

AN AETIOPATHOLOGICAL STUDY OF EXFOLIATIVE DERMATITISSadeep Melathil Sadanandan¹, Celine Machiyanicckal Issac², Sobhanakumari Kunjumoni³, Anuj Kumar⁴¹Professor, Department of Dermatology, Mount Zion Medical College, Adoor, Kerala.²Additional Professor, Department of Dermatology, Government Medical College, Kottayam, Kerala.³Professor, Department of Dermatology, T.D. Government Medical College, Alappuzha, Kerala.⁴Junior Resident, Department of Dermatology, Government Medical College, Kottayam, Kerala.**ABSTRACT****BACKGROUND**

Erythroderma or exfoliative dermatitis is an inflammatory disorder in which erythema and scaling occur in a generalized distribution involving more than 90% of body surface. It is a reaction pattern of skin due to various pre-existing dermatoses, malignancy– cutaneous or internal. 100 clinically diagnosed cases of exfoliative dermatitis were included in this study.

The objectives of this study were- to evaluate clinical profile and aetiology of exfoliative dermatitis and to correlate histopathological findings with clinical diagnosis.

MATERIALS AND METHODS

100 clinically diagnosed cases of exfoliative dermatitis were included for this cross-sectional study, during a period of 18 months (from March 2014 to August 2015). A detailed history and clinical examination were done. Investigations including complete blood count, peripheral smear, urine routine examination, LFT, RFT, chest X-Ray, ECG, blood sugar, FNAC lymph node and skin biopsy were done in all patients. An approval from institutional review board for ethics committee and informed consent from all patients were obtained. All data was collected in a proforma and evaluated by using epidemiological investigative software SPSS.

RESULTS

Male to female ratio was 5:1:1. Mean age of patients was 57.7 years. 57% of patients were manual labourers. 82% of patients develop exfoliative dermatitis from pre-existing skin diseases and psoriasis was present in 42%. The interval between pre-existing skin disease and Erythroderma was 1 week to 1 year in 61% of patients. Drugs caused exfoliative dermatitis in 11% of patients. Lymphadenopathy was seen in 80% of cases. Anaemia was found in 61% of patients. LFT abnormality was noted in 48% of cases. Histopathology of skin correlated with clinical diagnosis in 51% of patients.

CONCLUSION

Erythroderma mainly a disease affecting persons of 40-70 yrs. Psoriasis is the common single disease causing exfoliative dermatitis. Histopathology helps in diagnosis only in 50% of cases.

KEYWORDS

Exfoliative Dermatitis, Skin Biopsy, Psoriasis.

HOW TO CITE THIS ARTICLE: Sadanandan SM, Issac CM, Kunjumoni S, et al. An aetiopathological study of exfoliative dermatitis. J. Evid. Based Med. Healthc. 2018; 5(8), 667-672. DOI: 10.18410/jebmh/2018/136

BACKGROUND

Erythroderma or exfoliative dermatitis is an inflammatory disorder in which erythema and scaling involving more than 90% of the body surface.¹ It is usually accompanied by other systemic manifestations resulting in hemodynamic and metabolic derangements.

Erythroderma is a morphological reaction pattern of skin to pre-existing dermatoses like psoriasis, atopic dermatitis, contact dermatitis, systemic skin conditions including malignancy and drug reaction. Pre-existing dermatoses or

Financial or Other, Competing Interest: None.

Submission 30-01-2018, Peer Review 31-01-2018,

Acceptance 17-02-2018, Published 19-02-2018.

Corresponding Author:

Dr. Celine Machiyanicckal Issac,

Additional Professor,

Department of Dermatology,

Government Medical College, Kottayam, Kerala.

E-mail: dr.miceline@gmail.com

DOI: 10.18410/jebmh/2018/136



their therapy can result in erythroderma and this is the most common cause of Erythroderma in adults.^{2,3,4,5,6,7} Psoriasis is the most common cause of exfoliative dermatitis amongst dermatological disorders.^{2,7,8,9}

Irrespective of etiology the clinical features of erythroderma were almost identical. Thus, the importance of trying to find the etiology with special emphasis on histopathology, allowing early and appropriate intervention for each case.¹⁰ The number of new erythroderma cases in dermatology department of government medical college Kottayam for 18 months (from March 2014 to August 2015) was 115 and we include first 100 patients who full filled inclusion and exclusion criteria in this study.

