Original Article

Cutaneous manifestations of systemic lupus erythematosus: experience from a tertiary care hospital of Bangladesh

Asifuzzaman M[a], Ara R[b], Biswas T[c], Hassan R[d], Choudhury MR[e]

ABSTRACT

Background: *Systemic lupus erythematosus (SLE) is a chronic, multisystem disorder that can affect any organ of the body. Approximately 80 percent of patients develop skin disease at some point in their disease course. The association with SLE varies among the subtypes of cutaneous lupus erythematosus (LE). Better understanding of cutaneous manifestations can help in more effective management. This study aimed to evaluate the pattern of cutaneous manifestations of SLE and to find out association with organ involvement.*

Methods: *This cross-sectional observational study was conducted in the Green Life Medical College Hospital from January 2019 to December 2020. Sixty four lupus patients who fulfilled the SLICC 2012 classification criteria and having new onset or preexisting skin complaints were enrolled. Mixed connective tissue disease and other overlap syndromes were excluded. All patients were evaluated by a dermatologist and diagnosis was done as per modified Gilliam Classification criteria.*

Results: *Out of 64 patients, 56 were female and 8 were male. Female and male ratio was 7:1. Mean age was 28.4±9.6 years. Among the cutaneous manifestations, LE specific was 38 (59.4%), LE non-specific was 41 (64.1%). Among LE specific, 66% were acute (ACLE), 42% were sub-acute (SCLE) and 37% patients were chronic (CCLE). Among ACLE, 72% had malar rash and 84% had photosensitivity. Among SCLE, most common was papulosqumous (68%). DLE (86%) was the most common CCLE. Among LE non-specific, 85% had non-scarring alopecia, 52% had vascular abnormalities. Most common organ involvement was musculoskeletal (84%), then renal (56%). DLE had negative association with renal involvement [OR (-0.04)]. No other cutaneous manifestations showed any significant association with any other organ involvement.*

Conclusion: *Cutaneous manifestations are important feature in SLE. LE non-specific was more common than LE specific manifestations in this study. Better understanding can help in efficient diagnosis and management.*

Key words: *Acute cutaneous lupus erythematosus, cutaneous lupus erythematosus, chronic cutaneous lupus erythematosus, discoid lupus erythematosus, sub-acute cutaneous lupus erythematosus.*

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INTRODUCTION

Systemic lupus erythematosus (SLE) is a chronic, multisystem immune-mediated disorder that can affect any organ of the body. Approximately 80 percent of patients develop skin disease at some point in their disease course.[1] Cutaneous involvement causes considerable morbidity by producing alopecia, scarring lesions, disfigurement, etc. and for these reasons about 45% of patients experience some degree of vocational handicap.[2] According to the modified Gilliam grouping system for cutaneous manifestations, LE includes three subsets of LE-specific skin diseases: acute cutaneous lupus erythematosus (ACLE), subacute cutaneous lupus erythematosus (SCLE) and chronic cutaneous lupus erythematosus (CCLE) and a variety of LE-

nonspecific skin diseases. The major clinical variants for ACLE include: localized (ie, malar rash, butterfly rash), generalized and toxic epidermal necrolysis-like; SCLE include annular, papulosquamous, drug-induced and less common variants: erythrodermic, poikilo dermatous, erythema multiforme-like (Rowell syndrome) and vesiculobullous annular SCLE; CCLE **include discoid** lupus erythematosus (DLE), lupus erythematosus tumidus, lupus profundus (also known as lupus panniculitis), chilblain lupus erythematosus and lichenoid cutaneous lupus erythematosus-lichen planus overlap syndrome (LE-LP overlap syndrome). LE-nonspecific skin disease occurs with increased frequency among patients with SLE but are not specific to SLE and lack histopathologic features of cutaneous LE comprises vascular abnormalities (periungual erythema , livedo reticularis, raynaud phenomenon and vasculitis), nonscarring alopecia, sclerodactyly, calcinosis cutis, nonspecific bullous eruptions, urticaria, erythema multiforme, leg ulcers, etc.[3] The association with SLE varies among the subtypes of cutaneous LE. Cutaneous LE may undergo flares in the absence of any other systemic exacerbation or can be part of a multiorgan flare.[4] Moreover, lupus-specific skin lesions serve primarily as an important diagnostic clue whereas lupus non-specific skin lesions are associated with active disease.[5] Many of the time a multidisciplinary approach among dermatologists, rheumatologists, internists and other specialists as per organ involvement is required to manage these patients. Better understanding of cutaneous manifestations of SLE can help in effective management plan for this patient group. This study aimed to evaluate pattern of cutaneous manifestations of SLE in a tertiary care hospital of Bangladesh and find out its association with organ involvement.

METHODS

This cross-sectional observational study was conducted in the Department of Dermatology, Department of Medicine and Green Life center for rheumatic care and research from January 2019 to December 2020. After inclusion and exclusion criteria 64 lupus patient was enrolled consecutively in this study. All SLE patients fulfilling the SLICC 2012 classification criteria[6] having new onset or preexisting skin complaints were included and patient diagnosed as mixed connective tissue disease or other overlap syndrome and unwilling to participate were excluded from the study.

