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Mucocutaneous manifestations of Systemic Lupus Erythematosus and their correlation with disease activity assessed by SLEDAI in a tertiary care hospital of North-East India: a cross-sectional study

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ABSTRACT

Background: Systemic lupus erythematosus (SLE) is a chronic autoimmune disorder with mucocutaneous manifestations, which can precede or co-exist with other systemic features and provide important clues to diagnosis and management. Regional variations in the phenotypic expression of these features remain insufficiently documented. **Aims and objectives:** To study the mucocutaneous manifestations among patients with SLE and their correlation with disease severity. **Materials and Methods**: A cross-sectional observational study was conducted among SLE patients in a tertiary centre in Northeast India for 1 year. 64 patients were examined. The mucocutaneous manifestations were classified as lupus-specific or lupus-nonspecific and their correlation with disease severity was assessed by the Systemic Lupus erythematosus Disease Severity Index (SLEDAI) score. **Results**: Lupus-specific manifestations included malar rash in 92.19% of patients, maculopapular eruption in 40.63%, and chronic discoid lupus lesions in 12.5%. Lupus-nonspecific manifestations comprised photosensitivity in 93.75%, alopecia in 92.19%, mucosal ulceration in 64.07%, facial edema in 26.56%, purpuric lesions in 20.31%, telangiectasia in 17.19%, vasculitis in 12.5%, and Raynaud's phenomenon in 3.13%. High disease activity, defined as a SLEDAI score above 10, was observed in 50% of patients. Photosensitivity, malar rash, alopecia, mucosal ulceration, maculopapular eruption, purpura, and vasculitic manifestations demonstrated significant associations with disease activity, while active mucosal ulcers were particularly frequent among patients with very high SLEDAI scores. **Conclusion**: Mucocutaneous features are highly prevalent and diverse among SLE patients from the Indian subcontinent and their recognition along with systematic assessment of disease activity may facilitate early diagnosis and timely intervention through multidisciplinary management.

Keywords: *SLE, mucocutaneous, SLEDAI, disease severity, cutaneous lupus.*

INTRODUCTION

Systemic Lupus Erythematosus (SLE) is a systemic disease is a chronic, heterogenous autoimmune disorder characterized by the association of immunological abnormalities and widespread inflammation affecting various organ systems, particularly affecting young women.[1,2] This complex condition results in diverse clinical features including hematological, renal and neurological abnormalities.[3] Mucocutaneous involvement serves as one of the most significant features of this disease, appearing in approximately 70-85% of patients at some point of time and may precede systemic involvement in 20-25% of patients[2]. Considering that cutaneous lesions frequently precede severe organ involvement, their prompt identification is crucial to improve clinical management and prevent morbidity[4]. Genetic predisposition and regional environmental factors in a particular demographic may also influence the phenotypic expression and frequency of

mucocutaneous manifestations in SLE[5]. Monitoring of these mucocutaneous lesions may help in assessing disease severity and monitor prognosis.

The mucocutaneous manifestations of SLE are classified according to Gillian and Sontheimer into lupus specific lesions which include acute cutaneous lupus erythematosus (ACLE), subacute cutaneous lupus erythematosus (SCLE), and chronic cutaneous lupus erythematosus (CCLE) —and lupus-nonspecific lesions, including alopecia, oral ulcers, photosensitivity, Raynaud's phenomenon, vasculitis, livedo reticularis, purpura, and bullous lesions [6]. This distinction gives important clues regarding the disease as lupus specific lesions help in diagnosing the disease whereas lupus non-specific lesions may indicate concurrent systemic activity [7].

Clinical observation in Indian patients indicate a particularly high prevalence of malar rash, photosensitivity, oral ulceration and alopecia [2] . Malar rash is reported by 80% of patients by Kole and Ghosh [8] becoming the most frequently reported LE specific lesion, followed by photosensitivity and diffuse maculopapular rash.

Another study in the Indian subcontinent indicate a particularly high prevalence of photosensitivity and chronic discoid lesions, often appearing as key diagnostic indicators of disease activity [9] . Beyond these specific lesions, non-specific findings such as alopecia, periungual telangiectasias, and vasculitic changes are frequently observed, necessitating histopathological verification to differentiate them from common dermatoses [10]

There are several disease severity indices used to monitor progress of disease in SLE and CLE (Cutaneous Lupus Erythematosus) such as SLEDAI (Systemic Lupus Erythematosus Disease Activity Index), SLEDAI-2K (Systemic Lupus Erythematosus Disease Activity Index-2000), CLASI (Cutaneous Lupus Erythematosus Disease Area and Severity Index) and SLICC/ACR Damage Index. The goal of these indices is to control activity and prevent damage which is often irreversible. [7]

SLEDAI incorporates selected mucocutaneous manifestations assigning points for alopecia, oral or nasal ulcers, new inflammatory rash, and vasculitis, with vasculitic features receiving greater weight because of their association with potentially severe vascular and systemic involvement [7]. SLEDAI-2K retains the same structure and scoring range, however allows for scoring of persistent inflammatory rash and other ongoing manifestations , thereby improves follow up assessments. Both SLEDAI and SLEDAI-2K are mainly systemic indices and evaluate skin only as a limited component of overall disease activity. In contrast, the CLASI was developed s[specifically for cutaneous activity and damage, distinguishing reversible erythema, scale and mucosal disease from irreversible dyspigmentation, scarring, atrophy and alopecia. [11]

Accordingly, SLEDAI or SLEDAI-2K is appropriate for estimating overall disease activity, whereas CLASI provides a more sensitive measure of cutaneous burden, longitudinal change and accumulated dermatological damage.

