Epidemiology of exfoliative dermatitis at the University of Santo Tomas Hospital (Department of Dermatology) from 2008-2012: a five-year review

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ABSTRACT

Introduction: Exfoliative dermatitis is a potentially life- threatening inflammatory reaction that poses a significant risk for morbidity and mortality. Several underlying etiologies of this dermatologic condition include pre-existing dermatoses, drugs and malignancy. Although it is a common disease entity, local studies on exfoliative dermatitis published in literature are very limited.

Objective: The primary objective of this study is to determine the epidemiological profile of patients with exfoliative dermatitis diagnosed at University of Santo Tomas Hospital Dermatology department from January 2008 to December 2012. Methods: Inpatient and outpatient clinical records of patients diagnosed and treated as exfoliative dermatitis were retrieved. The prevalence, clinical presentation, history of previous dermatoses or use of any drugs/topical medications, family history and accompanying systemic symptoms were reviewed and analyzed.

Results: A total of 67 patients were included in this retrospective study. The prevalence among patients with exfoliative dermatitis in this study was computed at 1 per 1000 dermatologic patients. The highest number of cases belonged to the group aged seventy-one to seventy-nine (25.4%) with a mean age of 56.62 years. There was a male predilection (65.7%). Clinical presentation of patients included pruritus, generalized scaling and erythema, accompanied by bipedal edema (41.8%), chills (22.4%), fever (T ≥ 38 °C), lymphadenopathies (6%) and joint pains (4.5%). Several etiologic factors of exfoliative dermatitis recorded were: pre-existing dermatosis (67.2%), idiopathic or undetermined causes (19.4%), drug-induced (10.4%) and malignancy (3%).

Conclusion: Exfoliative dermatitis is a condition more commonly found in the older age group. Pre-existing dermatoses, drugs and malignancy are etiologic factors. The most common pre-existing dermatosis causing exfoliative dermatitis in this study is psoriasis while the most implicated drug is allopurinol.

Key words: exfoliative dermatitis, erythroderma, epidemiology

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Source of funding: none
Conflict of interest: none

INTRODUCTION

Exfoliative dermatitis, also known as erythroderma, is a reaction pattern characterized by generalized and confluent erythema with desquamation affecting more than 90% of body surface.[1] This is usually accompanied by other systemic manifestations, resulting in hemodynamic, metabolic and biochemical derangements. Common underlying etiologies include pre-existing dermatoses such as psoriasis, atopic dermatitis, drug hypersensitivity reactions, and malignancies.[2] The identification of triggering factors and its etiopathology is just as important for accurate therapeutic management. Without immediate recognition and proper treatment, this condition can be fatal because of its possible complications.

Exfoliative dermatitis was first described by Herba in 1868[3] and several international studies and only a few local case reports[4,5,6] have been published since; hence, the need for a more systematic review on the epidemiology of exfoliative dermatitis. This is the first retrospective study done locally to describe the epidemiology of exfoliative dermatitis at University of Santo Tomas Hospital, department of Dermatology.

OBJECTIVES

The primary objective of this study is to determine the epidemiological profile of patients with exfoliative dermatitis diagnosed at University of Santo Tomas Hospital Dermatology department from January 2008 to December 2012.

The secondary objectives of this study are 1) to determine the prevalence of exfoliative dermatitis, 2) to describe the clinical presentation of patients with exfoliative dermatitis, 3) to determine history of previous dermatoses of patients with exfoliative dermatitis, and 4) to identify possible precipitating factors and /or underlying diseases among patients with exfoliative dermatitis.

METHODS

All inpatient (pay and clinical division) and outpatient (clinical division) clinical records with a diagnosis of either exfoliative dermatitis or erythroderma seen at University of Santo Tomas Hospital Dermatology department from January 2008 to December 2012 were retrieved and reviewed through the department's patient logbook. Data gathered included: sex, age, history of previous dermatoses or use of any drugs/topical medications, family history, as well as accompanying systemic symptoms. Results were then tabulated and analyzed.

RESULTS:

A total of 70 cases of exfoliative dermatitis were diagnosed at University of Santo Tomas Hospital, department of Dermatology from January 2008 to December 2012. The prevalence is 1 per 1000 dermatologic patients. There were 47 males and 23 females with a male to female ratio of 2:1.

