of psoriasis. 1 patient who was clinically undiagnosed, considered to be idiopathic, was found to have psoriasis on histopathology. Total number of patients with psoriasis on histopathology was thus 13.

Seborrhoeic Dermatitis: Total patients clinically diagnosed to have seborrhoeic dermatitis were 8. Out of the 8 patients, on histopathology, 3 had features of eczema, 4 had nonspecific features and 1 patient had features of ichthyosiform erythroderma. So the final number of patients with seborrhoeic dermatitis was 3.

Air Borne Contact Dermatitis (ABCD): Total number of patients clinically diagnosed as having air borne contact dermatitis was 8.0. On histopathology of these patients, we got features of spongiotic dermatitis (eczema) in 3 patients, whereas in 5 cases, features were nonspecific. Final number of patients with air borne contact dermatitis is 3.

Drug Induced Erythroderma: 7 patients were correlated both clinically and histopathologically as having drug induced erythroderma.

Atopic Dermatitis: We diagnosed atopic dermatitis as the cause of erythroderma in 5 patients. Out of the five, 2 patients showed eczema on histopathology, 3 patients had nonspecific feature. So the final aetiology in 2 patients was atopic dermatitis.
2 cases of pemphigus foliaceus, 2 cases of pityriasis rubra pilaris and 1 case of dermatophyte infection were correlated clinically & histopathologically. Patient with dermatophytosis had positive KOH test.

**Ichthyosiform Disorder:** Clinically we got 3 cases of ichthyosiform diseases. They were correlated histopathologically. However 1 patient who was clinically diagnosed as seborrhoeic dermatitis, was found to have ichthyosiform disease on biopsy. So the total number of patients with ichthyosiform disorder was 4.

**Malignancy Induced Erythroderma:** Though on histopathology, there were no significant findings, however from the clinical examination and lymph node biopsy findings, it was taken as a case of Non-Hodgkin’s lymphoma.

**Idiopathic Erythroderma:** Clinically there were 3 undiagnosed cases. On histopathology of these 3 cases, 2 showed nonspecific features, while 1 showed features of psoriasis.

Total cases with nonspecific features tallied to a total of 14 cases, attributing them to idiopathic erythroderma. [Patient with Non-Hodgkin’s Lymphoma with nonspecific histopathology was confirmed following lymphnode biopsy].

| Aetiology                  | Number of Patients | Percentage |
|----------------------------|--------------------|------------|
| Preexisting dermatoses     | 30                 | 57.69%     |
| Drugs                      | 07                 | 13.46%     |
| Malignancy                 | 01                 | 1.92%      |
| Idiopathic                 | 14                 | 26.92%     |
| **Total**                  | **52**             | **100%**   |

*Table 4: Aetiologies of erythroderma*

| Dermatoses                  | Number of Patients | Percentage |
|-----------------------------|--------------------|------------|
| Psoriasis                   | 13                 | 25%        |
| Ichthyosis                  | 04                 | 7.69%      |
| ABCD                        | 03                 | 5.76%      |
| Seborrhoeic dermatitis      | 03                 | 5.76%      |
| Atopic dermatitis           | 02                 | 3.84%      |
| Pityriasis Rubra Pilaris    | 02                 | 3.84%      |
| Pemphigus foliaceus         | 02                 | 3.84%      |
| Dermatophyte infection      | 01                 | 1.9%       |

*Table 5: Preexisting dermatoses incrimination in erythroderma*

In this study we found 7 cases of drug induced erythroderma. Amongst the drug, there was 1 case related to each phenytoin, carbamazepine, nevirapine, nimesulide and allopurinol (14.28% each). 2 patients (28.57%) gave history of ingestion of ayurvedic painkillers for some other illness prior to the development of erythroderma.
Out of 15 patients with lymphadenopathy, 7 patients refused to give consent for lymph node biopsy. 87.5% of the cases (7 cases) revealed dermatopathic lymphadenopathy, while 12.5% case (1 case) revealed malignancy (NHL).

