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PAPER

The study of Cutaneous Lupus Erythematosus Disease Area and Severity Index in Indian patients with systemic lupus erythematosus

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Abstract The Cutaneous Lupus Erythematosus Disease Area and Severity Index (CLASI) is a newly described tool used to assess the activity of and damage caused by cutaneous lupus erythematosus (CLE). There is a paucity of data on CLASI from the Indian subcontinent. We sought to determine the applicability of CLASI in specific lesions of CLE in patients with systemic lupus erythematosus (SLE) attending a tertiary care hospital in India. In this prospective, cross-sectional study, 93 patients of SLE with cutaneous lesions were recruited. CLASI activity and damage scores of lupus erythematosus (LE)-specific skin lesions were done in 75 patients with SLE. The mean CLASI activity score was 15.4 ± 9.4 (range 0–39) and the mean damage score was 6.87 ± 7.75 (range 0–30). Higher mean CLASI activity scores were seen in patients with a combination of acute, subacute and chronic CLE and in those with widespread lesions. Patients with longstanding disease and long duration of skin lesions had higher damage scores. This study shows that CLASI is an effective tool to assess cutaneous activity of LE-specific lesions, and the damage caused by them, in Indian patients. *Lupus* (2011) **20,** 1510–1517.

Key words: activity; CLASI; cutaneous lupus; damage; systemic lupus erythematosus

Introduction

Cutaneous manifestations are among the most frequent presenting signs of systemic lupus erythematosus (SLE) and remain a major source of disease flares throughout the course of the illness.[1] Most of the indices for systemic disease activity assessment in SLE include cutaneous manifestations as one of their components. The Cutaneous Lupus Erythematosus Disease Area and Severity Index (CLASI) was designed in 2005 to convert subjective observations seen in cutaneous lupus erythematosus (CLE) into objective data using a scoring system. It describes the extent of the disease in terms of intensity of involvement of anatomical areas.[2] It has separate scores for quantifying activity and damage, which makes it possible to monitor a patient's disease course and response to therapy. It has so far been applied to only LE-specific skin lesions.[3] The activity measurement attempts to quantify the level of active inflammation in the skin, scalp and oral mucosa. The damage measurement attempts to quantify the 'footprint' of destruction left behind by the previous inflammation.[4] Mucocutaneous lesions are very common manifestations, reported in 52–98% of patients from Asia.[5] Our aim was to study the extent and severity of skin and mucosal involvement in patients with SLE using the CLASI activity and damage scores, as there are no large scale studies addressing this aspect of disease activity in SLE from India.

Patients and methods

Study design

This prospective, cross-sectional study was conducted from May 2007 to August 2008

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(16 months) in the dermatology clinic of a tertiary care, university-affiliated hospital.

Patients

Patients with SLE were recruited from the dermatology clinic and the inpatient services of Rheumatology, General Medicine, Paediatrics and Nephrology. Patients with SLE but without cutaneous manifestations and those not willing to participate were excluded. They were informed about the purpose of the study and informed consent obtained. Separate child and adolescent consent forms were used for patients in the age groups of 7–12 years and 13–17 years, respectively. The patients were examined by the principal investigator. A structured proforma designed by the team of investigators involved in the study was completed at the first patient visit for all patients. The demographic data, clinical profile, details of clinical examination and the CLASI activity and damage scores were recorded. Treatment given to the patient in the previous 3 months was also recorded. The skin lesions were classified as specific or non-specific according to the Gilliam classification for skin lesions of LE.[3] The diagnosis of CLE was based on clinical features and confirmed by biopsy of the lesional skin for histopathology and direct immunofluorescence. Basic laboratory tests included a haemogram, urine microscopy, urine albumin, 24-h urine protein, antinuclear antibody (ANA), total serum complement, C3 and C4 estimation, and anti-double stranded DNA (anti-dsDNA) for all patients. Additional tests such as direct Coomb's test, liver function test, renal biopsy and muscle enzymes were done when indicated.

