Epidemiological and clinical features of hospitalized erythroderma patients: a cross-sectional study

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Erythroderma or generalized scaling dermatitis is a condition marked by redness and scaling of more than 90% of the body surface. This study aimed to review the epidemiological and clinical features of erythroderma patients hospitalized in the Dermatology Ward of Shahid Faghihi Hospital, Shiraz, Iran. This retrospective cross-sectional was conducted from 2001 to 2017 using patient records. All patients with a diagnosis of erythroderma on record were included in the survey, and those whose data were missing or were not compatible with the clinical diagnosis were excluded. Data were analyzed with SPSS version 22 and Stata version 14.2. Overall, 217 erythroderma patients were admitted to this ward, including 119 (54.8%) men and 98 (45.2%) women. The mean age of the patients was 47.27 ± 19.68 years (range: 4-92 years). Moreover, the most frequent cause of erythroderma was drug reaction (67%); lamotrigine, with a frequency of 12 patients, was the most prevalent prescribed medication in patients with drug reaction-induced erythroderma. The mean duration of hospital stay was 6.64 ± 4.50 days; this parameter was directly associated with the erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP) level. Pruritus (41.9%) and fever (15.2%) were the most frequent clinical manifestations among these patients. As erythroderma is a dermatologic condition that medications can induce, patients should be informed about the warning signals and course of the disease before certain medications are prescribed.

Keywords: dermatitis, skin disease, inflammation, erythroderma, epidemiology

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INTRODUCTION

Erythroderma is an extreme skin redness that Von Hebra first identified in 1868. This inflammatory condition is triggered by severe impairment of the cutaneous metabolism, which induces redness and scaling throughout the body. Usually, this disorder involves about 90% of the body surface. This disease may be a morphological manifestation of diverse dermatologic and systemic disorders and drug reactions. Several studies indicate that most erythroderma patients are diagnosed with psoriasis, spongiform dermatitis, pharmaceutical reaction, or T-cell lymphoma (CTCL) [1,2]. However, the probable erythroderma processes and etiologies are yet to be completely known [3].

Patients with erythroderma may experience hair loss, nail loss or nail malformation, and involvement

of the palms and soles [4]. In addition, the emergence of lymphadenopathy and hepatosplenomegaly can suggest drug susceptibility or malignancies, especially when accompanied by liver disease and fever [5].

According to the literature, the etiology of erythroderma has a significant role in the prognosis of the disease. Erythroderma develops rapidly in drug oversensitivity, lymphoma, leukemia, allergens, viral infections, or staphylococcal desquamation syndrome. Nevertheless, slow progression is found with primary skin conditions, including psoriasis and atopic dermatitis [1,2,6,7]. Nowadays, through quick evaluation and treatment, patients with drug-induced erythroderma recover sooner [1,2]. The details of idiopathic erythroderma have not been clarified, though several mechanisms have been suggested in this regard. Long-term corticosteroid usage is usually present in this process [2,8].

To the best of our knowledge, there are few studies on erythroderma in Iran. Therefore, this study aimed to explain the epidemiology and clinical features in hospitalized patients with erythroderma in Shiraz, Southwestern Iran, as one of Iran's main dermatology referral centers.

MATERIALS AND METHODS

Study design and population

This study was cross-sectional and descriptive in nature. The study population included all patients admitted to the Dermatology Ward of Shahid Faghihi Hospital, Shiraz, Iran, with the diagnosis of cutaneous erythroderma between 2001-2017.

Inclusion and exclusion criteria

The inclusion criteria encompassed patients with a diagnosis of redness and scaling that affected more than 90% of the body surface. Documents with incorrect diagnoses and missing files were excluded from the study.

Data collection

The patients' documents were closely verified, and the following details were registered: patient age, sex, medical background (including the history of skin diseases), suspected history of medication use, manifestations, and evidence of physical findings (with a particular focus on skin, mucus, hair, nails, lymph nodes, temperature, edema, and even hepatosplenomegaly). Laboratory measures included hematological variables (specifically hemoglobin, white blood cells, and eosinophil percentage), ESR (erythrocyte sedimentation rate), and C-reactive protein (CRP) as part of standard monitoring for all admitted erythrodermic patients in the dermatology unit. Provided that samples were used for the ultimate diagnosis, an etiological review prompted us to report patient details under the name of the etiology.