Of the 70 cases, only 67 charts were available for review. There were 44 males and 23 females, with male to female ratio of 1.9:1. The prevalence was highest in the 8th decade (25.4 %). The mean age was 56.42 years; the youngest was 3 months of age while the oldest was 89 years of age. **(Table 1)**

Table 1. Gender and age distribution of patients with exfoliative dermatitis

	n=67	(%)
Gender:		
Male	44	65.7
Female	23	34.3
Age:		
0-9 years old	4	6
10-19 years old	1	1.5
20-29 years old	2	3
30-39 years old	6	9
40-49 years old	12	17.9
50-59 years old	4	6
60-69 years old	13	19.4
70-79 years old	17	25.4
80-89 years old	8	11.9

In the etiological classification, pre-existing dermatoses topped the list (67.2%), followed by idiopathic or undetermined causes (19.4%), drug-induced (10.4%), and 2 cases of malignancy (3%), one is of pulmonary origin and the other is cutaneous T-cell lymphoma. **(Table 2)**

Table 2. Etiological classification of exfoliative dermatitis (n=67)

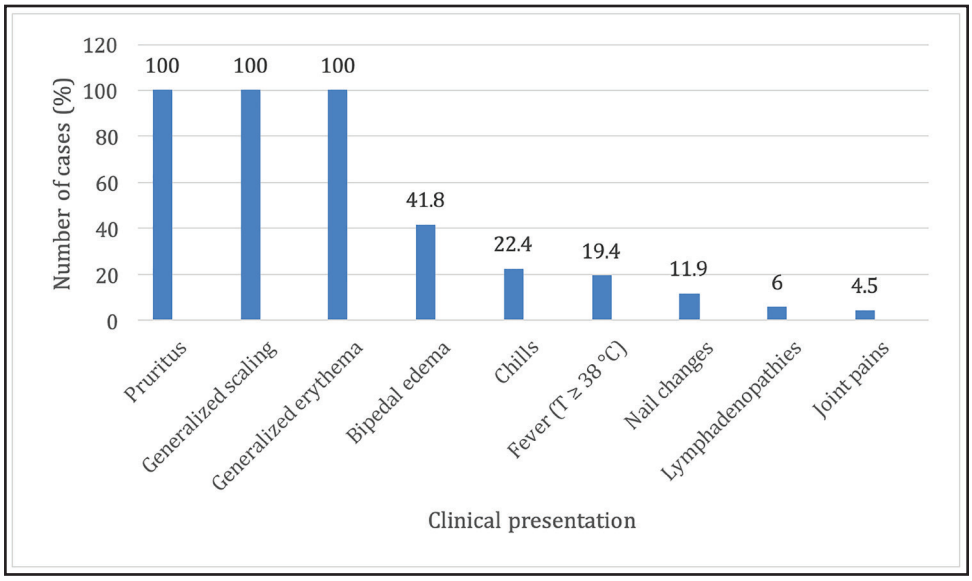
		(%)
Pre-existing dermatosis		45 (67.2%)
Psoriasis	23	
Contact dermatitis	16	
Xerotic eczema	3	
Atopic dermatitis	2	
Seborrheic dermatitis	1	
Idiopathic or undetermined		13 (19.4%)
Drug-induced		7 (10.4%)
Allopurinol	3	
Dapsone	1	
Antibiotic (cefexime)	1	
Hydrochlorthiazide	1	
Statin	1	
Malignancy		2 (3%)
T-cell lymphoma	1	
Non-cutaneous (Pulmonary)	1	

Among the pre-existing dermatoses, the most common cause of exfoliative dermatitis was psoriasis. Among these patients, 8 (34.8%) had a family history of psoriasis. On the other hand, the most common cause of contact dermatitis was secondary to the application of topical herbal medications such as guava, cilantro, atis and tamarind extracts.

Seven patients presented with drug-induced exfoliative dermatitis. These drugs were graded as possible causes of exfoliative dermatitis based on the Naranjo adverse drug reaction probability scale.[7] The relationship between a drug and exfoliative dermatitis was established from the antecedent intake of the offending drug in the days or weeks preceding the onset of exfoliative dermatitis and improvement of the manifestations upon withdrawal of the drug. Implicated drugs in this study included: allopurinol, dapsone, cefixime, thiazide, and statin.