After taking ethical clearance from the ethical review committee of Green Life Medical College**,** a preformed questionnaire to determine pattern of skin manifestations was administered to all the patients diagnosed as lupus from the Department of Dermatology both, OPD and IPD**,** from Green Life Center for Rheumatic Care and Research and Department of Medicine, Green Life Medical College Hospital. All patients were evaluated by a dermatologist to determine the type of skin lesions. Modified Gilliam classification criteria were followed to classify skin lesions**.**[3] Biopsy was arranged by the Department of Dermatology in appropriate cases. A through physical examination and review of previous medical records were done. Relevant data and laboratory parameters were recorded in data sheet. Written informed consent was taken from all participants.

Data was checked for inconsistencies and then entered into a computer and was analyzed by using SPSS windows version 22. Frequency and percentage were calculated to see the pattern of cutaneous manifestations of SLE. Multivariate logistic regression analysis was done to see association with organ involvement.

RESULTS

Out of 64 patients 56 were female and 8 were male. Female and male ratio was7:1. Mean age ± SD was 28.4±9.6 years. Most of them were married (51.6%), student (45.5%), graduate (37.5%), and lived in urban area (68.7%) as shown in Table I. Among the cutaneous manifestations; LE specific was 38 (59.4%), LE non-specific was 41 (64.1%) and 17 (26.6%) patient had both LE-specific and LE-non specific variants as shown in Figure 1. LE specific skin lesions were found in 38 (59.4%) and LE non-specific skin lesions were found in 41 (64.1%) patients and 17 (26.6%) patients had both LE specific and LE non-specific skin lesions. As shown in Table IIa, among LE specific skin lesions 66% patients were ACLE, 42% patients were SCLE and 37% patients were diagnosed as CCLE. Among ACLE, 72% malar rash and 84% had photosensitive dermatitis, among SCLE most common was papulosqumous (68%) lesion. DLE (86%) was the most common CCLE. Four patients had lupus profundus. As shown in Table IIb, among LE non-specific skin lesions; 85% had non scarring alopecia, 52% vascular abnormalities, and among others 5 patient had leg ulcer, 4 had pyoderma gangrenosum and 3 had

bullous LE. Around 40% patient had coexisting non-lupus skin problems like fungal infection in 8 patients, herpes zoster in 5 patients, herpes simplex in 3 patients as shown in Table II. With cutaneous LE, most common organ involvement was musculoskeletal (84%), then renal (56%) as shown in Figure 2. DLE had negative association with renal involvement [OR = (-0.04)]. No other cutaneous manifestations showed any significant association with any other organ involvement. Auto-antibody profile showed that all patients were ANA positive, 70% anti-dsDNA and 15% anti-phospholipid positive.

Table I Socio-demographic characteristics of the study participants (N=64)

Variables	Frequency (%)
Mean age (SD) year	28.4 (9.6)
Gender	
• Male	8 (12.5)
• Female	56 (87.5)
Lives in	
• Urban	44 (68.7)
• Rural	20 (38.3)
Marital status	
• Unmarried	28 (43.7)
• Married	33 (51.6)
• Widow	1 (1.6)
• Separated	2 (3.1)
Educational status	
• Primary	5 (8)
• Secondary	10 (15.5)
• Higher secondary	12 (18.7)
• Graduate	24 (37.5)
• Postgraduate	12 (18.7)
• Uneducated	1 (1.6)
Occupation	
• Student	31(48.5)
• Home maker	26 (40.6)
• Others	7 (10.9)

Table IIa LE specific skin lesion

Traits	Number (percentage)
Acute cutaneous LE	25 (65.8)
Malar rash	18 (72)
Photosensitivity	21 (84)
Sub-acute cutaneous LE	16 (42.1)
Annular	7 (43.7)
Papulosqumous	11 (68.7)
Drug induced	1 (6.2)
Chronic cutaneous LE	14 (36.8)
DLE	12 (85.8)
Lupus profundus	4 (28.6)
Lupus timidus	0

Table IIb LE non-specific skin lesion

Traits	Number (percentage)
Non scarring alopecia	35 (85.4)
Vascular abnormalities	21 (52.2)
Raynaud's	9 (21.9)
Vasculitis	10 (24.4)
Others	16 (39)
Leg ulcer	5 (12.2)
Pyoderma gangrenosum	4 (9.7)
Bullous LE	3 (7.3)
Periungual erythema	2 (4.9)
Psoriasiform LE	1 (2.4)
Livido reticularis	1 (2.4)

Table III Coexisting non-lupus skin disease in cutaneous LE patients

Traits	Number	Percentage
Fungal infection	8	14
Drug rash	5	8.3
Herpes zoster	5	6
Herpes simplex	3	5
Eczema	2	3
Other skin conditions (Acne, cellulitis, venous ulcer, paronychia, scabies)	3	5