Methods

The activity and the damage scores of specific CLE lesions were calculated using physician rating as described by Albrecht et al.[2] Thirteen anatomical sites were examined for the most severely affected cutaneous lupus-specific lesion.

Activity was assessed by examination of erythema, scale/hypertrophy, mucous membrane disease, acute hair loss, and non-scarring alopecia. Erythema was graded on a scale of 0–3 ranging from its absence to dark red/purple/violaceous/crusted/haemorrhagic lesions. Scaling was graded on a 0–2 scale, from absent scaling to verrucous or hypertrophic lesions. The presence of mucous membrane involvement was noted. Acute hair loss was defined as occurring within the last 30 days or as reported by the patient. Scalp alopecia was graded on a scale of 0–3 from absent alopecia to focal or patchy alopecia in more than one scalp quadrant. The total activity score was calculated by summation of the scores of erythema, scale, mucosal involvement and alopecia.

Damage was assessed by noting dyspigmentation, cutaneous scarring/atrophy, and scarring alopecia. These parameters were assessed in similar body locations as those used in activity assessment. If the dyspigmentation occurred in a skin lesion and had lasted at least 12 months, it was taken as permanent and the score of the same was doubled. Scarring / atrophy were graded from absent to severe atrophic scarring or panniculitis on a 0–2 scale. Scalp scarring was graded on a 0–6 scale from absent scarring to involvement of the whole scalp. If a particular scalp lesion had both scarring and non-scarring alopecia, both were scored independently. The total damage score was calculated by the summation of the score for dyspigmentation, scarring of skin and scarring alopecia.

Statistical analysis

Statistical software SPSS version 16.0 was used for the data analysis. The dependent variable of CLASI damage score and the independent variables of duration of the systemic disease and the duration of skin lesions were analysed. Spearman's rank correlation coefficient (ρ) as non-parametric measure of statistical dependence between the two variables was applied to establish the relationship between the duration of disease and the duration of skin lesions with the CLASI damage score. A two-tailed test was done to establish the significance of the correlation coefficient. Linear regression analysis was carried out to quantify the strength of the relationship between the duration of systemic disease and of the skin lesions with the CLASI damage score. The coefficient of determination (R^2) was calculated to find out the amount variation in the dependent variable in relation to the independent variables. The regression line was fitted using the method of least squares. The slope of regression line was calculated to investigate the change in the dependent variable for a unit increase in the independent variable. Analysis of variance (ANOVA) was performed to find the significance of the regression model.

The study was approved by the Ethics committee of the Institutional Review Board.

Results

Patient characteristics

In total, 93 patients who were diagnosed to have SLE according to the 1997 modification of the ACR criteria[6] were included. LE-specific lesions alone or in combination with non-LE-specific lesion were observed in 75 (80.65%) patients. Figure 1 summarizes the patient characteristics in this study. There were 87 (93.5%) adults (>15 years) and six (6.45%) children (<15 years). The male to female ratio was 1:14.5 and 1:5 among adults and children, respectively. The mean age of the patients was 29.8 ± 12.73 (range 5–65). The mean age of males and females was 29.9 ± 10.46 and 28.5 ± 10.46, respectively. Of the 75 patients, 41 (54.6%) were on prior therapy with prednisolone and/or methylprednisolone and 11 patients (14.6%) were on deflazacort. 32 patients (42.6%) were on hydroxychloroquine. Other drugs taken were mycophenolate mofetil in 4 patients (5.3%), azathioprine in 4 patients (5.3%), methotrexate in 3 patients (4%) and cyclosporine and cyclophosphamide in one patient each.

