

# Cutaneous Manifestations of Systemic Lupus Erythematosus - A Retrospective Study

K Uma Maheswari<sup>1</sup>, B Vijayalakshmi<sup>1</sup>, M Vasantha Kumar<sup>2</sup>, E K Jaleena<sup>3</sup>, Heber Anandan<sup>4</sup>

<sup>1</sup>Assistant Professor, Department of Dermatology, Madras Medical College and Rajiv Gandhi Government General Hospital, Chennai, Tamil Nadu, India, <sup>2</sup>Assistant Professor, Department of General Medicine, Kilpauk Medical College and Hospital, Chennai, Tamil Nadu, India, <sup>3</sup>Junior Resident, Department of Dermatology, Madras Medical College and Rajiv Gandhi Government General Hospital, Chennai, Tamil Nadu, India, <sup>4</sup>Senior Clinical Scientist, Department of Clinical Research, Dr. Agarwal's Healthcare Limited, Chennai, Tamil Nadu, India

## Abstract

**Background:** Lupus erythematosus is a systemic autoimmune disorder with polyclonal B cell activation resulting from interplay of genetic, environmental, and hormonal elements. Heterogenous clinical expression is considered a continuum or spectrum extending from limited cutaneous disorder to life-threatening systemic disease process.

**Aims:** The aim of the present study is to find the age and sex incidence, precipitating or exacerbating factors, clinical features, cutaneous manifestation of systemic lupus erythematosus (SLE) and relationship with systemic manifestations if any, laboratory profile and its relationship with disease activity.

**Materials and Methods:** A retrospective study was carried out over 1 year from May 2015 to April 2016. A total of 110 SLE patient's details who attended our hospital were collected from the medical records.

**Results:** The most common age group affected was between 2<sup>nd</sup> and 3<sup>rd</sup> decades. Female preponderance with a female to male ratio of 9:1. Photosensitivity was the most common precipitating and exacerbating factor followed by infections, mental stress, and pregnancy. The most common symptoms were fever, easy fatigability, diffuse hair loss, and arthralgia. The most common disease specific skin lesion was malar rash and nonspecific but disease related skin disease was diffuse hair loss. Musculoskeletal system was the most common system involved. Renal failure was the most common cause of death. Malar rash and oral ulcer had a parallel course with disease activity. Antinuclear antibody was positive in all patients. Patients with dsDNA positivity had severe renal involvement.

**Conclusion:** Examination of skin for disease specific as well as nonspecific lesions is important in SLE as skin is one of the most important target organs. A good knowledge about the various cutaneous manifestations will help not only in diagnosis and management but also in predicting the prognosis.

**Key words:** Antinuclear antibody, Cutaneous manifestations, Disease activity, Systemic lupus erythematosus

## INTRODUCTION

Lupus erythematosus is a systemic autoimmune disorder associated with polyclonal B cell activation that is thought to result from interplay of genetic, environmental, and hormonal elements. It is convenient to consider the heterogenous clinical expression of this disorder as

constituting disease continuum or spectrum extending from a limited cutaneous disorder to a life-threatening systemic disease process.<sup>1</sup>

Cutaneous lesions in patients with LE can be divided into two broad categories.

- LE specific skin lesions
- LE nonspecific skin lesions.

It is important to divide cutaneous lesions into LE specific and nonspecific because it is possible to make a diagnosis of LE from the histopathology of specific lesion only and not from nonspecific lesion. Nonspecific lesions are important in assessing the disease activity and are seen frequently in patients with systemic lupus erythematosus (SLE).<sup>2</sup> LE

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**Corresponding Author:** Heber Anandan, No. 10, South By-pass Road, Vannarpettai, Tirunelveli - 627 003, Tamil Nadu, India.  
Phone: +91-9894067910. E-mail: clinicalresearch@dragarwal.com

specific skin lesions are further subdivided into:

- Chronic cutaneous LE (discoid lupus erythematosus [DLE]) - localized DLE, generalized DLE, hypertrophic DLE, lupus panniculitis (lupus profundus)
- Subacute cutaneous LE (SCLE) - papulosquamous (psoriasiform) SCLE, annular polycyclic SCLE
- Acute cutaneous LE (SLE) - malar rash, wide spread erythema of sun exposed area, bullous, or toxic epidermal necrolysis (TEN) like acute cutaneous lupus erythematosus lesion.<sup>2,3</sup>

A variety of factors have been proposed to be etiologic for SLE<sup>4</sup> which include genetic factors, environmental factors, abnormalities in immune regulation, viral infection, drugs, and ultra violet rays.

