Morphological Pattern of Cutaneous Manifestations in Systemic Lupus Erythematosus Patients

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Abstract

Background:
SLE is a chronic, autoimmune, inflammatory disease with multiorgan involvement. The Skin is the second most commonly affected organ and manifestations occur 70%-80% of all SLE patients. Cutaneous lesions in patient with SLE may be specific (LE specific) or may be non specific (LE-non specific).There are little or scanty data about the prevalence and morphological pattern of cutaneous lesions in SLE patients in our country. So a study was conducted to find out the morphological pattern of cutaneous lesions in SLE.

Objective:
The aim of the study to evaluate the morphological pattern and spectrum of cutaneous lesions in SLE patients.

Method:
This was a prospective type of observational study conducted among thirty patients with SLE with cutaneous manifestations attending at Department of Dermatology and Venereology, Department of Medicine and Department of Nephrology, Rangpur Medical College & Hospital, Rangpur from April, 2017 to September, 2017.

Result:
The study revealed that the mean age was 25.93 years with a standard deviation of ±8.37. Most of the patients were female, 28 (93.33%) and male were only 2 (6.6%). Within study group of patients LE specific skin manifestations were noted as follows: Butterfly rash or malar rash 22(73.33%), photosensitivity 18(60%), maculopapular rashes 6(20%), oral ulcers 10(33.33%), discoid rash 3(10%). Non specific LE skin manifestations included vasculitic rash 14(46%), alopecia (non scarring) 16(53%), Raynaud's phenomenon 2(6.6%), palmar erythema 6(20%,) livedo reticularis 1(3.3%), hyper pigmentation 4(13.33%), leg ulcers 1(3.33%). Patients having LE specific skin manifestations like malar rash and discoid rash were more likely to have internal organ involvement, while with those having LE non specific skin manifestations were seen with acute flare of disease. ANA and anti-ds DNA antibodies were positive in 96.66% and 66.66% patients respectively.

Conclusion:
Skin manifestations in SLE are significant clues in diagnosis that can give valuable information regarding diagnosis (SLE-specific), as well as, disease activity (SLE-nonspecific skin manifestations are associated with disease activity). Skin manifestations are responsible for increased morbidity also. However, there is a need for large multicentered, randomized trials to know the more precise figures in our population.

Key wrods: SLE, Morphological of cutaneous, Lupus

Introduction:

Systemic Lupus Erythematosus (SLE) is a chronic, autoimmune, inflammatory disease characterized by a spectrum of clinical forms where skin being the second most commonly affected organ and skin involvement occurs in 70%-85% of all patients with SLE[1,9]. This disorder usually is life-long and a potentially fatal autoimmune disease[11]. The disease is more commonly seen among female population. It is about 9 times as common in women as in men, with a peak age of onset between 20-40 years[4,7].

Etiology of SLE is still not fully known but there are several predisposing factors. Multiple

genes confer susceptibility to disease development, the loss of immune tolerance, increased antigenic load, excess T helper cells, defective B cell suppression, and shifting of Th1 to Th2 immune responses lead to cytokine imbalance, B cell hyperactivity, and the production of pathogenic auto antibodies. Finally, certain environmental factors are probably needed to precipitate the onset of the disease[5,7].

SLE is perhaps the best example of multi system disorder in which cutaneous components of the disease, can yield valuable diagnostic and prognostic information2. There is a tremendous variability and diversity in the type of involvement ranging from classical butterfly rash and atrophic hyperkaratotic lesions of discoid lupus to bullae, alopecia and vasculitis[6].

For purpose of identifying patients in clinical studies American Rheumatology Association (ARA) revised criteria for classification of lupus erythematosus is used. A person is said to have SLE if any four or more of the 11 criteria are present, serially or simultaneously during any interval of observation. Cutaneous lesions are important as a diagnostic aid as reflected by fact that they are account for four of the 11 revised American Rheumatology Association criteria of Systemic Lupus Erythematosus[6].