Profile of mucocutaneous lesions

The most common specific cutaneous lesions were discoid lesions, seen in 51(54.8%) patients followed by malar rash in 29 patients (31%) and generalized acute CLE in 26 patients (27.9%). Papulosquamous lesions of subacute CLE (SCLE) were seen in seven (7.5%) patients. Five patients had nodular lesions, of which four were clinically suggestive of tumid lupus, but histopathology of these lesions was non-specific; the remaining one patient had a vasculopathic picture on histology. Among the non-specific lesions, non-scarring alopecia was the most common, seen in 60 (64.5%) patients, followed by palpable purpura (Table 1).

CLASI activity and damage scores

CLASI was scored for 75 patients with LE-specific lesions (Figure 1). Mean CLASI activity score was 15.4 ± 9.4 (range 0–39) out of a maximum score of 70. The average number of sites scored was 6.5 (range 0–13). The CLASI activity score was >20 in 27 patients, of whom 16 (59.3%) patients had 10 or more sites of involvement. There was a

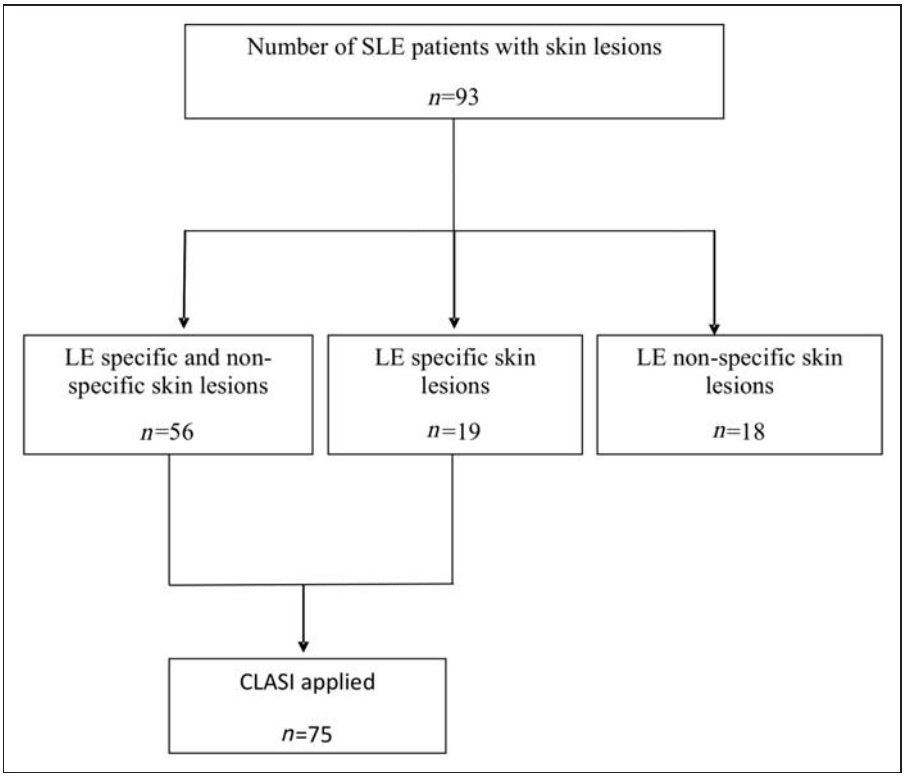

Figure 1 Patient characteristics in this study.

trend towards increasing activity scores in patients with higher number of involved sites (Table 2).

Of the 440 anatomical sites that were examined for erythema, Grade 1 erythema (pink, faint erythema) (Figure 2A) was seen in 249 (56.6%) sites while Grade 2 (red) (Figure 2B) and Grade 3 (dark red/ crusted / haemorrhagic) (Figure 2C) erythema was seen in 152 (34.54%) and 39 (8.86%) sites, respectively. Erythema was most commonly observed in lesions of the face and the ears. On the face, 28 (46.7%) patients had Grade 1 erythema, 24 (40%) had Grade 2 erythema and eight (13.3%) had a Grade 3 erythema. Erythema was less frequent on the covered areas (legs, feet, and abdomen).

