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RESEARCH ARTICLE

Clinical evaluation of skin lesions among patients with systemic lupus erythematosus: Experience from a tertiary care centre

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ABSTRACT

Background: Lupus patients frequently exhibit specific and nonspecific skin lesions and lesions associated with skin infections. This study aimed to determine the frequency of lupus-specific and non-specific skin lesions and the incidence of skin infections.

Methods: This study was conducted in the Department of Rheumatology at Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh, from 2014 to 2016. After obtaining ethical clearance from the Institutional Review Board of BSMMU, 136 consecutive patients fulfilling the ACR criteria for SLE were enrolled and followed up for at least one year. A dermatologist confirmed lupus-specific, non-specific, and skin lesions related to infections and noted them in a datasheet. Relevant investigations were performed at baseline and during subsequent follow-up visits.

Results: One hundred thirty-one patients completed their follow-up period. The mean (standard deviation) follow-up period was 13.3 (2.0) months. The patients' mean (standard deviation) age was 28.8 (8.2) years. Skin lesions and skin infections were present in 71.8% and 26.7%, respectively of patients. Common lupus-specific lesions were malar rash (75.4%) and DLE (12.3%). Photosensitivity (72.6%), non-scarring alopecia (67.9%), mucosal ulcers (47.6%), Raynaud's phenomenon (23.8%), and hyperpigmentation (23.8%) were the prevalent lupus non-specific skin lesions. The common skin infections were tinea (42.9%), herpes infection (34.3%), paronychia (20%), and scabies (17%).

Conclusions: Skin lesions related to infections were common, along with lupus-specific and nonspecific lesions skin lesions. Tinea and herpes infections were more common skin infections.

Keywords: *systemic lupus erythematosus; skin lesions; skin infections*

INTRODUCTION

Systemic lupus erythematosus (SLE) is a chronic autoimmune disease affecting multiple organs, including the skin, muscles, joints, blood, kidneys, brain, and other tissues.[1, 2] Skin involvement occurs in 70-85% of SLE patients.[3] Cutaneous manifestations are classified as LE-specific and LE-nonspecific lesions.[4] Lupus-specific lesions confirm cutaneous LE,[5] while nonspecific lesions are related LE[5] but not specific to SLE and also appear in other autoimmune diseases. Identifying these lesions is essential as they imply systemic involvement[6] An Italian study detected 31% nonspecific lesions in the active disease phase.[3] In a Swedish study, nonspecific lesions were 43%, almost twice as frequent as lupus-specific chronic lupus erythematosus (CLE-23%).[7]

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HIGHLIGHTS

1. Lupus-specific and non-specific skin lesions were frequent among the SLE patients.
2. Skin lesions related to infections were also common, along with lupus-specific and nonspecific lesions.
3. Tineasis and herpes infections were common skin infections.

Despite improved survival rates over recent decades, infections remain a major cause of morbidity and mortality in SLE patients.[8] In a Spanish study, skin and mucous membrane infections were the most frequent (16%) among SLE patients.[9] A Mexican study found skin infections were the second most common (23%), following urinary tract infections in outpatients with SLE.[10] Rabbani *et al.* reported 7.5% of skin infections among SLE patients in Pakistan.[11] Zhou and Yang found 8.3% skin and mucous membrane infections among 487 hospitalised SLE patients.[12] Herpes Zoster infections also occur more frequently in SLE patients, causing significant morbidity.[13] Active lupus influences mucocutaneous infections regardless of other variables. There are minimal studies in Bangladesh on skin lesions and infections in SLE patients. Understanding skin infections in SLE patients may help in early diagnosis and effective interventions to reduce morbidity and mortality. This study aimed to determine the frequency of lupus-specific and non-specific skin lesions and identify the skin infection in SLE patients.

METHODS

This observational study was conducted among patients with SLE who attended the Departments of Rheumatology at Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, from October 2014 to April 2016. After obtaining informed written consent, 136 consecutive patients fulfilling ACR 1997 criteria for SLE were enrolled. Consent was also taken to obtain a photograph of their skin lesions. Patients were followed for at least one year, with follow-up visits every three months or as needed, especially when new skin lesions appeared. Baseline characteristics, disease activity, routine investigation findings, types of skin lesions, skin infections, and potential risk factors for skin infections were documented in a semistructured questionnaire. According to Gilliam[4] classification, both LE-specific and LE-nonspecific skin lesions were recorded, drug reactions and skin infections were recorded separately. The investigator initially evaluated skin lesions and infections, then these were confirmed by a dermatologist, with suspicious infections confirmed by laboratory tests. We measured disease activity during each visit.