A case file evaluation of each patient's clinical manifestations showed a series of symptoms (itching, peripheral edema, hepatosplenomegaly, lymphadenopathy, hyperchromatosis, and pyrexia) based on incidence registrations for all patients. Retrospective examination and case studies for each patient were registered with Excel software by analyzing the variables including age, sex, hospitalization period in the dermatology unit, etiology, clinical manifestations, experimental data, and the medical background of patients.

Statistical analysis

SPSS version 22 (IMB, Inc., Armonk, USA) and Stata 14.2 (Stata/MP 14.2 for Windows, Revision 29 Jan 2018, StataCrop LLC, 4905 Lakeway Drive, College Station, TX77845, USA) were conducted for statistical analyses. Independent t-test and ANOVA were used to assess the association between the variables. Moreover, standard mean difference (Cohen's d) was used to measure the effect sizes. P-values equal to and less than 0.05 were considered statistically significant.

Ethics statement

The protocol of this study was approved by the Ethics Committee of Shiraz University of Medical Sciences (IR.SUMS.MED.REC.1399.253).

RESULTS

A total of 217 erythrodermic patients were admitted to the Dermatology Ward of Shahid Faghihi Hospital between 2001-2017 and were subjected to a final examination throughout this

research; 54.8% of the admitted patients with erythrodermic were men, so the men to women ratio was 1.21. The patients' age range was 4-92 years (mean age 47.27 ± 19.53 years). In erythrodermic patients, the lowest average age (42 years) was attributed to T-cell lymphoma, and, in these participants, the maximum mean age (60.75 years) was associated with other factors. The mean age of men was significantly more than that of women (men: 51.00 ± 19.87; women: 42.74 ± 18.43 years, $P = 0.002$). The mean duration of hospitalization of the erythrodermic patients in our study was 6.64 ± 4.58 days. The shorter hospitalization was for erythrodermic patients with adverse medication reactions (6.09 days), while the longer duration of hospitalization was in patients with erythrodermic psoriasis (9.93 ± 6.81 days) (Table 1). According to the results of this study, there was no significant difference between hospital stay in men and women with erythroderma (men: 7.07 ± 4.94 days; women: 6.12 ± 4.07 days; $P = 0.128$).

The erythroderma patients were categorized into six classes etiologically. According to the results of this study, the most common cause of erythroderma was drug complications (67%), and lamotrigine was the most often administered medicine among the patients. On the other hand, T-cell lymphoma (1%) had the lowest frequency among the causes of the erythroderma. Other causes of erythroderma in order of frequency were idiopathic, eczema, psoriasis, and other triggers (pityriasis rubra pilaris, pemphigus foliaceous, and subacute lupus erythematosus).

Table 2 shows the most common clinical

Table 1. Etiology, age, and average hospitalization duration in patients with erythroderma

Etiology	Frequency (%)	Age (years) Mean ± SD	Hospital stay (days) Mean ± SD
Psoriasis	15 (6.9)	48.60 ± 18.96	9.93 ± 6.81
Drug reaction	146 (67.3)	44.13± 19.80	6.09 ± 3.74
Eczema	22 (10.1)	54.09 ± 14.85	7.41 ± 5.50
T-cell lymphoma	2(0.09)	42.00 ± 16.97	9.5 ± 6.36
Idiopathic	24 (11.1)	55.21 ± 18.97	6.12 ± 5.33
Other factors	8 (3.7)	60.75 ± 19.36	9.25 ± 5.70
Total	217 (100)	47.27 ± 19.53	6.64 ± 4.50
P-value [a]		0.013 [b]	0.014 [c]

a. *P*-value equal to or less than 0.05 was considered significant; b. The post hoc LSD test showed that the statistically significant difference was related to differences in means between drug reaction and eczema ($P = 0.024$), idiopathic causes ($P = 0.009$), and other causes ($P = 0.018$). c. The post hoc LSD test revealed that this significant result was related to the difference between the days of hospital stay among erythrodermic patients with the etiology of psoriasis and drug reaction ($P = 0.002$) and idiopathic causes ($P = 0.011$).