AIMS AND OBJECTIVES:

1. To study the mucocutaneous manifestations in patients of SLE.
2. To study the correlation between mucocutaneous manifestations with disease severity in SLE using the SLEDAI score.

MATERIALS AND METHODS:

Study setting:

This was a cross sectional observational study carried out among the SLE patients attending the Dermatology and Medicine Outpatient Department of a tertiary hospital from the north eastern part of India. The study was conducted for a period of 1 year.

Inclusion criteria:

All patients who presented to the Dermatology or Medicine outpatient department during the study period and fulfilled the ACR criteria of SLE irrespective of age and sex and gave written informed consent were included in the study.

Exclusion criteria:

1. Patients who presented with features of overlap syndrome or mixed connective tissue disorder.
2. Patients who were on medications with a potential to alter findings of mucocutaneous examination such as cytotoxic drugs for non SLE indications.
3. Patients who denied to give written and informed consent.

Data Collection and study procedure:

After obtaining written and informed consent, the patients were enrolled in the study and detailed history was obtained from each patient. Each patient was asked thoroughly about age, duration of illness, the initial manifestations, constitutional symptoms like fever, malaise, weight loss, anorexia, nausea and generalized weakness, type of skin lesions and their

distribution and other systemic illnesses. They were being asked about the factors responsible for initiation of the disease and the factors which may lead to flare up of the disease process especially intercurrent infection, mental and physical stress, occupation, drugs and duration of sun exposure . The premenstrual flareups, menstrual irregularity, about the use of oral contraceptive pills and a thorough obstetrical history regarding any flareup during or after pregnancy was recorded in the proforma. The patients were also asked about their family history, past illnesses and any associated diseases and recorded in the proforma.

General physical examination, relevant systemic examination followed by a detailed mucocutaneous examination was done for each patient. Special care was taken to look for both LE specific and LE non-specific lesions as per a pre-defined proforma based on the classification given by Gillian et al. Photographic evidence of mucocutaneous lesions were obtained from each patient.

Complete Blood Count (CBC), Liver Function test (LFT), Renal Function Test (RFT), blood sugar profile, 24 hours urinary protein test, serological test for syphilis, chest Xray (CXR), ANA Profile test and test for Rheumatoid Factor (RF) was done for all patients.

Other investigations such as Electrocardiography (ECG), Ultrasonography (USG) , Magnetic resonance imaging (MRI) and skin biopsy for histopathology were done if indicated.

ASSESSMENT OF SEVERITY OF DISEASE ACTIVITY IN SLE:

The criteria for assessment of severity of disease process of SLE were based on the Systemic Lupus Erythematosus Disease Activity index (SLEDAI). The grading was done as follows:

SLEDAI score= 0 : no disease activity
SLEDAI score = 1-5 : mild disease activity
SLEDAI score = 6 to 10 : moderate disease activity
SLEDAI score >10 and <20 : high disease activity
SLEDAI score >20 : very high disease activity. [12, 13]

STATISTICAL CORRELATION:

In this study, the statistical correlation between cutaneous lesions and SLEDAI was done through factor analysis. Factor loading with more than 0.6 indicates very good association between variables under study so far as health data is concerned.

0.8 – 1.0	Very Strong
0.6 – 0.8	Strong
0.4 – 0.6	Moderate
0.2 – 0.4	Weak
0.0 – 0.2	Very Weak

RESULTS:

The study enrolled a total of 64 patients who presented to the outpatient departments of Dermatology and Medicine of a tertiary medical centre in North-East India over a 12-month duration. Participants were selected based on the American College of Rheumatology criteria for the diagnosis of SLE, ensuring consistency in the identification of systemic involvement All patients underwent a comprehensive dermatological assessment to document specific mucocutaneous lesions, which were subsequently analysed for their correlation with systemic disease activity markers.

Out of a total of 14393 patients who attended the Dermatology and Medicine OPD during the study period, only 64 were diagnosed as SLE, the incidence rate being 0.44% (2.76/1,00,000). Out of the 64 patients, 61 (95.31%) were females and only 3 (4.61%) were males. The age of the patients ranged from 10 to 58 years. (Table 1)

Table 1: shows the demographic profile of the study population.

Parameter	**Number and percentage (%)**
Total patients	64
Female	61 (95.31%)
Male	3 (4.61%)
Age group (in years)	
0-10	2 (3.13%)
11-20	16 (25%)
21-30	27 (42.19%)
31-40	15 (23%)
41-50	3 (4.69%)
51-60	1 (1.56%)

Table 1: shows the demographic profile of the study population.

Family history was positive in only 1 patient (1.56%) . Fourteen (21.86%) of total 64 cases, had a duration of illness in the range of less than 1 year, followed by 28 (43.75%) cases had a duration of illness in the range of 2 year to less than 5 years; 19 (29.69%) cases had duration of illness in the range of 6 years to less than 10 years and only 2 (3.13%) cases in the range of 11 years to less than 15 years duration. Only 1 (1.56%) case had duration of illness over 15 years. A total of 42 (65.61%) cases presented within a period of 5 years. Mean duration of illness was 3.5 years. The shortest period recorded being 20 days and the longest duration observed was 17 years (Figure 1).