Pathogenesis of SLE include abnormal production of auto antibodies and immune complexes, failure to suppress the production and proliferation of forbidden clones.<sup>5</sup> The American College of Rheumatology (ACR) criteria is used for diagnosis of SLE. Four main cutaneous manifestations are included in the ACR criteria which are malar rash, discoid rash, painless oral ulcer, and photosensitivity. Cutaneous lupus erythematosus disease area and severity index is used to assess the disease activity. It includes erythema, scaling, mucosal lesion, and nonscarring alopecia.<sup>6</sup> A better understanding of the various cutaneous manifestation of SLE is required for diagnosis, assessing the severity and prognosis, for choosing the optimum treatment option.

## MATERIALS AND METHODS

A retrospective study of the various cutaneous manifestations in SLE was conducted in the Department of Dermatology, Madras Medical College and Rajiv Gandhi Government General Hospital. Data of SLE patients who attended skin department at our hospital from May 2015 to April 2016. History regarding nature of onset, progression, precipitating or exacerbating factors and symptomatology of skin lesion and systemic manifestation was taken. Patient's clinical examination details with reference to symptomatology, morphology, and distribution of skin lesion were also noted.

Biopsy was performed to confirm the diagnosis. Specific investigation including anti-nuclear antibody titer, anti-dsDNA estimation as well as nonspecific investigation such as total count, differential count, erythrocyte sedimentation rate (ESR), hemoglobin, red blood cells and platelet count, urine examination for albumin, sugar and deposits, renal function test, liver function test, electrocardiogram, X-ray chest, physical therapy (PT), activated partial

thromboplastin time, bleeding and clotting time, Voluntary Counseling and Testing Centers, Venereal Diseases Research Laboratory was done. In addition, based on the symptoms clinical and laboratory abnormalities further tests were done if necessary including echocardiography, ultrasound abdomen, computed tomography brain, bone marrow aspiration, endoscopy, and renal biopsy.

## RESULTS

Of 110 patients, maximum patients 52 among 110 were in the age group 21-30 years (47.2%). Male to female ratio was 1:9. Youngest patient was 9-year-old girl and eldest was 65-year-old female. The mean age of onset was 27 years (Table 1).

The probable precipitating or exacerbating factor was found in 79 of the total patients. The most common precipitating or exacerbating factor was found to be photosensitivity which was seen in 66 patients (60%). Infections such as typhoid, malaria, viral fever preceded the onset of SLE in 7 patients. One patient was diagnosed to have extra pulmonary tuberculosis and was started on anti tuberculous treatment. A total of 6 patients reported worsening of symptoms with mental stress. Two patients had exacerbation of disease during pregnancy. One patient had second trimester miscarriage due to exacerbation of disease and disease worsened further after abortion (Table 2).

Fever and fatiguability was present in 100% of cases. Malar rash was the most common specific skin lesion in 73 patients (66.36%). Discoid rash was seen in 20% of patients. Two patients had DLE lesion on scalp with

**Table 1: Distribution of study patients in age group and gender**

Age group	Female	Male	Total
0-10	1	-	1
11-20	7	1	8
21-30	46	6	52
31-40	37	4	41
41-50	3	-	3
51-60	4	-	4
61-71	1	-	1
	99	11	110

**Table 2: Distribution of precipitating or exacerbating factor in study group**

Precipitating/exacerbating factor	Number of patients
Photosensitivity	66
Infection	7
Mental stress	6
Pregnancy	2

scarring alopecia and depigmentation. Mucous membrane lesion was seen in 70% of patients, most commonly involving hard palate and buccal mucosa. Other mucosal lesions seen were gingivitis, glossitis, nasal ulceration, blepharitis, and conjunctivitis. Two patients had extensive erosions of oral cavity and erosion over labia majora.

Diffuse hair loss was mainly in the form of non-scarring alopecia in 88 patients (80%). Scarring alopecia was seen in only seven patients (6.36%). Bluish discoloration of finger nail and or toe nail was seen in 18 patients (16.36%). Among this, three patients had discoloration from the onset of disease. 2 patients were on chloroquine treatment for 3 months and showed bluish discoloration of all finger and toe nail and in one patient lunula was absent. Raynaud's phenomenon was present in 11 patients (10%). Other vascular lesions noticed were leg ulcers in 11 patients (10%), palpable purpura, peripheral gangrene, and erythema multiforme.