Among the presenting symptoms, pruritus, generalized scaling and erythema were the most consistent features (100%). Eight cases (11.9 %) showed nail changes in the form of nail pitting, oil spots and dystrophy, mostly exhibited by patients diagnosed to have psoriatic exfoliative dermatitis. Systemic manifestations included bipedal edema (41.8%), chills (22.4%), fever (T≥ 38 °C) (19.4%), lymphadenopathies (6%) and joint pains (4.5%). **(Figure 1)**

Figure 1. Etiological classification of exfoliative dermatitis (n=67)



The most common laboratory finding in patients with exfoliative dermatitis was anemia (41.8%), followed by leukocytosis (31.3%) and hypoalbuminemia (31.3%). (Figure 2)

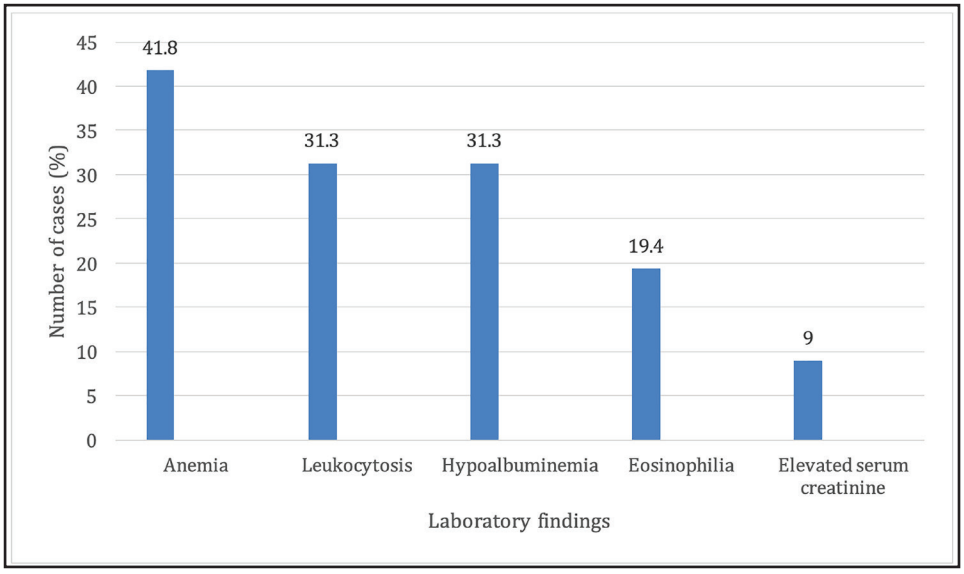


Figure 2. Laboratory findings in patients with exfoliative dermatitis

Skin punch biopsy was only performed on 8 cases during the active phase of the condition. On histopathology, three cases revealed subacute dermatitis, four cases were consistent with psoriasis while one case revealed cutaneous T-cell lymphoma. Patients with exfoliative dermatitis secondary to psoriasis have been previously diagnosed with psoriasis prior to the onset of the exfoliative dermatitis. Since these patients had no other co-morbidities or other concomitant underlying conditions, the underlying psoriasis most probably have caused the occurrence of the exfoliative dermatitis.

DISCUSSION

A major challenge lies in establishing the underlying cause of exfoliative dermatitis. It is very important to understand its etiology in every patient since the clinical features of exfoliative dermatitis are non-specific and certain manifestations cannot be easily traced to a specific cause.

In this study, the mean age of onset was 56.42 years (range: 3 months to 89 years). The condition was also more commonly found in the older age group. Males were affected more compared to females. These findings were in accordance to previously published studies.[2,8,9,10,11] This may be due to the fact that men are exposed to more toxic substances and have different environmental circumstances. Moreover, men are less likely to seek immediate medical consult as compared to women; therefore, making them more likely to develop this condition. The highest prevalence of exfoliative dermatitis belonged to the group aged 71-79 (25.4%), followed by the group aged 60-69 (19.4%), and the group aged 40-49 years old (17.9%). Elderly patients are more prone to developing exfoliative dermatitis due to several reasons. As one ages, the immune system gets weaker. The presence of other co-morbid conditions that can possibly cause exfoliative dermatitis, such as malignancy are more common among this age group. Furthermore, along with the presence of other co-morbid conditions is the intake of more drugs that can also potentiate the development of exfoliative dermatitis in the older age group. On the other hand, 2 patients in this study aged 3 months and 5 months, were also diagnosed with exfoliative dermatitis, secondary to seborrheic dermatitis and contact dermatitis secondary to herbal extracts, respectively. According to Pruszkowski *et al*.[12], the most common cause observed in neonatal and infantile erythrodermas is immunodeficiency such as Omenn's syndrome and Leinner's disease. However, the 2 pediatric patients in this study did not have other manifestations pointing to immunodeficiency as the cause of their erythroderma. Other underlying conditions associated with neonatal and infantile exfoliative dermatitis include ichthyosis, Netherton syndrome and eczematous or papulosquamous dermatitis,[12]