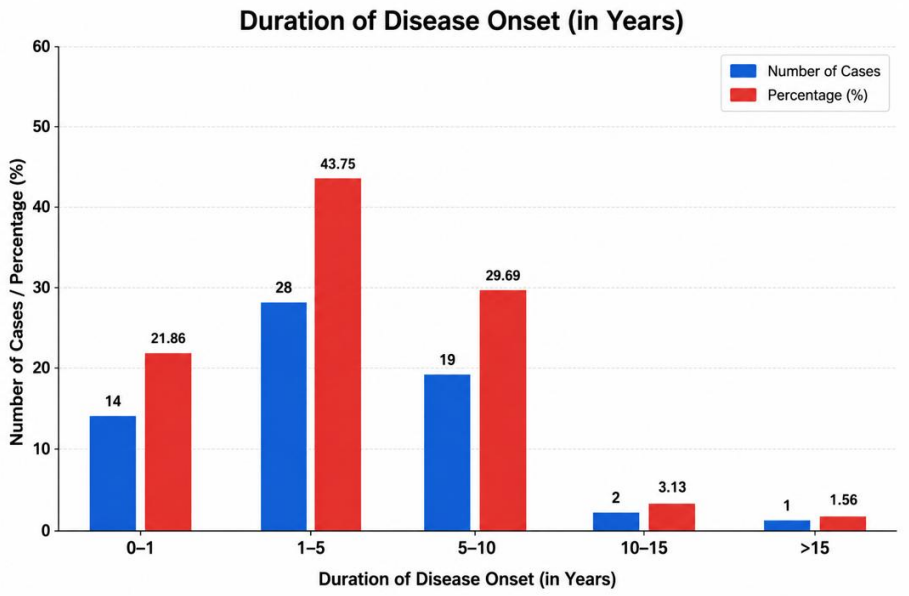

Figure 1: Represents the duration of disease onset in the study population.

It was seen that stress played a major role in precipitating the disease. Out of 64 patients 32 (50%) had stress as a precipitating factor in which mental stress was found in 22 (34.38%) patients, followed by physical stress in 10 (15.62%) patients and both were present in 10 (15.62%) patients. The next important precipitating factor was prolonged sun-exposure in 22 (34.38%) patients, premenstrual flareup was present in 10 (15.62%) patients, postpartum flareup found in 7 (10.94%) patients and intercurrent infection was found in 5 (7.81%) patients. (Table 2)

Table 2: shows the precipitating factors of the disease in our patients.

PRECIPITATING FACTORS	NUMBER OF CASES	PERCENTAGE (%)
Stress:	32	**50.00**
◆ **Mental**	22	**34.38**
◆ **Physical**	10	**15.62**
◆ **Both**	10	**15.62**
Prolonged Sun Exposure	22	**34.38**
Premenstrual Flare Up	10	**15.63**
Postpartum Flare Up	7	**10.94**
Intercurrent Infection	5	**7.81**
Drugs	0	**0.00**
OCP	**0**	**0.00**

Table 2: shows the precipitating factors of the disease in our patients.

It was found that constitutional symptoms were present in 48 (75%) patients out of 64 patients at the time of presentation. All the 48 patients had multiple constitutional symptoms present at the time of examination. (Table 3)

Table 3: shows the constitutional symptoms present in our study population.

CONSTITUTIONAL SYMPTOM	NUMBER OF CASES	PERCENTAGE (%)
Fever	37	57.81
Malaise	37	57.81

Generalised Weakness	34	53.12
Anorexia	33	51.56
Nausea	15	23.44
Weight Loss	6	9.38

Table 3: shows the constitutional symptoms present in our study population.

All of the patients had mucocutaneous involvement at the time of presentation (100%). Photosensitivity was the most frequent mucocutaneous manifestation, occurring in 60 patients (93.75%), followed by malar rash and alopecia in 59 patients each (92.19%); diffuse non-scarring alopecia accounted for most cases of hair loss (87.5%). Oral ulcers were present in 41 patients (64.06%), while maculopapular eruptions occurred in 26 (40.63%), facial oedema in 17 (26.56%), purpuric lesions in 13 (20.31%), telangiectasia in 11 (17.19%), and chronic discoid lesions and vasculitis in 8 patients each (12.5%). (Figures 2,3) .