MATERIALS AND METHODS

100 clinically diagnosed cases of exfoliative dermatitis were included in this cross-sectional study during the given period of 18 months (from March 2014 to August 2015). Patients were clinically evaluated with detailed history including the

occupation, socioeconomic status, onset, duration, evolution of disease, pre-existing dermatoses, aggravating /precipitating factors, previous treatment, personal history, family history and any associated disorder. A detailed clinical examination was carried out.

Extent of erythema and scaling were calculated according to the "Wallace's rule of nine". Changes in palms, soles and nail were noted; also, mucous membrane were examined.

Systemic examination was done, to detect clinical evidence of cardiac failure, hepatomegaly and any lung changes. Per rectal examination was done, in all old male patients and per vaginal examination in all married females. Investigations like haemoglobin, total and differential white cell count, erythrocyte sedimentation rate, peripheral smear for abnormal cell, urine routine examination, liver function test, renal function test, serum electrolytes, X-ray chest, ECG and blood sugar estimation were done. FNAC examination done in patients with significant lymph node enlargement and suspected cases of malignancy, skin biopsy was taken from all patients.

An approval from Institutional Review Board for Ethics Committee and informed consent from all patients who participated in the study were obtained. All data was collected on a proforma and evaluated by using epidemiological investigative software SPSS.

OBSERVATION AND RESULTS

100 patients were included in this study from March 2014 to August 2015. In these 83 were males and 17 were females. Male to female sex ratio was 5.12:1 Maximum patients (30%) were of 7th decade followed by 18% of 6th decade. Youngest patient was a 10 months old boy and the oldest was 89 years old man. Mean age of our patients was 57.7 years. Most of the patients in this study were manual labourers 57% followed by farmers with 17%. In majority of patients (63%) the duration of disease was <3 months. Minimum duration of 2 days was seen in a case of irritant contact dermatitis due to application of some Ayurvedic preparation and a case of drug reaction with amoxicillin. While maximum duration (12 years) was in a case of psoriatic erythroderma. 82% developed Erythroderma due to pre-existing dermatoses in which most common was psoriasis. Drug reaction was responsible for 11%, malignancy for 2% and rest 5% left without definite diagnosis as idiopathic. (Figure - 1 & 2)