Similar to other reports[13], pruritus, generalized scaling and erythema were found to be the most common clinical presentation of patients with exfoliative dermatitis. Other accompanying symptoms were bipedal edema, fever (T≥38°C), chills, lymphadenopathies and joint pains. A subjective chilly, sensation independent to recorded temperature is common due to excessive vasodilatation and heat loss. In other series, generalized lymphadenopathy was reported in majority of patients.[14,15] However, in this study, only 2 patients were reported to have regional (cervical and inguinal) lymphadenopathies. This could be attributed to the fact that the examining physician may have missed the others at the time of consult.

Several nail changes that can be found in exfoliative dermatitis are onycholysis, subungal hyperkeratosis, splinter hemorrhages, paronychia, and Beau's lines.[14,16] In drug- induced exfoliative dermatitis, shore-line nails with alternating bands of nail plate discontinuity can also be observed.[17] In this study, the most common nail changes recorded were nail pits and oil spots, mostly in patients with psoriatic exfoliative dermatitis. However, in a study by Jowkar *et al*. [18], onycholysis and subungal hyperkeratosis were the most reported nail findings observed in patients with exfoliative dermatitis.

Laboratory findings are most often not diagnostic for the etiology of exfoliative dermatitis. Common laboratory findings in these patients include leukocytosis, anemia, elevated erythrocyte sedimentation rate, lymphocytosis, eosinophilia, and increased serum IgE.[2,8] Other findings include elevated creatinine level, elevated uric acid level and lowered serum protein levels[8,10] In this study, the most common findings were anemia, leukocytosis and hypoalbuminemia. In a study by Kondo *et al*.[19], the most commonly reported laboratory finding associated with exfoliative dermatitis was anemia. This could be due to folic deficiency, iron deficiency, or a chronic inflammatory state.

Several factors associated with exfoliative dermatitis include previous dermatoses, drugs, and malignancy.[2,3,8,9,13] As in previous studies[2,8-10,13,14,20], the data corroborated in this study showed that pre-existing skin diseases contributed the highest percentage of exfoliative dermatitis. Among the

pre-existing dermatoses, psoriasis was the most common (34.3%) which is consistent with the other studies.[10,16,20-22] Other dermatoses associated with exfoliative dermatitis included contact dermatitis (13.4%), xerotic eczema (4.5%), atopic dermatitis (3%) and malignancy (3%) which were also mentioned by Rothe *et. al*.[23]

Topical herbal medications, which include *Psidium guajava* (guava), *Annona squamosa* (atis), *Coriandrum sativum* (cilantro) and *Tamarindus indica* (sampaloc) extracts were the leading causes of exfoliative dermatitis secondary to contact dermatitis. Skin lesions have been observed as early as 1 day after application of the said topical herbal medications.

Antiepileptic drugs, anti-hypertensive agents, antibiotics, calcium channel blockers are some of the drugs associated with exfoliative dermatitis.24 The most common oral drug that caused exfoliative dermatitis in this study was allopurinol (4.5%), which was consistent in most series.[8,10,23,25] However, this contradicted the study by Jowkar *et al*.[18], which reported an anti-epileptic drug (carbamazepine) to be the most common cause of erythroderma. Other drugs implicated in this study included dapsone (1.5%)[26,27], cefixime (1.5%), thiazide (1.5%) and statin (1.5%).