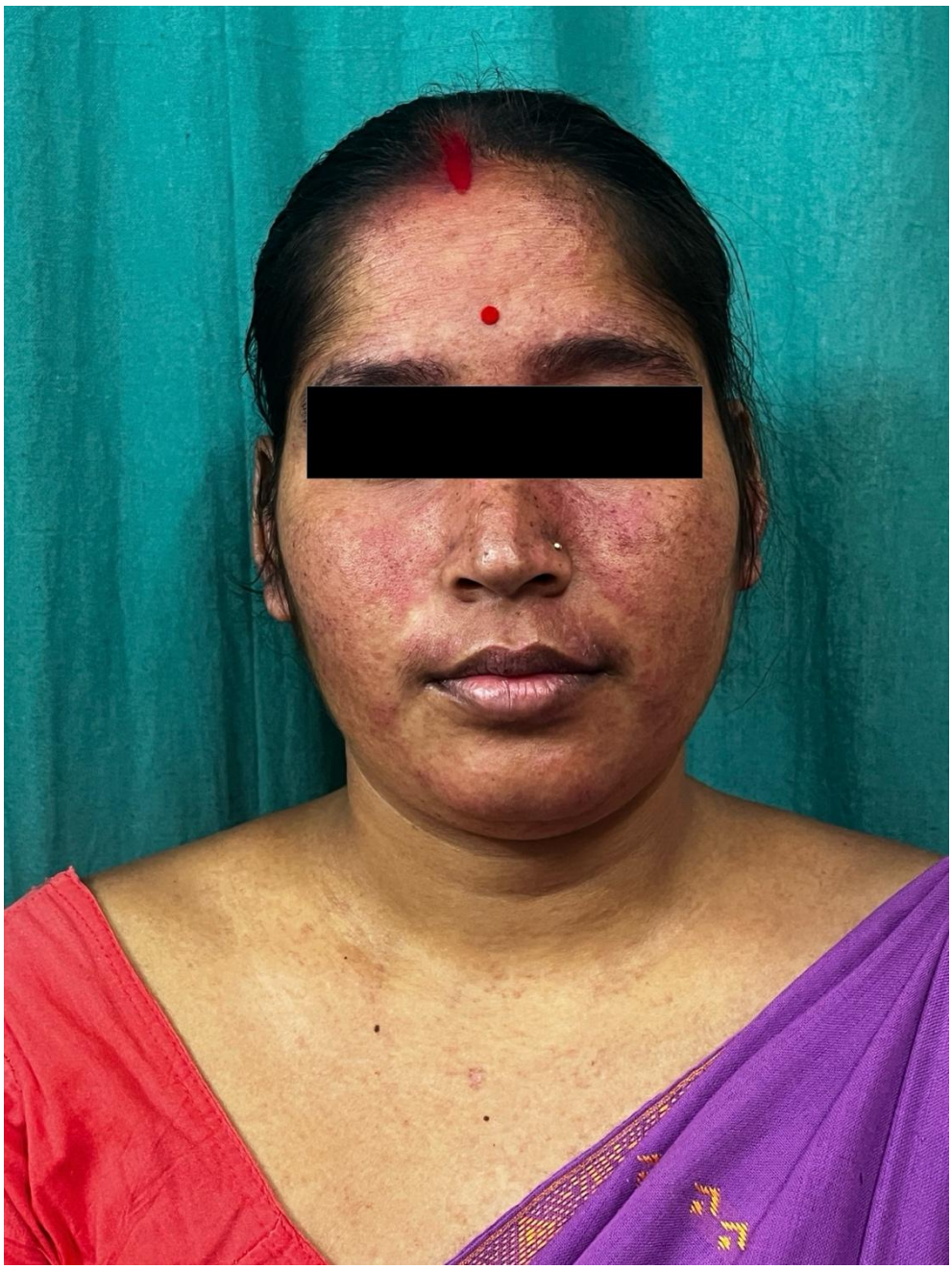

Figure 2: 38 year old female with malar rash and photosensitivity.

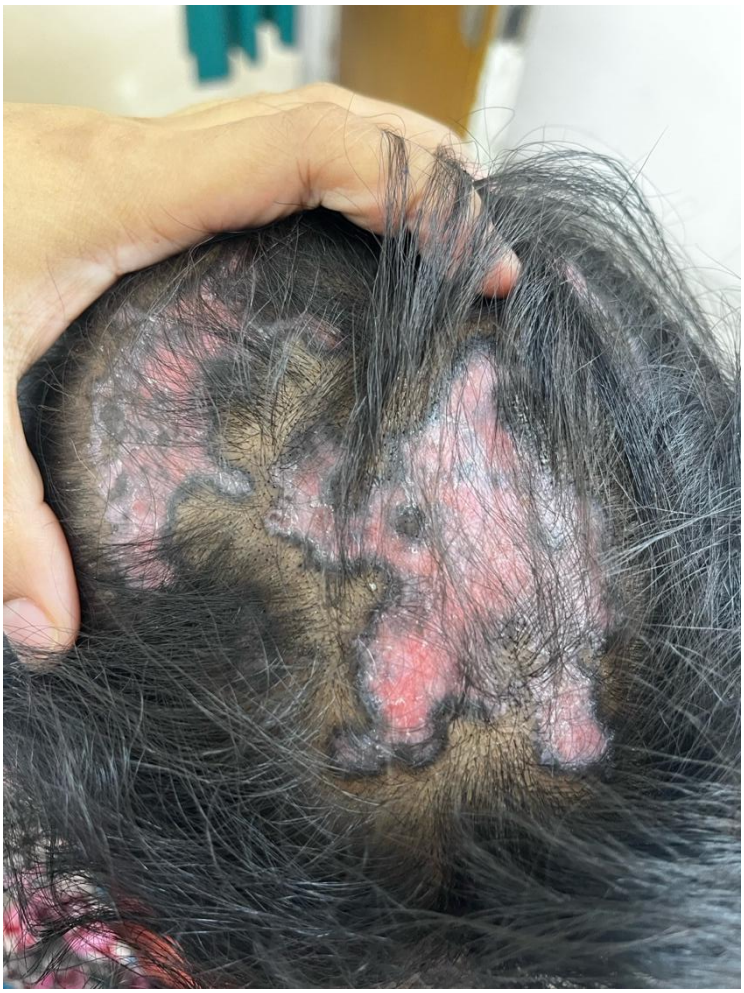

Figure 3. Chronic discoid lupus erythematous lesion present on the scalp of a 26-year-old female.

Out of 64 patients 33 (51.56%) patients had skin manifestations as the initial presenting sign of the disease. The rest developed skin lesions during the disease process. (Table 4)

Table 4 represents the various mucocutaneous manifestations seen in our patients.