Disease activity was measured as a categorical variable: SLEDAI score: 0 (no activity), 1–3 (mild), 4-12 (moderate), and >12 (severe). Proteinuria with or without active sediments was recorded as renal activity. Extrarenal activity was defined as flares in systems other than the renal system. Disease duration was recorded in months. Treatment was categorised by the presence and absence of prednisone therapy and other immunosuppressive therapies (cyclophosphamide, azathioprine, mycophenolate mofetil, and methotrexate). The laboratory tests, such as complete blood count, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), urine for routine and microscopic examinations with culture and sensitivity, ultrasonography of kidney ureter and bladder, antinuclear antibody (ANA), anti-double stranded DNA (Anti-dsDNA), serum complement 3 and serum complement 4 (C3, C4) were performed as needed.

Statistical analyses

Patient characteristics were expressed as numbers, means (standard deviation, SD) and medians as appropriate. The frequency of identified lesions was expressed in percentage. The outcome variable, infection, was dichotomised into two groups: those who developed a skin infection and those who did not. Comparisons between categorical variables were performed using the chi-square test.

RESULTS

One thirty-one participants completed the follow-up period. The participants' mean (SD) follow-up period was 13.4 (1.2) months. The patient's mean (SD) age was 28.75 (8.17) years. The frequency of skin lesions and infections was 71.76% and 26.7%, respectively. Baseline socio-demographic features are shown in **TABLE 1.**

TABLE 1 Background characteristics and baseline findings of study participants (n=131)

Characteristics	Frequency (%)
Sex	
Male	5 (3.8)
Female	126 (96.2)
Marital status	
Married	103 (78.6)
Unmarried	21 (16.0)
Others[a]	7 (5.3)
Disease activity	
SELENA-SLEDAI score<3	71 (54.2)
SELENA-SLEDAI score≥3[b]	60 (45.8)
White blood cell count	
<4000/cmm	60 (45.8)
4000-11000/cmm	8 (6.1)
>11000/cmm	108 (82.4)
Erythrocyte sedimentation rate	
Normal (<15 mm/first hour	15 (11.4)
Raised	70 (53.4)
C-reactive protein	
Normal (≤1.0 mg/dL)	61 (46.5)
Raised	92 (70.2)
Anti-dsDNA	
Positive>25 IU/mL	18 (13.7)
Negative	106 (80.9)
Serum complement 3 or complement 4	
Normal (C3: 75 - 175 mg/dL, C4: 22-45 units/mL)	21 (16.0)
Reduced	41 (31.3)

[a]Others included divorced and widow; [b]SELENA-SLEDAI, Safety of Estrogens in Lupus Erythematosus National Assessment- Systemic Lupus Erythematosus Disease Activity Index, SELENA-SLEDAI ≥3 means moderate to high flare present

Among the study population, 94 (71.8%) patients developed skin lesions. The most common lupus-specific lesion was malar rash, affecting 75.4% of patients. Other lupus-specific skin lesions are detailed in **TABLE 2.**

The most common nonspecific skin lesion in lupus was photosensitivity, which affected 72.6% of patients. Other nonspecific lesions of lupus are shown in the **TABLE 3.** We found drug reactions in 1 (1.2%) patient and drug-induced Cushing striae in 1 (1.2%) patient.

TABLE 2 Distribution of lupus-specific skin lesions among the study population (n=57)

Lupus-specific skin lesions	Frequency	Percent
Acute cutaneous lupus erythematosus		
Malar rash	43	75.4
Bullous	2	3.5
Generalised	4	7.0
Total	49	85.9
Subacute cutaneous lupus erythematosus		
Annular	1	1.7
Papulo-squamous	1	1.7
Total	2	3.5
Chronic cutaneous lupus erythematosus		
Classic localised discoid	4	7.0
Classic generalised discoid	3	5.4
Both (localised and generalized)	2	3.6
Lupus profundus	1	1.7
Total	10	17.6

We found 26.7% (n=35) of 131 patients had skin infections. The most frequent skin infection was tinea, affecting 42.9% of patients, followed by herpes infection (34.3%). The frequency of skin infections is shown in **FIGURE 1.**