Table 2. The clinical manifestations of the patients with erythroderma and their effect on hospital stay compared to those who did not have these clinical manifestations

Clinical manifestation	Frequency (%)	Mean difference in hospitalization days[a] (95% CI)[b]	*P*-value[c]	Standard mean difference[d] (95% CI)
Signs and symptoms				
Pruritus	91 (41.9)	0.50 (-0.74 to 1.75)	0.424	0.11 (-0.15 to 0.37)
Peripheral edema	26 (12)	-0.36 (-2.21 to 1.58)	0.742	-0.06 (-0.48 to 0.37)
Hepatosplenomegaly	2 (0.9)	-5.40 (-11.80 to 0.99)	0.097	-1.18 (-2.58 to 0.22)
Pyrexia	33 (15.2)	0.05 (-1.67 to 1.76)	0.958	0.01 (-0.36 to 0.38)
Palmoplantar keratoderma	5 (2.3)	-4.05 (-8.11 to 0.02)	0.050	-0.89 (-.1.78 to 0.01)
Nail alterations	5 (2.3)	-2.41 (-6.50 to 1.68)	0.246	- 0.53 (-1.41 to 0.36)
Lymphadenopathy	3 (1.4)	-3.74 (-8.99 to 1.51)	0.161	-0.82 (-1.96 to 0.33)
Laboratory tests				
Anemia	32 (14.75)	-1.30 (-3.02 to 0.43)	0.140	-0.28 (-0.66 to 0.09)
Eosinophilia	10 (4.61)	-0.21 (-4.14 to 1.72	0.416	-0.26 (-0.90 to 0.37)
Leukocytosis	68 (31.34)	-0.60 (-1.92 to 0.72)	0.371	-0.13 (-0.42 to 0.16)
Increased ESR or CRP levels	93 (43.86)	-1.64 (-2.86 to -0.41)	0.009	-0.36 (-0.63 to -0.09)

a. The mean differences of hospitalization days for each row were calculated by subtracting the average number of hospitalization days in patients without that manifestation (negatives) from the average number of hospitalization days in patients with that manifestation (positives); c. A *P*-value equal to or less than 0.05 was considered significant; d. CI: confidence interval; c. Cohen's *d*

symptoms associated with erythroderma. Itching (41.9%) and pyrexia (15.2%) were the most common clinical symptoms in these patients. Furthermore, this table shows that increasing ESR or CRP levels was the only factor associated with a prolonged duration of hospital stay [P = 0.009, Cohen's d = -0.36 (%95 CI: -0.63 to -0.09)].

The laboratory test results revealed that the most common pathological phenomenon was a rise in ESR or CRP (42.9%), more typical in erythrodermic patients with drug complications. Further laboratory data were anemia (4.6%), leukocytosis (14.7%), and eosinophilia (31.3%). Moreover, diabetes, hypertension, and epilepsy were the most common non-cutaneous comorbid diseases among patients with erythroderma. The details of changes in the laboratory findings and frequency of non-cutaneous underlying diseases in our study patients are reported in Table 3.

DISCUSSION

This study showed that erythroderma was more common among men, especially in the fifth decade of life. Furthermore, an increased ESR/CPR level was the most common laboratory finding in these patients, sharing a direct association with the hospital stay duration. Moreover, drug reaction was the most common cause of erythroderma.

Although erythroderma typically develops in the sixth decade of life and is more common in men [9], according to the study of Aqil *et al.* in Morocco [10] and Akhyani *et al.* in Iran [11], erythroderma is more prevalent in the fifth decade of life. These results are in line with our study. Our study revealed that the disease was more prevalent among men. During a prospective review of 309 patients by Miyashiro *et al.*, the male to female ratio was recorded at 2.2 [9]. In the research conducted by Aqil *et al.*, a female preponderance was recorded, and this proportion was stated as 0.7 [10].

Drug reactions were the most common cause of erythroderma in our study. However, in several studies [9,10,12-14], psoriasis was the most crucial factor, followed by a history of exacerbation of dermatosis disorders. Aqil *et al.* showed that the underlying skin conditions that resulted in the hospitalization of erythrodermic patients were mainly psoriasis and other triggers of the condition, including idiopathic diseases, eczema, T-cell lymphoma, and, to a lesser extent, subacute cutaneous lupus, pemphigus foliaceous, and pityriasis rubra pilaris. This variation in etiology may be attributed to hereditary, regional, and cultural distinctions [10].