MUCOCUTANEOUS SYMPTOMS	NO. OF CASES	PERCENTAGE (%)
Photosensitivity	60	93.75
Malar Rash	59	92.19
Alopecia	59	92.19
• Diffuse Non–Scarring Alopecia	56	87.5
• Lupus Hair	2	3.13
• Scarring Alopecia	1	1.56
Maculopapular Eruption	26	40.63
Oral Ulcers	41	64.06
• Healed Oral Ulcers	26	40.63
• Active Oral Ulcers	15	23.44
Facial Oedema	17	26.56
Purpura, Petechiae, Ecchymosis	13	20.31
Telangiectasia	11	17.19
Chronic DLE	8	12.50
Vasculitis	8	12.50
Urticaria	5	7.81
Palmo – Plantar Erythema	3	4.69
Raynaud's Phenomenon	2	3.13

Pigmentary Changes	2	3.13
Digital Ulceration	2	3.13
Leg Ulcers	1	1.56

Table 4 represents the various mucocutaneous manifestations seen in our patients.

Systemic involvement was predominantly musculoskeletal (92.19%) and renal (59.36%), with additional gastrointestinal, cardiac, respiratory, and central nervous system involvement documented in 35.94%, 20.31%, 14.06%, and 10.94% of patients, respectively.

Laboratory abnormalities included raised erythrocyte sedimentation rate (81.25%), albuminuria (68.75%), anaemia (51.56%), proteinuria exceeding 0.5 g/day (43.75%), thrombocytopenia (23.44%), and increased serum creatinine (17.19%); ANA was positive in 87.5% and anti-dsDNA antibodies in 31.25% of cases.
Disease activity was mild in 10 (15.63%) , moderate in 22 (34.37%), high in 27 (42.19%), and very high in 5 (7.81%) patients, with photosensitivity, facial oedema, maculopapular eruption, alopecia, mucosal ulcers, purpura, and Raynaud's phenomenon or vasculitis showing significant associations with higher SLEDAI scores. (Figure 4)

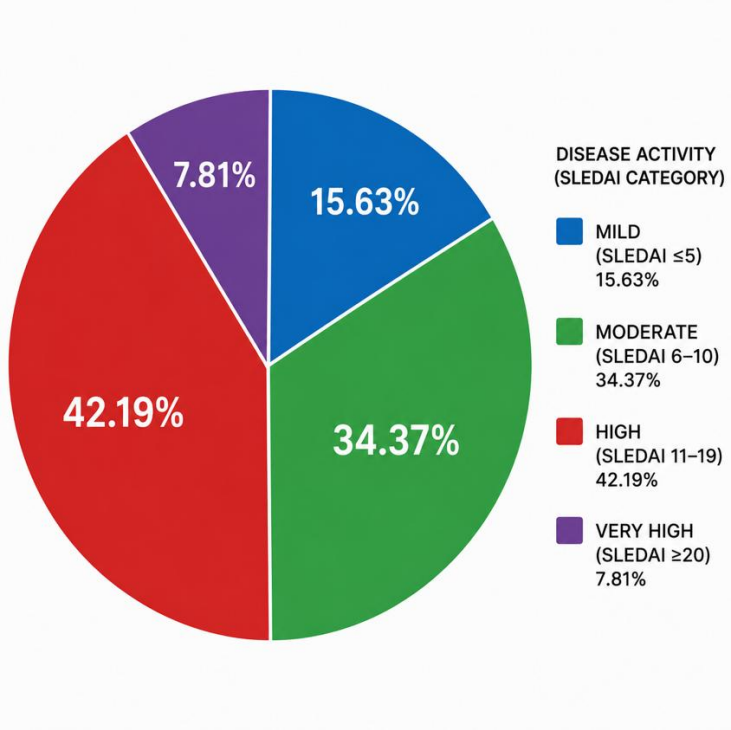

Figure 4 shows the percentage of patients in each disease activity category as per the SLEDAI score.

Most patients with malar rash, photosensitivity, and alopecia had moderate-to-high disease activity, with the largest numbers in the SLEDAI 11–19 category. Among the 59 patients with malar rash, 6 had SLEDAI 0-5, 19 had scores of 6–10, 29 had scores of 11–19, and 5 had scores above 20. Similarly, of the 60 patients with photosensitivity, 7 had SLEDAI ≤ 5, 19 had scores of 6–10, 29 had scores of 11–19,, and 5 had scores above 20. Of the 59 patients with alopecia, 5 had SLEDAI ≤ 5 , 23 had scores of 5–10, 26 had scores of 11–19, and 5 had scores above 20.

Mucosal ulcers and maculopapular eruptions were also more frequent among patients with moderate-to-high disease activity. Of the 41 patients with mucosal ulcers, 2 had SLEDAI ≤ 5, 16 had scores of 6–10, 18 had scores of 11–19, and 5 had scores above 20. Among the 26 patients with maculopapular eruptions, 3 had SLEDAI ≤ 5, 9 had scores of 5–10, 10 had scores of 11–19, and 4 had scores above 20.