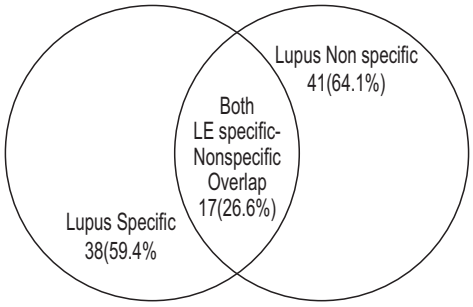

Figure 1 Venn Diagram of Lupus Specific and Lupus Non-Specific cutaneous manifestations

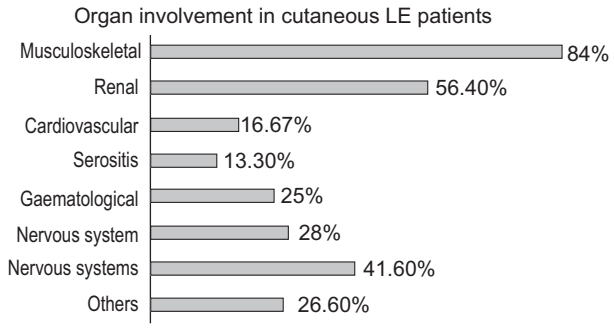

Figure 2 Frequency of organ involvement in cutaneous LE patients

DISCUSSION

In this study, most of the participants were female which was consistent with universal epidemiology of lupus[7]; female and male ratio was 7:1 which was ranges from 7:1 to 15:1 in different studies.[8,9] Mean age of our patients was similar with different studies done in India where age ranges from 25 to 29 years.[10,11] In this study LE non-specific skin lesions were a bit higher than LE specific skin lesions (64 % vs 59%). YI Bae et al. has found lupus specific manifestations more common in Korean population.[12] Around 26 % patients had both LE specific and LE non-specific overlap. In an European study there were 30% overlap in between sub sets was reported.[13] Among LE specific, ACLE was most common (66%), then SCLE (42%) and then CCLE (37%). This finding widely varies among the studies. CCLE was found to have most common in a Korean study[12], again ACLE was found to have more common in many Indian and European studies.[13-16] Among ACLE, photosensitive dermatitis was most common (84%), then malar rash (72%) in our study. Malar rash was the most common lesion (80%) and photosensitive dermatitis in 50% cases was noted in a study done by Kole KA et al.[11] Again, Wysenbeek, et al.[14] reported 49% malar rash and Vaidya, et al.[15] reported 53.2% malar rash from western India. Our finding of 42.1% SCLE was higher than some other studies. Kole KA et al.[11] reported 3.34% SCLE, whereas Wysenbeek et al.[14] reported13% cases of SCLE. Like this study, DLE was the most common CCLE in many other studies.[12-16] Among LE non-specific manifestations, nonscarring alopecia (85.4%) was the most common in this study that finding was consistent with the study done by Kole KA et al.[11] who reported non scarring alopecia 86.7% and again 57% by Wysenbeek et al.[14] Raynaud's was found in 21% cases in our study. Malaviya et al[10] reported 32 % cases of Reynaud's phenomenon and approximately 40% was reported by Koch K et al[17] in South African population. This may be attributed to seasonal and environmental variation. We had 4 cases of pyoderma gangrenosum, 3 bullous LE that more or less consistent with other studies.[11,14] We had found around 40% co-existing non lupus skin problems like fungal infection, herpes zoster, herpes simplex etc that was not been evaluated in other studies. In this study most common organ involvement was MSK that was consistent with other studies.[10,14,15] No positive association was found with any cutaneous sub sets and organ involvement in our study. Unlike ours Koch K et al[17] found positive association with ACLE and renal involvement (OR =2.6). Our finding of negative association in DLE and renal involvement [OR = (-0.04)] was consistent with other studies.[18,19]

The strengths and limitations of this study

This was a first study in Bangladesh with adequate sample size that evaluated pattern of cutaneous manifestations in SLE, in which skin manifestations are very important for diagnosis and management. This study had some limitations as well. It was a single center study, there may be referral bias and biopsy and histopathology were not done in most of the patients.

Conclusions

In this study, LE non-specific was more common than LE specific skin involvement. 26 % patients had both LE specific and LE non-specific overlap. *Around 40% had co-existing non lupus skin problems. No positive association was found with any cutaneous sub sets and organ involvement in except DLE had negative*

association with renal involvement. Though SLE is a multisystem disorder, skin manifestations are very important in diagnosis, management and predict other organ involvement, disease flare and prognosis. Moreover, being the most visible part of the body, cutaneous manifestations pose significant psychosocial implications. So, better understanding of skin manifestations can help in efficient diagnosis and management of SLE to improve outcome.

Recommendations

A larger multicenter study with long term follow up is required to get better understanding of pattern of cutaneous manifestations in our population and find out the association between different subset of cutaneous LE with organ involvement, and predict long term prognosis of SLE.

Author's contribution: MA and RA planned the study, searched literature, wrote protocol, took ethical clearance, recruited patients, planned data analysis, wrote and reviewed manuscript; both of them contributed equally as first author. TB and RH helped in data collection, data analysis and review of manuscript. MRC guided and reviewed the manuscript. All the authors read and approved the final manuscript before submission.

Conflicts of interests: Nothing to declare.

Consent: Written informed consent was taken from all the participant before enrollment.

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