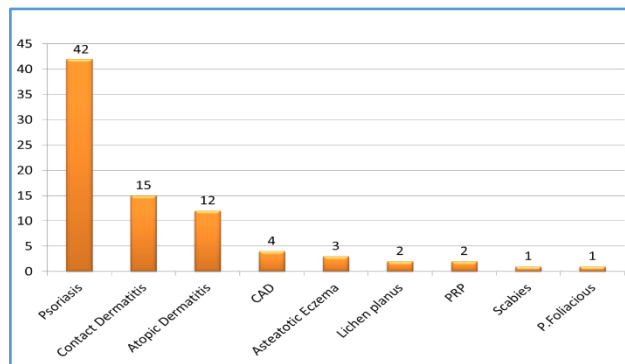


Figure 2. Types of Pre-existing Dermatoses



Figure 3. Erythroderma Secondary to Pustular Psoriasis

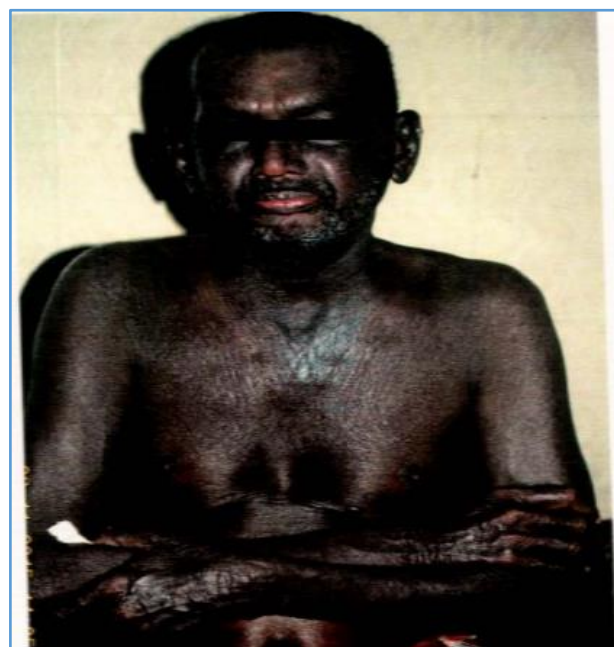


Figure 4. Erythroderma Secondary to Chronic Actinic Dermatitis

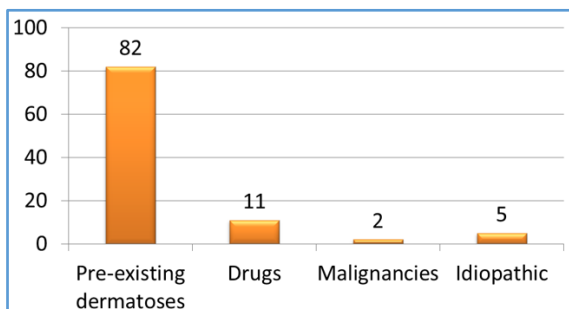


Figure 1. Aetiological Factors of Erythroderma

History of psoriasis was noted in 42% (Figure 3) contact dermatitis in 15%, and atopic dermatitis in 12%, chronic actinic dermatitis (CAD)/ Photodermatoses (Figure 4) in 4%, and asteatotic eczema in 3%, lichen planus in 2%, pityriasis rubra pilaris (PRP) in 2%, pemphigus foliaceus and scabies in 1% each. Time interval between PED and erythroderma was 1 week to 1 year in 61% patients with minimum of <1 week in 2% cases and maximum >10 years in 4%. Mean duration of this interval was 2.5 years. Total number of drug induced erythroderma patients were 11 and the most common drug causing erythroderma was Phenytoin sodium in 5 cases followed by INH and Dapsone 2 cases each and 1 case each of sodium valproate and penicillin's (amoxicillin + cloxacillin). 2 cases of malignancy were found in this study. One case each of CTCL and papillary carcinoma of thyroid. With our best efforts of thorough evaluation, we could not find out exact aetiology in 5 patients. History of AYUSH (Ayurvedic, Unani, Siddha, and Homeopathy) therapy, home remedies or other indigenous medication was present in 30%, infections in 18%, photo-exacerbation in 6%, drug intake was in 11%, drug withdrawal in 8%, irritant applications in 6%, stress and winter season in 2% cases each. Itching was present in 87%. Chills, rigor, malaise were present in 62%, fever in 58% and burning sensations in 4% cases.

Diffuse non-scarring hair loss was present in 21 cases, majority (9 cases) were of contact dermatitis followed by 8 cases of psoriasis while 2 cases from CAD and 1 each from atopic dermatitis and idiopathic. Most common finding on oral examination was dental carries in 54% cases, followed by mucosal changes (46%) white lacy pattern, hyper-pigmentations, atrophic glossitis, scrotal tongue and candidiasis. Nail changes were found in 71% of cases. Most common nail changes were longitudinal ridges in 63% cases. The specific nail change for psoriasis, oil drop sign was present only in 8 cases of psoriatic erythroderma. While other suggestive nail changes were pitting, subungual hyperkeratosis (SUHK) and onycholysis. Enlargement of lymph node were present in 80% cases, of these 30% cases had generalized lymphadenopathy and 50 % cases had localized involvement in inguinal and/or axillary group of lymph nodes.

FNAC was done in 17 suspected cases of malignancy out of which 8 showed reactive changes and remaining 9 cases showed lipomelanotic reticulosis (dermatopathic lymphadenopathy). These 8 patients with reactive changes were further investigated by lymph node biopsy; in them one case came as CTCL and was confirmed by skin biopsy also. In one case FNAC and biopsy was taken from hard thyroid swelling and result came as papillary carcinoma of thyroid. 87% cases had dependent pitting pedal oedema along with 12 cases of facial puffiness. Most common finding on

haemogram was anaemia which was present in 61% cases, followed by eosinophilia in 54%, neutrophilia, leucocytosis and lymphocytosis were present in 47%, 25%, and 4% respectively. All the haemogram findings had no association to any specific aetiology.