Table 1 Profile of mucocutaneous lesions

Type of lesions	*Number of patients (n = 93)*	*Percentage (%)*
Discoid lesions	51	54.8
Malar rash	29	31.2
Generalised acute cutaneous LE	26	27.9
Papulosquamous rash (SCLE)	7	7.5
Panniculitus	1	1.1
Non-scarring alopecia	60	64.5
Telogen effluvium	44	73.3
Lupus hair	15	25
Alopecia areata	1	1.7
Nodules	5	5.4
Oral mucosal ulcers	39	41.9
Palpable purpura	18	19.4
Erythema multiforme	9	9.7
Livedo reticularis	7	7.5
Raynaud's phenomenon	4	4.3
Leg ulcers	3	3.2
Digital ulcers	3	3.2
Urticaria	2	2.2
Sclerodactyly	1	1.1
Bullous lesions	1	1.1
Urticarial vasculitis	1	1.1

LE, lupus erythematosus; SCLE, subacute cutaneous lupus erythematosus.

Grade 1 scaling (Figure 2D) was most commonly observed on the ear and facial lesions (100%), followed by that on the scalp (97.5%). Grade 2 scaling (verrucous, hypertrophic) was observed in five (6.75%) patients.

There was a relationship between the morphology of the lesions and mean CLASI activity scores. Patients with SCLE, and acute CLE (ACLE) occurring with other types of LE-specific lesions had higher activity scores than those with only discoid LE or ACLE.

Of the 75 patients, 59 (78.6%) had evidence of damage. The mean CLASI damage score was 6.87 ± 7.75 (range 0–30) out of the maximum score of 56. The mean number of sites scored for damage was 3.44 (range 0–12). 58 out of 75 patients (77.3%) showed dyspigmentation (Figure 2E). It was of less than 12 months duration in 37/75 (49.3%) patients. The mean number of sites scored for dyspigmentation was 3.22 (range 0–12). Scarring of the skin was seen in 18/75 (24%) patients. The mean number of sites scored for scarring was 0.55 (range 0–7). Scarring of the scalp was seen in 15/75 (20%) patients (Figure 2F). Seven (46.6%) patients had scarring alopecia affecting all four scalp quadrants. Fourteen patients (18.66%) were scored for both scarring and non-scarring alopecia as the two types co-existed in some lesions.

Statistical analysis

Spearman's rank correlation coefficient between the duration of disease and CLASI damage score ($\rho = 0.477$) and between the duration of skin lesions and CLASI damage score ($\rho = 0.472$) was significant at $p < 0.001$. Linear regression analysis showed that for a unit increase in the duration of disease there is an increase of 0.104 units in damage score, which was significant at $p < 0.01$. It was also

Table 2 Mean number of affected sites and the mean CLASI activity and damage scores in relation to the LE-specific skin lesions

LE specific lesions	*Number of cases*	*Mean Duration of LE in months (Range)*	*Mean Duration of skin lesions in months (Range)*	*Mean CLASI activity score (Range)*	*Mean CLASI damage score (Range)*	*Mean number of sites for activity*	*Mean number of sites for damage*
DLE/SCLE	2	60(12–108)	6.5(5–8)	12(8–16)	5(0–10)	6.5	5
DLE	29	33(2–132)	17.88(0.8–84)	13.49(0–37)	8.69(0–30)	5.44	4.2
ACLE	20	19.34(2–108)	4.5(0.3–24)	15.2(2–30)	1.55(0–18)	7	1.1
ACLE/ DLE	18	21.9(2–60)	15.9(0.5–60)	18.2(6–39)	8(0–27)	7.5	4.3
ACLE/SCLE	1	12	12	20	8	7	4
ACLE/SCLE/DLE	2	6(4–8)	5.5(1–10)	21.5(15–28)	5(1–9)	8.5	5
SCLE	2	15(6–24)	9(6–12)	23(20–26)	11.5(9–14)	8.5	3.5

SCLE, sub acute cutaneous lupus erythematosus; DLE, discoid lupus erythematosus; ACLE, acute cutaneous lupus erythematosus; LE, lupus erythematosus; CLASI: Cutaneous Lupus Erythematosus Disease Area and Severity Index.