The study of Cesar *et al.* revealed that erythrodermic patients who experienced a rapid onset of medicine reaction had a shorter disease course and hospital stay [12]. In this regard, our study revealed that the shortest hospitalization period was seen when the etiology was a drug reaction. However, the most prolonged period occurred in patients with psoriasis. Like several other experiments [13,15], our study revealed that the disorder has no specific and diagnostic clinical signs or symptoms. Itching, irrespective of its origin, was the most frequent clinical symptom among our patients, followed

Table 3. Changes in the laboratory findings and frequency of non-cutaneous underlying diseases in patients with erythroderma based on etiology

Laboratory data & history	Etiology N %						
	Psoriasis N (%)	Drug reaction N (%)	Eczema N (%)	T-cell lymphoma N (%)	Idiopathic diseases N (%)	Other factors N (%)	Total N (%)
Laboratory tests							
Anemia	2 (13.35)	10 (6.8)	5 (22.7)	0 (0)	8 (33.3)	5 (62.5)	32 (14.75)
Eosinophilia	0 (0)	3 (2.1)	3 (13.6)	1 (50)	2 (8.3)	1 (12.5)	10 (4.6)
Leukocytosis	3 (20)	48 (32.9)	6 (27.3)	1 (50)	6 (25)	4 (50)	6 (31.3)
Increased ESR or CRP levels	6 (40)	67 (45.9)	10 (45.5)	0 (0)	7 (29.2)	1 (12.5)	93 (42.9)
Comorbidities							
Hypertension	1 (6.7)	13 (8.9)	1 (4.5)	1 (50)	2 (8.3)	1 (12.5)	19 (8.8)
Diabetes	1 (6.7)	12 (8.2)	3 (13.6)	0 (0)	4 (16.7)	1 (12.5)	21 (9.7)
Congestive heart failure	2 (13.3)	6 (4.1)	0 (0)	0 (0)	2 (8.3)	0 (0)	10 (4.6)
Chronic kidney disease	0 (0)	2 (1.4)	0 (0)	0 (0)	1 (4.2)	2 (25)	5 (2.3)
Dyslipidemia	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Epilepsy	0 (0)	14 (9.6)	2 (9.1)	0 (0)	0 (0)	0 (0)	16 (7.4)

by pyrexia. In this regard, the results of our study were close to those of Aqil *et al.* [10]. Other common symptoms were peripheral edema, palmoplantar keratoderma, nail alterations, lymphadenopathy, and hepatosplenomegaly. Some studies have demonstrated that nail alterations and palmoplantar keratoderma are more common in psoriatic patients [12,16].

Drug-induced pyrexia and edema have been established in erythrodermic patients [8]. The most prevalent experimental results in the Cesar *et al.* study were an increase in ESR/CRP, leukocytosis, and anemia [12]. The most prominent laboratory test results in a recent survey were elevated ESR/CRP levels, which are more common in erythrodermic patients. Other experimental results in order of frequency were leukocytosis, anemia, and eosinophilia. With regard to the drug reaction, some evidence indicates that hypereosinophilia is strongly correlated with erythroderma [10]. However, only a few erythrodermic patients in our study showed drug reaction-induced eosinophilia.

The differences between the results of our study and the other studies may be related to some factors, including ethnicity, race, and geographic conditions. Moreover, some erythrodermic patients suffering from underlying diseases may be admitted to the related hospital wards for their main disease, so the recorded erythroderma prevalence may be below the actual value. Moreover, increased ESR and CRP levels were the factors associated with increasing the duration of hospital stay. Still, this result is not conclusive because the confidence interval of the standard mean difference was wide.

There were some limitations to this study. First, it was a retrospective study, so the patients were not visited by ourselves, and we had to rely on the patients' information recorded in the documents. Second, it was probable that some of the patients with erythroderma were admitted and documented according to the final diagnosis of their underlying diseases (e.g., psoriasis), which may lead to a potential bias to present a low prevalence of erythroderma in Shiraz. Next, we had some data missing because of inappropriate data recording in a few patients' documents. Moreover, there were some changes in the patients' documents forms and the approach to diseases in the hospital during the study period, which may affect our results. Finally, as this study was a single-center investigation, the authors strongly recommend the conduction of multi-center studies on this topic in Iran.

CONCLUSIONS

It seems that several aspects of erythroderma remain ambiguous. Hence, further studies should be conducted to determine the main causes of erythroderma, the drugs, dosages, and drug interactions that could start or aggravate erythroderma, and patient characteristics that could modify the disease course.

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Conflict of Interest: None declared.

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