Systemic manifestations include musculoskeletal problems mainly arthralgia in 95 (86.36%), renal in 51 (46.36%), central nervous system including seizure, psychosis, hemiparesis, poor memory in 47 (42.72%), gastrointestinal and pulmonary complication in 15 (13.63%) patients each, eye involvement in the form of conjunctivitis, blepharitis, retinal hemorrhage, and lymphadenopathy were noted in 7 patients (6.36%) each. Menstrual irregularities were seen in 4 patients (3.63%).

Associated skin diseases were ichthyosis vulgaris in 11 patients (10%), chronic eczema in 8 patients (7.3%), superficial fungal infections including tinea cruris and pedis, pityriasis versicolor, oral candidiasis in 22 patients (20%), scabies in 7 patients (6.36%), and herpes zoster in 4 patients (3.63%) (Table 3).

**Table 3: Distribution of disease specific and nonspecific lesion in study group**

Lesions	Patients (%)
Disease specific lesions	
Malar rash	73 (66.36)
Discoid rash	22 (20)
Oral ulcer	77 (70)
Nonspecific lesion	
Alopecia	
Non scarring alopecia	88 (80)
Scarring alopecia	7 (6.36)
Nail change	18 (16.36)
Vascular	
Raynaud's phenomenon	11 (10)
Leg ulcer	11 (10)
Palpable purpura	7 (6.36)
Peripheral gangrene	4 (3.63)
Erythema multiforme	7 (6.36)

Laboratory abnormalities in 103 (93.63%) patients showed increased ESR, whereas 73(63.36%) patients had anemia. Thrombocytopenia was noted in 15 patients (13.63%). Deranged renal parameters were seen in 51 (46.36%) patients. All patients were positive for AntiNuclear Antibodies, 110 patients. Anti dsDNA was positive in 66 (60%) patients. Anti Cardiolipin antibodies and RF factor in 4 patients (3.63%). Renal biopsy with evidence of lupus nephritis was seen in 59 (53.63%).

Five patients had active disease flare up and succumbed to its complication. Three patients died due to end stage renal disease, one patient due to multiple cerebral infarctions and one patient due to TEN following anti tuberculous treatment.

## DISCUSSION

SLE is a multiorgan autoimmune disease of unknown etiology with many clinical manifestations. The skin is one of the target organs most variably affected by the disease.<sup>7</sup>

Evidence for genetic factor involvement is due to occurrence of SLE in monozygotic twins and familial cases, studies from dermatoglyphics, increased the incidence of connective tissue disease, antinuclear antibody (ANA) positivity, hyperglobulinemia in patients relatives and HLA association particularly HLA B8,HLA DR 3.<sup>7</sup>

Sex hormones are known to influence SLE, an autoimmune disease as estrogens enhance immuno enhancing, whereas androgens are immunosuppressive.<sup>8</sup> In this study, females predominated with female to male ratio of 9:1 comparable to study by Rowell *et al.*<sup>9</sup> and Malaviya, *et al.*<sup>10</sup> in which a female to male ratio was 8:1. Another study by Kole and Ghosh reported a ratio of 14:1.<sup>11</sup>

Peak age of onset was 27 years in this study. Higher mean age of onset was noted by Masi *et al.*<sup>12</sup> as 31 years and 3<sup>rd</sup> to 4<sup>th</sup> decade by Rowell<sup>9</sup> whereas 25 years by Kole and Ghosh<sup>11</sup> 24 years by Malaviya.<sup>10</sup> Even though SLE is considered a disease of young adults, the oldest age of onset was reported as 87 years by David *et al.*<sup>9</sup> In the present study group, the oldest age of onset was observed to be 65 years.