Hypertension peaked with 13 patients (25%), with evidence of diabetes mellitus in 11 patients (21.15%). There were 6 patients (11.53%) with chronic obstructive diseases (COPD) having history of long term smoking. Benign enlargement of prostate was found in 4 elderly patients (7.69%). Tuberculosis, either pulmonary or abdominal was seen in 4 patients (7.69%). Dyslipidemia was present in 3 cases (5.76%). 1 elderly patient (1.92%) had adenomyomatosis of gall bladder as USG finding.

Out of 52 patients of erythroderma, 38 patients showed consistent clinical and histopathological findings, while in 14 patients clinical and histopathological findings were not consistent. Thus in 73.07% clinical and histopathological findings were correlated.

DISCUSSION: The mean age at the time of diagnosis was 50.99±21.61 in this study. Choudhary A, Gupte PD⁴ and Mapar MA et al.,⁵ in their studies found the mean age to be 51.5 and 49.1 respectively. In this study the youngest patient was 2 months old and the oldest patient was 85 years of age. Similar age range was found by Yuan XY et al.,⁶ in their study, from the youngest of 1 month old to the oldest being 82 years of age. The male female ratio of 4.2:1 correlated with that found by Botella Estradas et al⁷ (4:1). In this study, scaling was found in 100% of the cases, which is similar to the observation made by Chaudhary and Gupte,⁴ Bharatia PR and Joshi,⁸ Akhyani M et al.,⁹ and Sudho R et al.,¹⁰ in their respective studies. Erythema was found in 100% cases in the present study which is similar to the observation made by Hulmani et al.,¹¹ Jowkar F et al.,¹² and Akhyani M et al.,⁹ in their respective studies. In our study, itching was observed in 88.46% cases. Pal S and Haroon TS¹³ reported pruritus in 86% of the cases.

The present study had 20 patients presenting with fever (38.46%). Chaudhary and Gupte⁴ reported fever in 32% of the patients at the time of admission. 15.38% of the patients had oliguria in our study. This finding is similar to the observation made by Nazeer M et al.,² who reported oliguria in 16.7% cases. In this study, lymphadenopathy was found in 15 cases (28.84%). This is similar to the observation made by Sudho R et al.,¹⁰ who found lymphadenopathy in 32% of the erythrodermic patients. Bandopadhyay et al.,¹⁴ reported lymphadenopathy in 22.67% of the cases. In this study we found generalized lymphadenopathy in 4 cases. In rest of the cases, the most commonly involved group was the inguinal group. Hepatomegaly was found in 3 cases (5.76%). This is similar to the observation made by Haeez J et al.,¹⁵ in their study who reported 4% cases of hepatomegaly. Nail changes in this study was present in 50% of the cases. Bharatia PR and Joshi¹⁸ in one study, found nail changes in 54.35% cases, in the form of discolouration, pitting, horizontal ridges and dystrophy.

In a study conducted by Sudho R et al.,¹⁰ alopecia was present in 24% of the cases, while Pal S and Haroon TS¹³ noted alopecia in 30% of the cases. In this study, hair changes in the form of alopecia were seen in 25% of the cases. This finding correlated with the findings of the above mentioned studies.