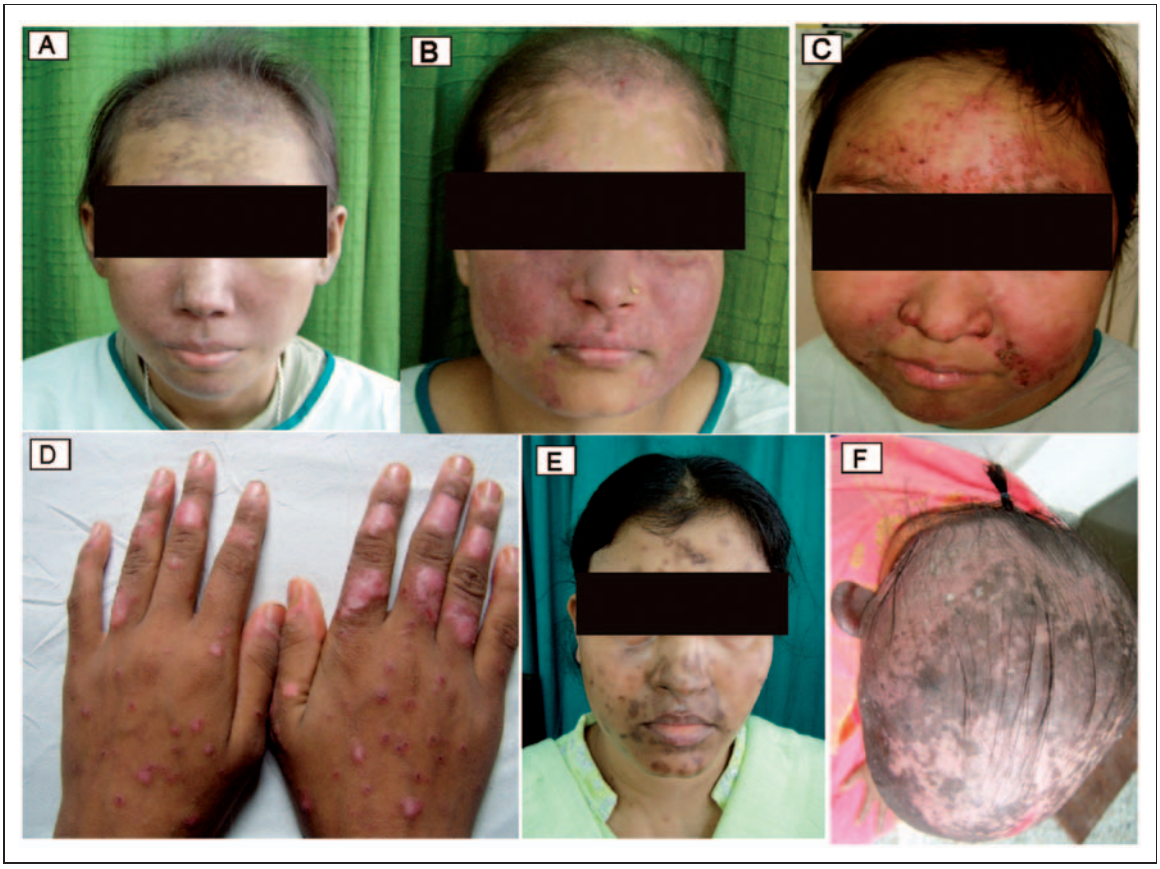

Figure 2 Grade 1 (A), Grade 2 (B) and Grade 3 (C) erythema in SLE patients with specific skin lesions. (D) Grade 1 scaling of the hands. (E) Patient with longstanding dyspigmentation. (F) Patient with scarring alopecia.

seen that for a unit increase in the duration of skin lesion there is an increase of 0.216 units in the damage score, that was also significant at $p < 0.001$. This analysis showed a significant result with coefficient of determination $R^2 = 0.168$ for duration of systemic disease and $R^2 = 0.267$ for duration of skin lesion. (Figures 3 and 4). The *p*-value of ANOVA was statistically significant.