TABLE 3 Distribution of lupus-specific skin lesions among the study population (n=84)

Nonspecific skin lesions	Frequency	Percent
Photosensitivity	61	72.6
Alopecia	57	67.9
Mucosal Ulcer	40	47.9
Raynaud's phenomenon	20	23.8
HCQ induced hyperpigmentation	20	23.8
Purpura/ ecchymosis	18	21.4
Urticaria	6	7.1
Acneiform lesion	5	6.0
Palpable purpura	4	4.8
Prurigo simplex	3	3.6
Post inflammatory hypopigmentation	2	2.4
Cutaneous ulcer	2	2.4
Purpuric infarction toes /fingers	2	2.4
Nail changes	2	2.4
Cushing striae	2	2.4
Undiagnosed skin changes	2	2.4
Seborrheic dermatitis	2	2.4
Others	6	7.1

The background information was similar between groups. The mean age of the study subjects was 28.2 (8.7) years in the skin-infected group and 29.0 (8.6)) years in the non-infected group. All skin-infected patients were female (100%). Among the non-infected group, 91 (94.8%) participants were female, and 5 (5.2%) were male. Other socio-demographic characteristics of both infected and noninfected groups are shown in **TABLE 4**.

DISCUSSION

Cutaneous manifestations are early and common presentations in SLE patients. SLE patients are more prone to infection, and skin infection is one of the most common infections in SLE patients.[14] As observed by others,[15, 16] females were the dominant gender in our study. However, our observation was extreme, which might be due to the tertiary care hospital setting. Male patients did not seek services until they were seriously ill.

The mean age of this study population was 28.8 years, which supported a study conducted in Japan.[17] Similar findings were also found in studies conducted in Europe

TABLE 4 Comparison of demographic variables between skin-infected and noninfected groups (n=131)

Characteristics	Infected (n=35)	Non-Infected (n=96)	*P*
Age (year)[a]			
Mean (Standard deviation)	28.2 (8.7)	29.0 (8.6)	0.62
Median (Range)	27 (18-50)	28 (18-50)	
Sex			
Male	0	5 (5.2)	0.32
Female	35 (100)	91 (94.8)	
Marital status			
Married	29 (82.9)	74 (77.1)	0.32
Unmarried	3 (8.6)	18 (18.8)	
Divorced or widowed	3 (8.5)	4 (4.2)	
Occupation			
Housewife	31 (88.6)	70 (72.9)	0.32
Student	4 (11.4)	13 (13.5)	
Others[b]	0 (-)	13 (13.5)	
Educational status			
Up to Primary	20 (57.1)	37 (38.5)	0.06
Secondary and more	15 (42.85)	59 (61.45)	
Residence			
Urban	21 (60)	60 (62.5)	0.89
Semi-urban	2 (5.7)	4 (4.2)	
Rural	12 (34.2)	32 (33.3)	

[a]One 60-year-old patient was excluded during the calculation;
[b]Others include service holders, tailors, drivers, and one unemployed.

(29 years),[18] Pakistan (31 years),[11] and a previous study in Bangladesh (29 years).[19] The disease appears to be more common in urban than rural areas.[15] Although Bangladesh is a rural dominant country in this series, the rural vs urban trend was 34% vs 63%, which supports the previous studies. Patients from distant rural areas have access challenges for economic and other reasons.

This study found LE nonspecific skin lesions in 64% of patients, higher than the Italian (31%)[3] and Swedish[7] studies (43%) but lower than another study (77.78%) conducted in Poland.[20] Though non-specific skin lesions are not specific to SLE, different non-specific skin lesions like photosensitivity, oral ulcers, and nonscaring alopecia were included in different diagnostic criteria for SLE, considering their importance. Photosensitivity appears to be an indicator of SLE and one of the most common skin findings of SLE that could also portend systemic spread of SLE. In this series, photosensitivity was found in 73% of SLE patients, consistent with the finding (75%) of a previous study done in Bangladesh. This finding was slightly higher than the English (63%)[6] and American (52.8%)[21] study. However, it was lower than that of another study (95%) conducted in