5 cases showed atypical lymphocytes in peripheral smear and on further investigation one case came as CTCL. 23 patients were found to be diabetic on blood sugar testing. Urine- abnormal in 19% cases in which significant increased pus cells (>5 in no. in males and >10 in females) were in 8% cases, other findings were proteinuria and glycosuria in 4% cases each, while RBC casts were present in 3% cases. LFT were done in all patients. Abnormality seen in 48% cases in which most common was hypoproteinaemia in 39%, hypo-albuminaemia in 32%, while enzymes were raised in 10 cases in which most of the cases (8) were of drug induced Erythroderma and rest 2 were in erythrodermic psoriasis cases. Serum bilirubin was raised in 4 cases, out of which 3 were of drug induced erythroderma and there was no relation in hypo-proteinemia/ hypo-albuminemia in different aetiologies of erythroderma. Most common finding in RFT was raised serum creatinine in 15% cases, raised blood urea in 7%. Electrolyte imbalance was present in 18 cases. Out of which hyponatremia in 8%, hypokalaemia in 3%, and hypocalcaemia in 7% cases. LDH done in 17 suspected cases of malignancy and raised LDH was present in 9 cases. 1 case came as malignancy (CTCL) after further investigations. Endoscopy was done in 2 cases and one case came as Barrett's oesophagus. USG abdomen were done in 52 cases out of which fatty liver were in 7 cases, liver fibrosis in 2 cases, BPH in 10 cases, hepatomegaly in 9 cases, splenomegaly in 3 cases, ascites in 2 cases, 1 case each of renal agenesis and renal cyst. ECG was done in 43 cases in which slight abnormality seen in 7 cases. Skin biopsy was performed in all cases. Total 106 samples were examined (6 repeat biopsy taken from 6 suspected cases of malignancy and for IHC). Histopathology was correlated with clinical diagnosis in 51%. (Table 1 & 2).

H/P Findings	Number of Cases (%)
Psoriasis	31
CAD	2
LP	2
PRP	2
P.F.	1
DRUGS	4
Spongiotic dermatitis	17
Psoriasiform dermatitis	15
Malignancy	2
Non-specific dermatitis	24

Table 1. Histopathological Diagnosis

Erythroderma Aetiology	Clinical Diagnosis	Histopathological (h/p) Diagnosis	Positive Correlation of h/p with Clinical Diagnosis (in %)
Psoriasis	42	31	73
Contact dermatitis	15	4	26.66
Atopic dermatitis	12	3	25
CAD / Photodermatoses	4	2	50

Asteatotic Eczema	3		
CTCL/Other Malignancy		2	-
Lichen planus	2	2	100
PRP	2	2	100
Scabies	1	-	-
Pemphigus foliaceus	1	1	100
Drugs	11	4	36.36
Idiopathic	7	-	-
Table 2. Clinco Histopathological Correlation			

DISCUSSION

ED is a distressing illness with high morbidity. In fully involved state, to identify its cause is very difficult and hence its management. It requires very detailed and prompt history, clinical and histological examination and other relevant lab investigations to know the etiology. 100 patients were studied in 18 months of period, male to female ratio among them were 5.12:1. Very high male: female sex ratios 11.27:1 and 14:1 were seen in Nicholas et al¹¹ and Hulmani et al⁴ studies respectively. Lowest ratio 1: 0.38 was seen in the study of Sehgal et al.² Hence this study is similar with other studies regarding male preponderance. Males are mostly affected due to more exposure to predisposing environmental factors. In the present study, the maximum numbers of patients (30%) were in the 61-70 (7th decade) age group. Studies of Abraham et al,¹² Nicolas et al,¹¹ Sehgal et al,² Bharatiya et al³ show maximum incidence in the age group of 50-59, which is almost similar to the present study. 57% of patients with ED were manual labourers including construction work, head load workers, painters, etc. These patients are likely to be subjected to maximum stress, exposure to sunlight, contact sensitization, infections, poor living conditions which may result in exfoliative dermatitis.