Discussion

CLASI was formulated in 2005 at the University of Pennsylvania and the Philadelphia V.A. Hospital.[2] It consists of physician-rated activity and damage scores. We compared the CLASI activity and damage scores in our study with results published in other studies (Table 3).[4,7–9] None of the studies listed have selectively studied patients of colour as in this report. We evaluated CLASI in 75 patients with SLE. A study by Klein et al. showed that CLASI can be applied to categorize patients into mild, moderate and severe disease groups that correspond to activity scores of 0–9, 10–20 and 21–70 respectively.[10] According to this grouping, 29 (38.7%) of our patients had moderate disease, followed by 24 (32%) and 22 (29.3%) with severe and mild disease, respectively.

The mean CLASI activity scores in our study in ACLE, SCLE and chronic CLE (CCLE) were 15.2 (range 2–30), 23 (range 20–26) and 13.03 (range 0–37), respectively. The largest study to date has been done by Moghadam-Kia et al., in which 47/114 patients studied were patients of colour.[8] In their study the mean CLASI activity scores in ACLE, SCLE and CCLE were 6.4, 11.1 and 7.5, respectively. The CLASI activity scores in the three subsets in our study were notably higher than those reported by Moghadam-Kia et al.[8] The mean CLASI activity scores in other published studies[4,7,9] ranged from 3.4 to 49. In a study done by Kreuter et al., only patients with SCLE were included.[9] Studies assessing the utilization of CLASI for treatment outcome have shown that it is applicable for follow-up of severity of the CLE lesions.[11,12]

The factors affecting the CLASI activity score in our patients were studied. In SLE it has been