Reticuloendothelial neoplasms, internal blood vessel malignancies, as well as lymphomas have also been implicated in exfoliative dermatitis. According to Yuan *et al*.[13], mycosis fungoides and Sezary syndrome are the most malignant causes of exfoliative dermatitis. In this study, 2 patients had exfoliative dermatitis secondary to malignancy, one of pulmonary origin, the other is cutaneous T- cell lymphoma as supported by the histopathological report. Nevertheless, 21.9% of patients had exfoliative dermatitis with idiopathic or undetermined cause. These patients may represent a pre-malignant phase, and therefore, a closer monitoring period should be done in order to identify the causes so that earlier treatment could be started.[28] A comparison of the etiology of exfoliative dermatitis in various studies, including the present study is shown in **(Table 3)**.

Study Causes	Number of patients (%)							
	Pal et al.[10] (n=90)	Rym et al.[20] (n=80)	Bandyopadhyay et al.[29] (n=75)	Sudho et al.[22] (n=25)	Chaudhary et al.[16] (n=30)	Hasan et al.[25] (n=50)	Hulmani et al [21]. (n=30)	Present study (n=67)
Psoriasis	37.8	51.25	33.33	32	40	10	33.3	34.3
Eczema	12.2	7.5	4.0	12	20	16	20	4.5
Ichthyosis	7.8	0	1.33	0	0	2	0	0
Pityriasis rubra pilaris	2.2	1.25	5.33	0	0	0	3.3	0
Scabies	2.2	1.25	1.33	0	0	0	0	0
Pemphigus foliaceus	5.6	6.25	5.33	4	0	0	0	0
Lichen planus	0	1.25	0	0	0	0	0	0
Atopic dermatitis	0	0	13.33	8	6.66	14	6.6	3
Other dermatoses	6.5	3.75	0	8	0	0	0	25.4
Drug reaction	5.5	11.25	12	24	10	22	16.6	10.4
Malignancy	5.5	8.75	2.67	4	6.66	4	3.3	3
Idiopathic	14.6	7.5	21.33	8	16.66	32	16.6	19.4

Figure 3. Comparison of etiology of exfoliative dermatitis in various studies

Skin punch biopsy was not routinely performed on all patients in this study. In patients who do not have any history of previous dermatoses or recent intake of new medications, the performance of skin punch biopsy becomes more essential[14] in order identify the possible underlying etiologic factor.

In this study, 65 out of 67 patients were discharged, improved based on the clinical and laboratory findings while 2 patients expired due to acute renal failure and cardiac problem. Overall, the disease prognosis varies, depending on the underlying etiology. Drug-induced exfoliative dermatitis has an excellent prognosis upon prompt recognition and withdrawal of the offending drug. On the other hand, this condition can be fatal, especially in elderly patients. Secondary infection, dehydration, temperature dysregulation and high output cardiac failure are potential complications in most cases.[30] In the initial documented studies, the recorded death rate varies from 18-64%.[2] However, mortality rate associated with exfoliative dermatitis has decreased over time. This could be attributed to advances in the diagnosis and therapy and more importantly, a regular and close follow-up period.

CONCLUSION

This is the first local retrospective study done to describe the epidemiology of exfoliative dermatitis at University of Santo Tomas Hospital, department of Dermatology. The prevalence of this condition was computed at 1 per 1000 dermatologic patients. All patients presented clinically with pruritus, generalized scaling and erythema. Bipedal edema, fever (T ≥ 38 °C) and chills were the most common systemic manifestations that accompanied the initial presentation. The most common cause of exfoliative dermatitis was a pre-existing dermatosis, the leading cause of which was psoriasis while the most common implicated oral drug in this study was allopurinol.

LIMITATIONS OF THE STUDY

Of the total 70 cases diagnosed with exfoliative dermatitis, only 67 charts were available for review. Other limitations include inadequacies in information gathering and documentation as seen in most retrospective studies.

RECOMMENDATION

The diagnosis, as well as the identification of the possible etiology of exfoliative dermatitis, has been a great challenge to dermatologists, as well as for other clinicians. Therefore, a more complete, detailed and systematic history taking and physical examination through the development of a checklist may be helpful in order to be able to properly identify all the possible triggering factors of exfoliative dermatitis through the course and evolution of the lesions.

The performance of skin punch biopsy, as well as a thorough work-up is highly recommended, specifically for those patients with no known or identifiable underlying dermatosis or drug intake, as this may open the possibility of a malignancy- related exfoliative dermatitis.

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