Facial oedema, purpura, Raynaud's phenomenon or vasculitis, and palmo-plantar erythema were less common but were mainly observed in patients with higher SLEDAI scores. None of the 17 patients with facial oedema had a SLEDAI score below 5; 5 patients had scores of 5–10, 9 had scores of 11–19, and 3 had scores above 20. Among the 13 patients with purpura, 1 had SLEDAI ≤ 5, 2 had scores of 5–10, 7 had scores of 11–20, and 3 had scores above 20. Of the 9 patients with Raynaud's phenomenon or vasculitis, 2 had scores of 5–10, 4 had scores of 11–19, and 3 had scores above 20. Of the 8 patients with palmo-plantar erythema, 1 had SLEDAI <5, 1 had scores of 5–10, 5 had scores of 11–19, and 1 had a score above 20. (Figures 5-7)

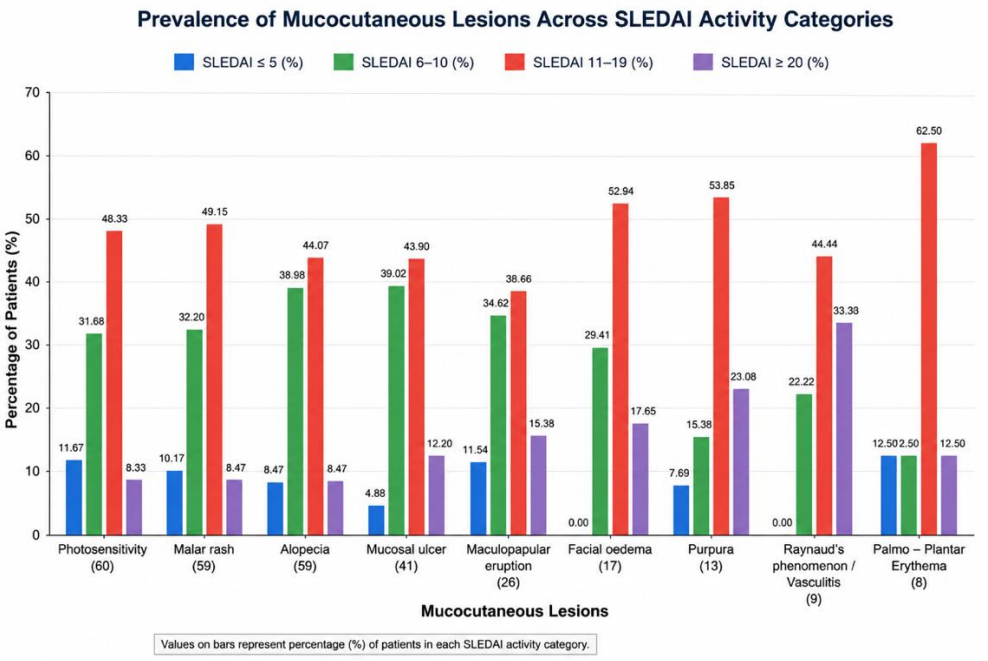

Figure 5 shows the various mucocutaneous manifestations across the different categories of disease severity as per SLEDAI.

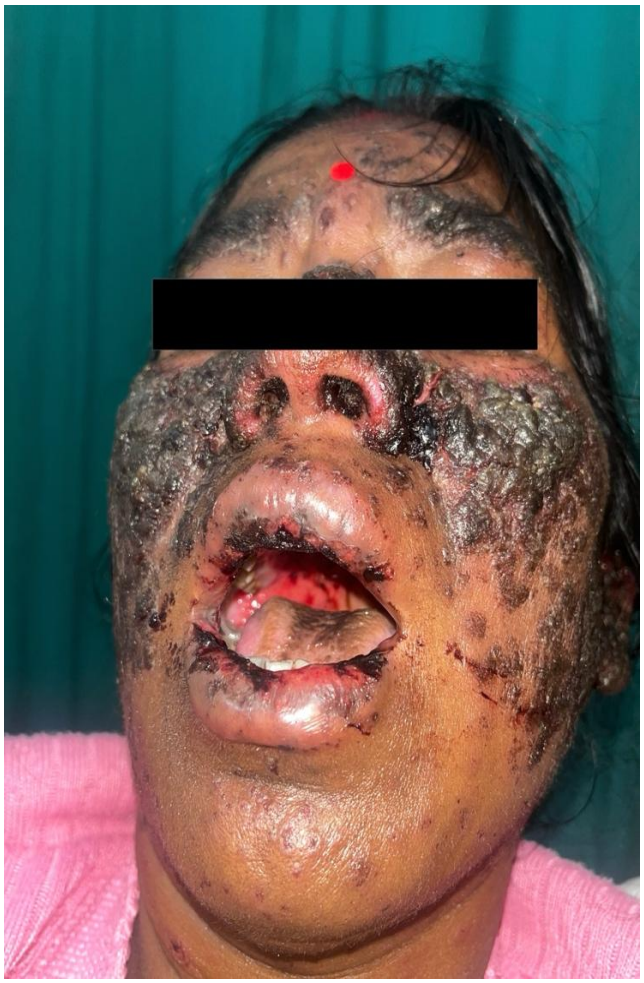

Figure 6 : 48 year old female with Toxic Epidermal Necrolysis (TEN) like presentation of SLE with bullous skin lesons and mucosal ulcers. Disease activity was very high , SLEDAI ≥20.