The duration of exfoliative dermatitis at the time of admission ranged from 2 days to 12 years. Most of the patients (63%) presented with duration of disease <3 months and 37% cases with duration >3 months. Bharatiya et al³; observed that 60.81% of patients had the duration of ED <3 months. This shows similarity with present study.

Shortest duration of 2 days was seen in a case of irritant contact dermatitis due to application of some Ayurvedic preparation and a case of drug reaction with amoxicillin. While maximum duration was in a case of psoriatic Erythroderma. Mean duration of erythroderma in this study was 1.59 years. This is almost similar to 1.44 years of one recent study done by Sudho et al⁸ from South India. In the study by Abraham et al¹² (1963) mean duration was 5 years showing a wide range in duration of illness. Many of the patients get initially treated with self-medication and indigenous medicines which often result in worsening of the condition. In this study, 82% of the cases developed Erythroderma due to pre-existing dermatoses. Present study is similar to other studies done by Hasan et al⁶ (42%), Shegal et al² (52.50%), Akhyani et al⁹ (59.80%), Pal et al⁷ (74.40%) regarding the most common etiology of Erythroderma pre-existing dermatoses. While study done by Nicholas et al¹¹, drug reaction was the major factor. Psoriasis was the most common etiology among pre-existing dermatoses (42%). Hasan et al⁶ study showed psoriasis as

an etiology in 10%, Bandyopadhyay et al¹³ in 33.33% cases, Pal et al⁷ in 37%. 15% of cases in this study were due to contact dermatitis. Similar finding was noted in the study done by Kondo et al,¹⁰ where 15.58% exfoliative dermatitis cases were due to contact dermatitis. In this study, 12% of cases of ED were due to atopic dermatitis. Akhyani et al⁹ had 13.4% of ED due to atopic dermatitis; Hasan et al⁶ had 14% cases due to atopic dermatitis, which almost correlate with this study. In this series 4% cases were due to CAD/Photodermatoses which is almost comparable to studies of Botella et al¹⁴ (5.4%) and exact correlate with Hasan et al⁶ who had (4%) cases due to this. The present study showed 2% of cases due to PRP which is similar to the observations made by Pal et al⁷ study (2.2%). While some other studies showed slightly higher incidence of Erythroderma due to PRP like 5.33% in Bandyopadhyay et al¹³ and 8.2% in Akhyani et al⁹ study. Asteatotic eczema was present in 3% cases which was correlate with study of Hasan et al⁶ with 2% cases. Lichen planus was present in 2% cases which were almost similar to Rymet al.¹⁵ Pemphigus foliaceus was present in 1% cases. Different studies have showed higher incidence of PF as a cause of ED as compared to this study, 4% in Sudho et al,⁸ 5.33% in Bandyopadhyay et al,¹³ 5.6% in Pal et al⁷ and 6.25% in Rym et al¹⁵ study.

Scabies as a cause of ED was present in 1% case. This is almost correlate with studies done by Rym et al¹⁵ (1.25%) and Bandyopadhyay et al¹³ (1.33%). Drugs as a cause of erythroderma were found in 11%. This was exactly match with study done by Rymet al¹⁵ (11.25%). Out of 11 cases in this study of which maximum 5 cases were due to phenytoin induced, 2 cases each of INH and Dapsone while one case each of sodium valproate and penicillin's (amoxicillin + cloxacillin). Sehgal et al² (1986) & Bharatiya et al³ (1995) noted INH & Kondo et al¹⁰ (2006) observed sulfone induced erythroderma. In this study only 2 cases found as cause of erythroderma, one case each of CTCL and papillary carcinoma of thyroid. This finding is almost correlate with several Indian studies done by Bandyopadhyay et al¹³ (2.67%), Sudho et al⁸ (4%) Bharatiya et al³ (4.35%). Abraham et al¹² had 8% of erythroderma cases due to lymphomas/leukaemia. Nicholas et al¹¹, Botella et al¹⁴ noted 21% & 12.5% cases of malignancy respectively in their studies, In 5% of patients of this study, an etiological diagnosis could not be reached. This study showed correlate with one study done by Sudho et al⁸ (8%) from South India. Maximum number of idiopathic cases was observed in western study by Abraham et al¹² (46.53%) and Indian study by Bandyopadhyay et al¹³ (21.33%). This study showed pruritus of varying intensity in most of the cases

(87%), chills and rigor in 62% of cases and fever in 58% cases. Pal et al⁷ noted pruritus in 86% and chills in 64.4% which is almost comparable to the results in the present study. Non-cicatricial diffuse hair loss of varying degree was noted in 21% of cases with maximum cases from contact dermatitis followed by psoriasis. The results are comparable with that of Pal et al⁷ & Nicolis et al¹¹ studies.