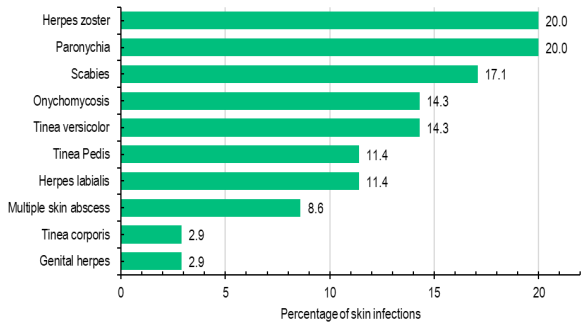

FIGURE 1 Distribution of skin infections in patients with systemic lupus erythematosus

Bangladesh.[19] The prevalence of non-scarring alopecia varies widely between countries, from 20% to 87% in Pakistan,[11] Italy,[3] UK,[6] Saudi Arabia,[22] Bangladesh[19] and India,[21] and Taiwan.[23] Das *et al.* found a highly significant association between systemic involvement in SLE and nonscarring alopecia, photosensitivity, oral ulcer and malar rash. However, we didn't search for this association in this study. Raynaud's phenomenon (RP) is one of the most common non-specific skin lesions in patients with SLE that herald a worse prognosis and is associated with higher disease activity scores.[24] We found RP in 24% of our SLE patients. RP is lower than the studies of the UK (60%)[6] and Italy (39.6%)[3] but higher than Hong Kong (14.8%)[25] and India (6.67%)[21]. Hyperpigmentation was found in 20 % and 22%% of SLE patients in other Bangladeshi[25] and Pakistani[11] studies, respectively. In our study population, hyperpigmentation was 24%, constituting most of these studies. Photosensitivity, skin damage and use of medications like hydroxychloroquine are thought to be the causes of hyperpigmentation. In this series, purpura/ecchymosis was found in 18% of patients, ranging from 7.5% to 19.8% in different studies.[3,25,27]

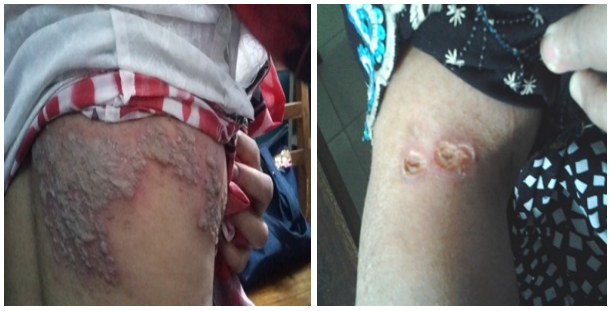

FIGURE 2 (a): Herpes zoster infection in one of our SLE patients; (b) Pyoderma gangenosum

The most common small vessel vasculitis in SLE patients is leukocytoclastic vasculitis (LCV), which usually presents as palpable petechiae or purpura in dependent areas. LCV may occur due to disease, infections, or drugs. We excluded drugs and infection causes before including purpura/ecchymoses in this study.

We found urticaria in 7% of SLE patients, which is comparable with the findings of a Pakistani (10%) study,[11] and the findings reported by Vitali *et al.* (6.3%) [26] and Dubois and Tuffanelli *et al.* (6.9%)[27], but our finding was relatively lower than that of a UK study (44%)[6]. Urticaria is found in SLE due to immune dysregulation and urticarial vasculitis; other causes of urticaria are drugs, medications and malignancy, which were ruled out before including in this study. The acneiform lesion was found in 6% of SLE patients in our series, whereas Van Vollenhoven *et al.*[28] found the same lesion in four patients out of ten patients, which is higher than that of our series. This higher rate may be because all study patients received dehydroepiandrosterone (DHEA). We found cutaneous ulcers in 2.4% of SLE patients. In contrast, these findings in other studies were 1% to 9.8%,[3, 8, 23] Cutaneous ulcers occur in systemic lupus erythematosus (SLE) owing to vasculitis, antiphospholipid antibodies, and, rarely, pyoderma gangrenosum or calcinosis cutis. In our study, cutaneous ulcer and pyoderma granulosum were recorded separately. Patients with SLE frequently show abnormalities of the vasculature of the nail folds marked by periungual erythema, splinter haemorrhages, and nail fold infarcts. Nail fold infarct was 2.4% in this series, consistent with an Indian study (1.34%)[21]. We found nail changes in 2.4% of SLE patients, whereas, in Indian21 studies, it was 26.31% of SLE patients, which was higher than our findings. Our study found pyoderma grangrenosum (PG) in 1.2% of SLE patients, although it is rarely associated with SLE. To our knowledge, 16 cases had been reported on PG in SLE until 2014.[29] Alakesh *et al.*[21] found PG in 1.34% of SLE patients, which is comparable to our study findings. Calcinosis cutis is rarely reported in patients with SLE. Only 36 cases in English-language medical published work had been reported on calcinosis cutis in SLE until 2010.[30] Calcinosis cutis was found in one patient (1.2%) in this series. In this series, other nonspecific skin lesions were prurigo simplex (3.6%), post-inflammatory hypopigmentation (2.4%), seborrheic dermatitis (2.4%), Cushing's striae (2.4%), prurigo nodularis (2.4%), hirsutism (1.2%), stomatitis (1.2%) and undiagnosed skin lesions (2.4%) which were not well reported in other studies.