Palmoplantar involvement was seen in 38.46% of the cases in the present study. King LE et al.,¹⁶ reported palmoplantar keratoderma in 37% of the cases. Mucosal changes in the form of congestion of conjunctiva, congestion and erosion of the oral mucosa and genital mucosa was seen in 17.30% of the cases. These changes were mostly seen in the drug induced erythroderma cases. In a study conducted by Pal S and Haroon TS,¹³ mucosal involvement was seen in 36.6% cases.
Among the laboratory data, anaemia was present in 36 patients (69.23%). Sehgal and Srivastava\(^\text{17}\) in their study of erythroderma of 80 patients, reported anaemia in 70% of their patients, while Pal S and Haroon TS\(^\text{13}\) reported anaemia in 72% of the patients. In this present study, raised ESR was present in 33 patients (63.46%). Hulmani et al.,\(^\text{11}\) in their study observed raised ESR in 53.3% cases. Hypoproteinemia was seen in 34.61% cases with altered albumin: globulin ratio in 23.07% cases. In a study conducted by Rafael and colleagues\(^\text{18}\) 34% of the patients had hypoproteinemia. Leucocytosis was seen in 28.84% cases in the present study. In a study conducted by Islam S et al.,\(^\text{19}\) 26% of the patients presented with leucocytosis. Serum electrolyte imbalance in the form of low serum sodium in 10 patients (19.23%) and low potassium in 7 patients (13.46%) was observed. Islam S et al.,\(^\text{19}\) conducted a study on biochemical changes in exfoliative dermatitis. Hyponatremia and hypokalemia were observed in 18% and 12% respectively in the study.

| Authors                  | Total cases | Preexisting dermatoses (%) | Drugs (%) | Malignancies (%) | Idiopathic (%) |
|--------------------------|-------------|----------------------------|-----------|------------------|----------------|
| Hasan & Jansen 1983\(^\text{20}\) | 50          | 54                         | 10        | 4                | 32             |
| Sehgal & Srivastava 1986\(^\text{17}\) | 80          | 52.5                       | 24.7      | 0                | 22.5           |
| Botella Estrada et al 1994\(^\text{7}\) | 56          | 62.5                       | 16        | 12.5             | 9              |
| Vas concellos et al 1995\(^\text{1}\) | 247         | 59.5                       | 7.3       | 4                | 29.2           |
| Mittal et al 1996\(^\text{21}\) | 50          | 50                         | 28        | 0                | 22             |
| Sigurdsson et al 1996\(^\text{22}\) | 102         | 53                         | 5         | 16               | 26             |
| Choudhary & Gupte 1997\(^\text{4}\) | 30          | 60                         | 16.6      | 6.7              | 16.6           |
| Pal & Haroon 1998\(^\text{13}\) | 90          | 74.4                       | 5.5       | 5.5              | 14.6           |
| Bandopadyay et al 1999\(^\text{14}\) | 75          | 64                         | 12        | 2.67             | 21.33          |
| Khaled A et al 2009\(^\text{23}\) | 82          | 43.9                       | 21.9      | 4.87             | 25.6           |
| Present study 2013-2014 | 52          | 57.69                      | 13.46     | 1.92             | 26.92          |

Table 6: Comparison of present study with previous studies

In this study, all the 52 cases were subjected to histopathology. Histopathology helped in correlating & confirming the aetiology of erythroderma in 38 cases (73.07%) and did not help in 14 cases (26.92%). Biopsies were repeated in 19 out of 52 patients. 5 cases showed features consistent with the clinical diagnosis after more than 1 repeat biopsy. In 14 cases, inspite of repeated biopsies, histopathology showed nonspecific features.

In a study by Rym BM et al.,\(^\text{24}\) clinico-histopathological correlation was found in 74% of patients. Study conducted by Kondo RN et al.,\(^\text{25}\) found a correlation of 72.54%. Thus the finding in the present study is similar to the observation made by the above studies.

CONCLUSION: In patients in whom no background aetiology could be ascertained, long term follow up is necessary. Awareness of the most frequent causes can help us to develop an efficient strategy for diagnosis and appropriate management of the disease. Experience from the study supports the view that erythroderma, although a very distressing disorder, may not pose a significant risk to the patient’s life; however the main challenge lies in identifying the underlying cause and managing it.
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Haematoxylin and eosin section from the involved skin shows hyperkeratosis with confluent parakeratosis. There is regular acanthosis with thinning of some suprapapillary plates. The papillary dermis shows dilated capillaries and an infiltrate of lymphocytes.

**Fig. 4:** Histopathology of non-Hodgkin’s lymphoma (Lymph node). Haematoxylin and eosin section of lymphnode in scanner view (4x) shows diffuse effacement of the nodal architexture by monomorphic population of lymphoid cells.

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