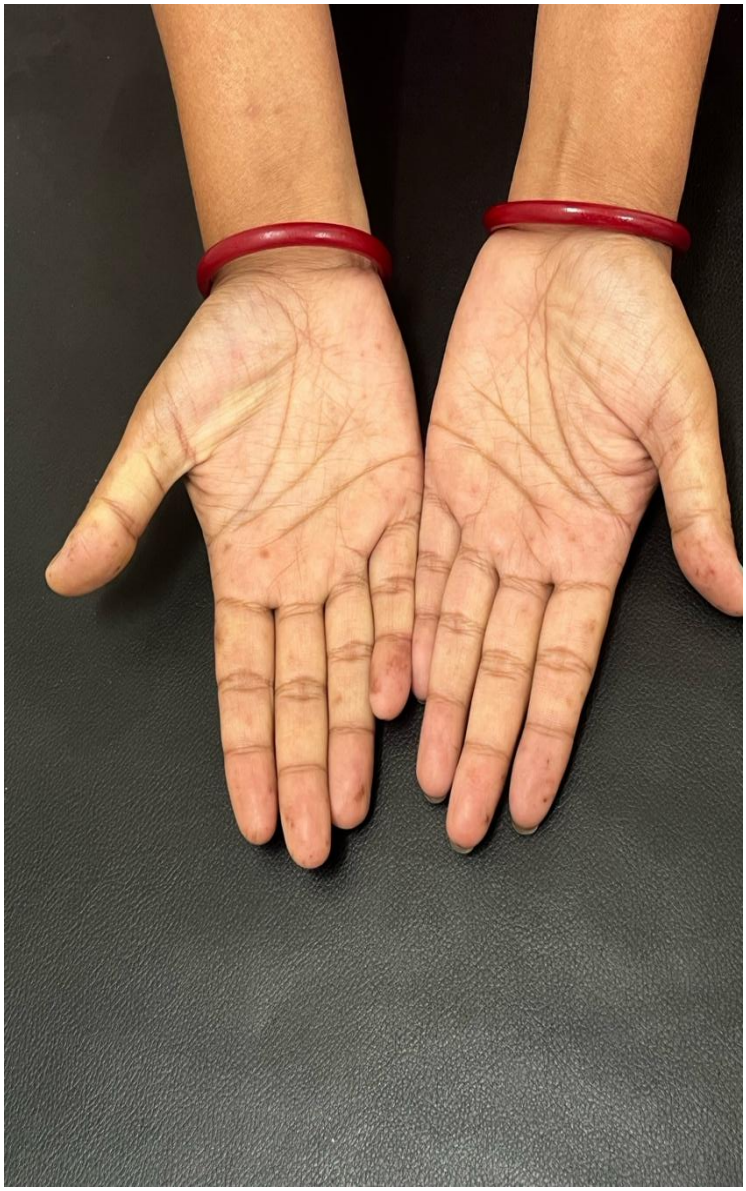

Figure 7 : Vasculitic lesions on the palms of a 45 year old female. Disease activity was very high, SLEDAI ≥20
Overall, the findings indicate that active cutaneous manifestations were more common in patients with moderate-to-high systemic disease activity.

The statistical correlation between cutaneous lesions and SLEDAI was done through factor analysis. Factor loading value of 0.0-0.2 indicates very weak (VW), 0.2-0.4 indicates Weak (W) association, 0.4-0.6 indicates Moderate (M) association, 0.6-0.8 indicates Strong (S) association and 0.8-1.0 indicates Very Strong (VS) association.

SLEDAI 6–10 shows a very strong association with photosensitivity (0.880) and facial oedema (0.821) whereas it shows a strong association with malar rash (0.689), maculopapular eruption (0.782), Palmo - Plantar erythema (0.686), alopecia (0.739), mucosal ulcer (0.783), purpura (0.776) and Raynaud's / vasculitis (0.635). There were no cases of facial oedema and vasculitis which had a SLEDAI ≤ 5 which signifies that their presence is almost always associated with high disease activity.

SLEDAI 10–19 shows a very strong association with maculopapular eruption (0.834), Palmo- Plantar erythema (0.926), photosensitivity (0.883), alopecia (0.837) and mucosal ulcer (0.846), whereas it shows a strong association with malar rash (0.793), facial oedema (0.796), purpura (0.787) and Raynaud's / vasculitis (0.734). (Figure 8)

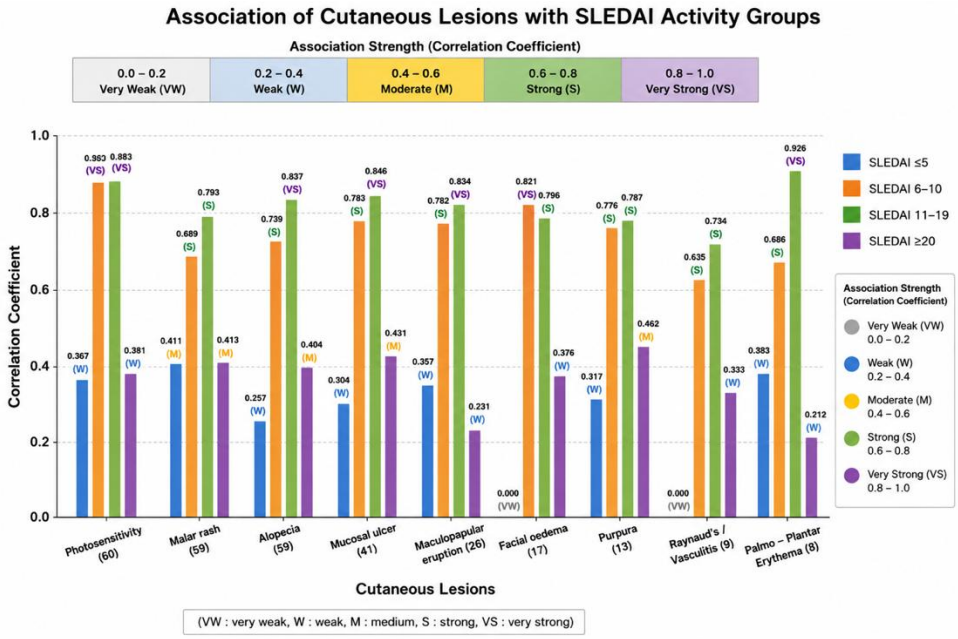

Figure 8 depicts the association of various mucocutaneous lesions with disease severity as per SLEDAI score.