We found skin infection in 26.7% of our SLE patients, comparable with a Mexican study (23%),[11] but higher than in Spain(16%).[9] Infections, including skin infections, are common in SLE due to its immunopathology and other risk factors like using steroids and immunosuppressant medications. Very few studies reported skin lesions related to skin infections in patients with SLE. Tinea was the most frequent infection (42.8%). Onychomycosis was one of the most common tinea infections (14.3%) in our study. In Mexico,[31] it was 24%, whereas in India,[32] it was 2.5% among the SLE patients. In this study, tinea versicolor, tinea pedis, and tinea corporis were other tinea infections. Although, to date, no tinea versicolor was reported in SLE patients, we found 14.3% tinea versicolor in our study. Bangladesh is a hot and humid country, and SLE is an immunocompromised state, which may cause developing tinea versicolor; its prevalence is also high in the general population. There has been no published report on the prevalence of tinea pedis in SLE till now; the prevalence was 11.4% in this study. Most of the participants of this study were homemakers, and they used excessive water in household work. Humidity and temperature are also well-known factors affecting fungal penetration through the skin.[33] In this series, tinea corporis was found in 2.9% of SLE patients. Rabbani et al.[11] Kapadia *et al.*[34] found 7% and 2.5% tinea corporis, respectively, in their study. Following tinea, herpes infections were the most common findings (34.3%). Herpes zoster was the most common herpes infection (20%), which was consistent with the USA (15%)[35] but lower than that of the results (46.6%) of a study from Japan.[36] Herpes labialis was found in 11.4% of SLE patients in this series, whereas it was 3% and 7.5% in two Pakistani studies[11], respectively, and in a survey of Saudi Arabia, it was 1%. Genital herpes infection was found in this series in 2.9% of SLE patients, comparable with the findings (2.5%) of

another Bangladeshi study.[10] We noticed paronychia in 20% of cases of infection. We found skin abscesses in 8.6% of patients in this series, consistent with the findings (5%) of a Pakistani study.[11] We found scabies in 17.1% (out of six patients, three had a family history of scabies) of SLE patients, which is similar to the findings (20%) of a Pakistani study.[11]

Conclusion

Our study has a limitation of short (one year) follow-up. Actual findings might differ from those of a long time follow-up. Skin lesions related to infections were also frequent, along with lupus-specific and nonspecific lesions. Tineasis and herpes infections were common skin infections. Infection-related skin lesions should be searched in SLE patients presenting with mucocutaneous manifestations. We also recommend further research on skin infections, including superficial fungal and herpes infections in SLE, with an adequate sample size. This may help guide further management of infections in SLE patients.

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Author contributions

Conception and design: MZH, MNI and ATMAZ. *Acquisition, analysis and interpretation of data:* MZH and MNI. *Manuscript drafting and critical revision:* MZH, MNI, ATMAZ, MSMM, MNS, MJA, NF. *Approval of the final version of the manuscript: MZH,* MNI, ATMAZ, MSMM, MNS, MJA, NF. *Guarantor of accuracy and integrity of the work: MZH and MNI.*

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Conflict of interest

None of the authors has any conflict of interest to disclose.

Ethical approval

During the study, the declaration of Helsinki's ethical criteria were followed. Ethical approval was obtained from the Institutional Review Board of BSMMU. Memo no. BSMMU/2014/2208 Date 29 -11-2024. Written (or thumb impression if unable to write) informed consent was obtained from the respondents in Bangla as per the Institutional Review Board guidelines.

Data availability statement

The data that support the findings of this study are available on request from the corresponding author .

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