In this study, photosensitivity was present in 60% of patients and was the probable precipitating or exacerbating factor and the incidence was same as noted by Rowell *et al.*<sup>11</sup> LE specific skin lesion malar rash was seen in 66.36% comparable to study by Sontheimer<sup>13</sup> who quotes that the maximum occurrence of about 61%. Wysenbeek, *et al.*<sup>14</sup> reported malar rash in 49% and Vaidya, *et al.*<sup>15</sup> 53.18% of

the patients. Discoid rash was present in 20% of patients comparable to the observed the incidence of 20-50% by David *et al.*<sup>8</sup> The incidence of oral ulcer was 70% in this study which was very high when compared to 9.1% reported by Dubois<sup>16</sup> 64% by Malaviya<sup>10</sup> 56.67% by Kole and Ghosh.<sup>11</sup> Malar rash and oral ulcer had a parallel course with disease activity.

Hair loss was present as nonscarring alopecia in 86% and scarring alopecia in 6.3%, comparable to study by Kole and Ghosh<sup>11</sup> as 86.67% higher number than reported by Gilliam *et al.*<sup>17</sup> as 60% and 57% noted by Wysenbeek<sup>14</sup> of nonscarring hair loss. Bluish nail discoloration was seen in 16.36 % similar reports by kapadia.<sup>18</sup>

Among vascular lesions Raynauds phenomenon was the most common in 10% of patients similar to study by Kole and Ghosh<sup>11</sup> 6.67% of the cases, higher numbers were reported by Malaviya, *et al.*<sup>10</sup> 32% and Vaidya, *et al.*<sup>15</sup> 15.5%. Three patients had oral ulcer along with Raynauds phenomenon. The incidence of peripheral gangrene was observed to be 3.63% compared to higher reports of 9% by Moschella.<sup>2</sup> Leg ulcers were present in 10% of patients in accordance with reports of 5 to 29% by David *et al.*<sup>8</sup> 2 patients with leg ulcers had classical SLE manifestation along with reduced platelet count and hypocomplementemia [c3,c4] which may account for chronicity of leg ulcer. In one patient who had associated rheumatoid arthritis the leg ulcer was chronic and persistent probably due to overlap of SLE and rheumatoid arthritis. 7 patients had SLE with EMF overlap (Rowells) with typical target lesions and extensive oral ulceration almost similar to incidence quoted by David *et al.*<sup>8</sup> In one case of childhood SLE the disease had a florid course with extensive photosensitivity, lymphadenopathy, pneumonia and peri orbital puffiness. In addition to increased ESR and mild thrombocytopenia, ANA and anti ds DNA were positive. In spite of all bad prognostic factors patient remarkably improved with systemic steroids.

Elderly patients with SLE are characterized by a milder serological picture, infrequent renal disease and more Serositis and arthritis.<sup>16</sup> The oldest patient in our study group with 65 years had severe arthritis, easy fatigability, fever, malar rash, nonscarring alopecia and contrary to reports had puffiness of face and evidence of renal involvement which is usually infrequent in elderly.

Among the hematological abnormalities, a raised ESR was found in 93.63%; even though, it may not be specific but helpful in assessing the severity of the disease. Anemia was detected in 63.36% of patients which was in accordance with reports of 50% by Dubois.<sup>16</sup> Anemias can result from chronic disease, auto immune hemolysis, iron deficiency,

and chronic renal failure. Thrombocytopenia was present in 13.63% of patients correlating well with 14% incidence reported by Dubois.<sup>16</sup> One patient had decrease in PT and partial thromboplastin time. This patient had a history of spontaneous abortion along with flare up of SLE and decreased complement level. ANA was positive in all patients in this study. Nearly 60% of patients had positive anti ds DNA positivity and had severe renal involvement. One case of antiphospholipid syndrome in a female patient with 24 years had a family history of dermatomyositis in father supporting genetic factor in etiology of SLE.

Vasculitic skin lesions in some cases are associated with neuropsychiatric manifestations of lupus.<sup>19</sup> Such an association was not seen in the present study. Patients having bullous skin lesions had systemic flares that were reported by Malcangi *et al.*<sup>20</sup> An association between concomitant lupus nephritis and bullous lesions had been documented by Ng *et al.*<sup>21</sup>

## CONCLUSION

Lupus erythematosus is a systemic disease with varied systemic as well as cutaneous manifestations. About 90% of patients have involvement of skin. Skin lesions can help in the diagnosis of SLE as well as to assess the severity, prognosis and also help in the management of SLE. Not only the specific lesion but nonspecific disease related skin lesions also play an important role in SLE as the disease severity is seen to go parallel with skin lesions. Better understanding of cutaneous lesions can help in providing better care to patients.

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