SLEDAI ≤ 5 and SLEDAI ≥ 20 do not show a significantly strong association with the cutaneous lesions.
The overall association ($\chi 2$) of 78.28 is significant at 27 d.f. with p value of 0.0027.

DISCUSSION

The present hospital based cross sectional study helps to confirm that mucocutaneous manifestations in SLE are not mere clinical features but they are useful indicators of systemic activity. Photosensitivity and malar rash were the predominant manifestations, followed by alopecia and mucosal ulcers, while facial oedema, purpura, Raynaud's phenomenon or vasculitis, and palmo-plantar erythema were less frequent. The concentration of photosensitivity, malar rash, alopecia, mucosal ulcers, maculopapular eruptions, facial oedema, purpura, and Raynaud's phenomenon or vasculitis in the SLEDAI 10–19 category suggests that these lesions may serve as useful clinical markers of active disease rather than merely representing isolated dermatological findings. In the present study, the factor-analysis coefficients further supported this relationship: SLEDAI 5–10 showed very strong associations with photosensitivity and facial oedema, whereas SLEDAI 10–19 showed very strong associations with maculopapular eruption, palmo-plantar erythema, photosensitivity, alopecia, and mucosal ulcers; the overall association was statistically significant, with $\chi^2 = 78.28$ and $p = 0.0027$. The absence of facial oedema and Raynaud's phenomenon or vasculitis in patients with SLEDAI <5 is clinically notable, suggesting that their presence may serve as warning for severe disease. An Indian retrospective study found that certain cutaneous features such as malar rash, photosensitivity, non-scarring alopecia, oral ulcers and vasculitis were associated with systemic involvement when assessment was done through SLEDAI-2K [14]. Another analytical observational study of 120 patients from India found that there was a significant association between higher SLEDAI scores and more severe cutaneous symptoms [15]. The very high frequency of photosensitivity, malar rash and alopecia in our cohort combined with the low frequency of some vascular and chronic discoid manifestations may reflect the clinical spectrum encountered in the Indian subcontinent where marked sun exposure, younger age of onset and differences in referral pattern may influence presentation. The findings of our study also corroborate with another study from the north eastern part of India which found that photosensitivity was the most common cutaneous manifestation followed by malar rash , non-scarring diffuse alopecia, discoid rash, oral ulcers and vasculitic rash respectively.[1] Furthermore, the high prevalence of these specific markers in the Indian demographic underscores the necessity of employing localized validation for activity tools like the Cutaneous Lupus Erythematosus Disease Area and Severity Index to better capture the nuance of both inflammatory activity and permanent cutaneous damage [16]. This overall pattern is consistent with findings of previous studies which showed that LE non-specific skin lesions, particularly alopecia, mucosal ulceration, vasculitis and inflammatory eruptions are more closely related to systemic activity than chronic lesions [17] . This interpretation is also reasonable because SLEDAI assigns points to alopecia, oral or nasal ulcers, vasculitis and new inflammatory rash, but photosensitivity and several other cutaneous manifestations are not independently scored [7] . Compared to SLEDAI, SLEDAI-2K improves longitudinal assessment by recording persistent disease activity such as rash, alopecia, mucous membrane ulcers or proteinuria that may not be new or recurrent, but persistent and hence represent active disease. Both SLEDAI and SLEDAI-2K remain mainly systemic indices and therefore CLASI can act as a complementary approach because it specifically quantifies reversible cutaneous activity and irreversible damage, including features such as erythema, scale/hypertrophy, dyspigmentation and scarring [7] . Hence, the findings of our study support the use of SLEDAI or SLEDAI-2K for assessing disease severity, but advocates the use of CLASI where detailed evaluation of mucocutaneous disease is required.

The findings of our study should be considered in light of limitations which include a small sample size, single centre and hospital based design, cross sectional assessment and failure to incorporate CLASI which could have complemented systemic activity indices.

CONCLUSION:

Our study demonstrates that mucocutaneous manifestations are common in SLE and provide valuable diagnostic clue as well as serve to monitor disease activity in Indian cohort. 33 (51.56%) patients in our study had skin manifestations as the initial presenting sign of the disease, which goes on to show that cutaneous manifestations may precede systemic disease and therefore should always be monitored.

New inflammatory eruptions, active mucosal ulcers, facial oedema, purpura, and vasculitis should prompt reassessment of renal, haematological, vascular, and other systemic domains rather than being managed as isolated skin disease; serial documentation of their onset, morphology, distribution, and resolution may help identify flares and evaluate treatment response.

Further studies should employ larger population in multicentre, prospective and longitudinal designs and incorporate SLEDAI-2K and CLASI to correlate mucocutaneous changes with systemic involvement and determine disease activity and treatment outcomes.

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