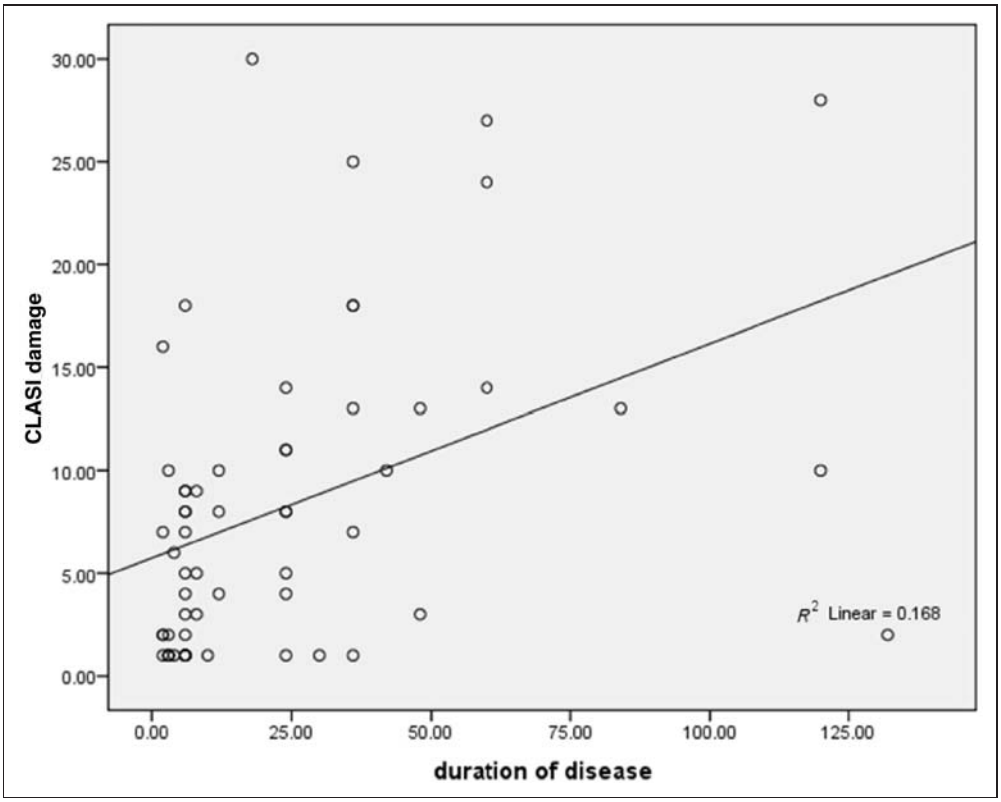

Figure 3 Scatter plot depicting the correlation between CLASI damage score and duration of disease in months.

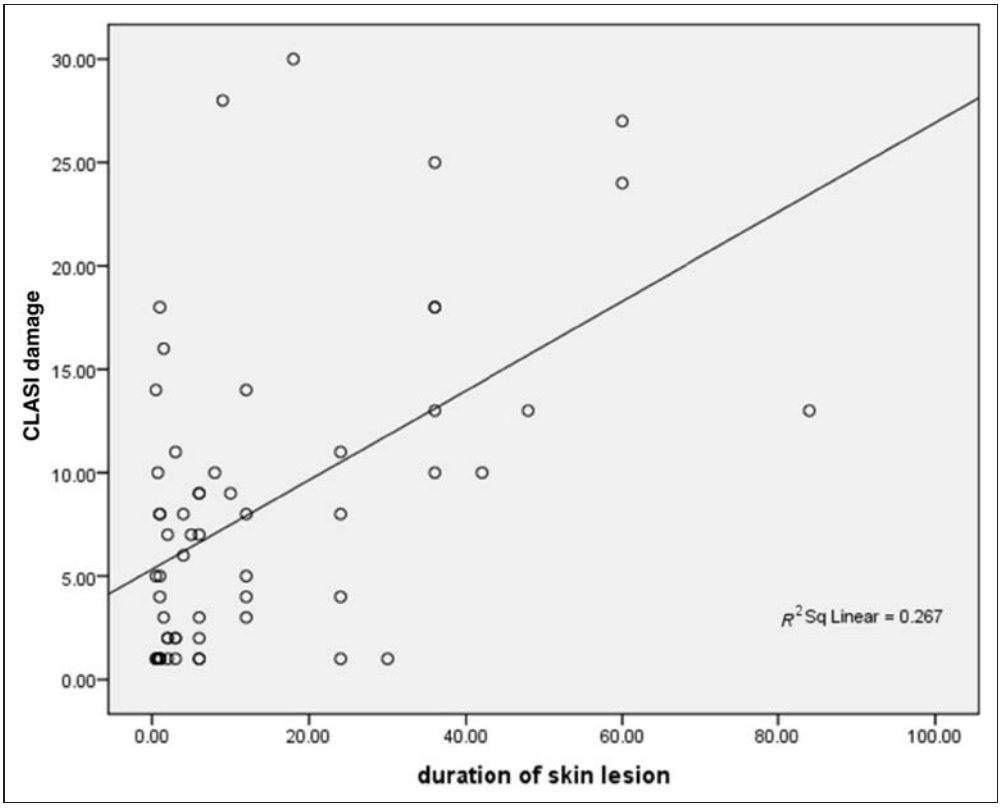

Figure 4 Scatter plot depicting the correlation between CLASI damage score and duration of skin lesions in months.