Most common finding on oral examination was dental carries in 54% cases, followed by other non-specific changes like hyper-pigmentations, atrophic glossitis, scrotal tongue and candidiasis. In this study mucosal involvement was present in 46% cases this is near to study done by Pal et al⁷ (36.6%). Nail changes of various types were found in 71% of cases. Most common nail changes were longitudinal ridges in 63% cases. 29% cases were having shiny nails. Pal et al⁷ study (80%) almost has the same results. Other changes are coarse pitting, subungual hyperkeratosis (SUHK) and nail destruction due to onycholysis.

Enlargement of lymph node were present in 80% cases, of these 30% cases had generalized lymphadenopathy and 50% cases had localized involvement in inguinal and/or axillary group of lymph nodes. Nicholas et al¹¹ and Sigurdsson et al¹⁶ have almost the same observation (71%). 87% cases had dependent pitting pedal oedema along with 12 cases of facial puffiness. Involvement compared to the studies of Sigurdsson et al,¹⁶ Bharatiya et al.⁹ Anaemia was noted in 61% cases (Hb<12 mg% in Males, Hb<11gm% in Females) Leucocytosis in 21% patients, eosinophilia in 45%, hypoproteinaemia in 39%. Percentage of anaemia in this study is similar to Nicolis et al,¹¹ Sehgal et al² and Pal et al⁷ studies Increased total leukocyte count is seen almost in the same manner as with Hasan et al⁶ and Pal et al⁷ study.

Peripheral Smear was done in all cases. 5 cases showed atypical lymphocytes. On further investigation one case came as CTCL. Abraham et al¹² had diagnosed 4 cases of leukaemia in their study after peripheral smear and bone marrow examination of 30 cases.

Histopathological results of clinically diagnosed dermatoses, like PRP, lichen planus and pemphigus foliaceus were 100% co-related. Pal et al,⁷ Botella et al¹⁴ noted that biopsy helped to detect pemphigus foliaceus, PRP, as in this study. In the rest of the cases the result came as psoriasis (31%), nonspecific dermatitis (24%), Spongiotic dermatitis (17%), Psoriasiform dermatitis (15%), photo dermatitis (2%), and drug (4%). Pal et al⁷ also noted that nonspecific and Spongiotic dermatitis picture of histopathology predominant in Erythroderma so this study also correlates with this view.

In 51% cases histopathology was well correlated with clinical diagnosis. This correlation is almost similar to Bandyopadhyay et al¹³ study (52%). Pal et al⁷ noted that in 27.7% of clinically diagnosed cases had correlation with skin biopsy. In 49% of cases no histologic correlation was obtained. Most of such cases were eczemas and few cases due to psoriasis. Because the histological feature of these often become non-specific in erythrodermic stage.

CONCLUSION

Erythroderma is a disease mainly affecting persons between 40-70 years old. Pre-existing dermatoses and their treatment are the most common causes among these; psoriasis is the common single dermatoses in the aetiology. Both endogenous and exogenous eczemas are other major group of dermatoses causes erythroderma followed by drugs. In full blown and chronic cases, the aetiology is often obscure. Detailed history, clinical & laboratory examination will help some extent to identify the cause.

Histopathological examination if performed early, preferably after subsidence of acute stage and repeatedly from multiple sites may help to identify and confirm the aetiology in around 50% of cases. Majority of histopathological reports were non-specific dermatitis, spongiform dermatitis and Psoriasiform dermatitis. Even though in about 10-20% of patients, aetiology remains unknown, continued follow up and repeated investigations are necessary in these patients.

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