Table 3 Published data on CLASI in the Western literature compared with data in this study

Study characteristics	*Present study*	*Krathen et al.*[4]	*Bonilla-Martinez et al.*[7]	*Moghadam-Kia et al.*[8]	*Kreuter et al.*[9]
Study design and aim	Prospective, cross sectional observational study	Validation study of CLASI for use by dermatologists and rheumatologists	Assessment of clinical responsiveness of CLASI after starting a new standard of care therapy	Assessment of disease severity in subsets of patients with CLE using outcome and quality of life measures	Prospective, nonrandomised study for efficacy of mycophenolate sodium in recalcitrant SCLE
Number of patients	93	14	8	114	10
Race(number of patients)	Asian(93)	African-American(10) Whites(4)	Blacks(3) Whites(3) Asian(1) Hispanic(1)	Whites(66) African -American(41) Asian(5) Hispanic(1)	Not Mentioned
Lesion type	LE specific and LE non-specific lesions	LE specific skin lesions	LE specific skin lesions	LE specific and non-specific lesions	Only SCLE lesions
Age range(years)	5–65	17–51	19–83	17–82	37–68
Mean age in years	29.8	39.6	49.25	NA	53.1
Females	87	13	8	93	8
Males	6	1	0	20	2
CLASI activity range at recruitment	ACLE 2–30 SCLE 20–26 CCLE 0–37	3.4–32.8	8–49	ACLE 0–19 SCLE 0–41 CCLE 0–32	4–25
Mean CLASI activity score at recruitment	ACLE -15.2 SCLE -23 CCLE -13.03	15.6 ± 10.6	NA	ACLE -6.4 SCLE -11.1 CCLE -7.5	10.8 ± 6.0
CLASI damage range at recruitment	ACLE 0–18 SCLE 9–14 CCLE 0–30	0.2-38.8	0-44	ACLE 0–11 SCLE 0–17 CCLE 0–40	ND
Mean CLASI damage score at recruitment	ACLE -1.55 SCLE -11.5 CCLE -8.67	20.2 ± 13.1	NA	ACLE 5.1 SCLE 1.6 CCLE 10.2	ND

LE, Lupus erythematosus; ACLE, Acute cutaneous lupus erythematosus; CCLE, Chronic cutaneous lupus erythematosus; SCLE, Subacute cutaneous lupus erythematosus; CLASI, Cutaneous lupus erythematosus disease area and severity index; NA, not available; ND, not done.

reported that the number of different types of skin lesions is highly indicative of disease activity so that the severity of disease increases with the number of lesions.[13] In our study it was found that the activity score increased proportionately with the number of anatomical areas involved. Higher CLASI activity scores were also seen in patients with SCLE, as in the study by Moghadam-Kia et al.,[8] and in ACLE occurring in combination with DLE as compared with those with only discoid lesions. This may be due to higher erythema scores in the former group as compared with those with only discoid lesions.

In our study, the CLASI damage showed a statistically significant correlation with the duration of SLE and the duration of skin lesions ($p < 0.01$). Among the parameters studied in CLASI damage, dyspigmentation was the most frequent, with 36% patients having had the dyspigmentation for more than 12 months at the time of inclusion into the study.

CLASI cannot be applied to non-specific skin lesions of SLE. Palpable purpura was seen in eighteen (19.4%) of our patients. In the assessment of cutaneous activity, a scoring system that takes into account the LE non-specific lesions will have to be devised. As of now, the CLASI provides an objective assessment of clinical activity and damage. The scores can be done periodically during follow-up and improvement or deterioration recorded.

One of the limitations of our study was that many of our patients were on disease-modifying treatment prior to inclusion into the study, which may have resulted in lower CLASI activity scores.

In summary, this is the largest study utilizing CLASI on patients with SLE from the Indian subcontinent. CLASI has been proved to be an effective tool in assessing cutaneous activity of LE in patients with pigmented skin. The present study has reinforced the findings of studies done in the West that CLASI is applicable to patients with pigmented skin.

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Conflict of interest

The authors declare they have no conflicts of interest.

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