The present study was conducted to evaluate the cutaneous manifestations of SLE in Bangladeshi patients

Methods :

This was a prospective type of observational study conducted among thirty patients with SLE with cutaneous manifestations attending at Department of Dermatology and Venereology, Department of Medicine and Department of Nephrology, Rangpur Medical College & Hospital, Rangpur from April, 2017 to September, 2017 through purposive sampling. On admission each patient was assessed thoroughly by history and clinical examination. Patients fulfilling the clinical and laboratory criteria of American Rheumatology Association (ARA revised criteria) and diagnosed by respective specialist were included into the study and patients and attendants who were unwilling to give consent, history of taking systemic steroid or drug induce cases, other collagen vascular diseases (DM, MCTD), other dermatoses (PMLE, Actinic keratosis, Lichen Planus, Lupus vulgaris, Psoriasis) and Pregnancy were excluded.

Data was entered in the template of statistical program SPSS-22 after necessary editing and coding. The qualitative data were presented as number and percentages while the quantitative data were presented as mean, standard deviations and ranges.

Results:

The main objective of the study was to determine the morphologic pattern of cutaneous lesions in systemic lupus erythematosus patient in respect of age, sex and occupation. Data were collected from 30 systemic lupus erythematosus patients those who attended in Department of Dermatology and Venereology, Department of Medicine and Department of Nephrology, Rangpur Medical College & Hospital, Rangpur, Bangladesh, during the period of April, 2017 to September, 2017. The mean age of the respondents was 25.93 years with a standard deviation of ±8.37. The findings of the study were presented here under (Table-I).

Table-I: Demographical pattern of patients with SLE (N=30)

Demographic Variable	Character	Value (N%)
Gender	Male	2(6.6%)
	Female	28(93.33%)
Marital Status	Married	22(73.33%)
	Unmarried	07(23.33%)
	Others	01(3.33%)
Occupation	House wife	21(70%)
	Student	5(16.66%)
	Service	3(10%)
	Others	01(3.33%)
Socioeconomic condition	Upper	3(10%)
	Middle	9(30%)
	Lower	18(60%)
Family history of SLE	Present	1(3.33%)
	Absent	29(96.66%)

Table-II showed that most of the patients were female 28 (93.33%) and only 2(6.66%) were male. Among them 29(96.66%) had no family history of SLE.

Table-II: Age and sex distribution of the respondents (N=30)

Age (Year)	Male	Female	Total
11-20	1(3.3%)	9(30%)	10(10)
21-30	1(3.3%)	11(36.66%)	12(12)
31-40	0	6(20.00%)	6(6)
41-50	0	2(6.66%)	2(2)
Total	2(6.66%)	28(93.33%)	30(30)
Mean (years)	21.50±6.36	26.25±8.50	25.93±8.37

Table-II showed the age distribution of the patients where mean age was 25.93±8.37 (years) and most of the patients (66.66%) belong to the age group 11-30 years of female.

Table-III: SLE Specific Skin Manifestations in study population (N=30)

Skin Manifestations	Frequency (N%)
Malar rash	22(73.3%)
Photosensitivity	18(60%)
Maculopapaular rashes	6(20%)
Oral ulcers	10(33.3%)
Discoid rash	3(10%)
Subacute cutaneous LE	1(3.3%)

Table-III showed that most of the patients were suffered from malar rash 73.3% and less were suffered from Subacute cutaneous LE 3.3%.

Table-IV: SLE-nonspecific manifestations in study population (N=30)

Nonspecific manifestations	Frequency (N%)
Vasculitic rash	14(46%)
Alopecia (non scarring)	16(53%)
Palmar erythema	6(20%)
Livedo reticularis	1(3.3%)
Raynaud's phenomenon	2(6.6%)
Hyper pigmentation	4(13.3%)
Leg ulcers	1(3.3%)

Table-IV showed that most of the patients were suffered from Alopecia (non scarring) 16 and the second most were suffered from Vasculitic rash.

Table-V: Laboratory findings in the study population.

Parameters	Frequency (N%)
Hb <10mg/dL	21(70%)
Leucopenia	2(6.6%)
Thrombocytopenia	3(10%)
ESR>50	26(86.66%)
ANA (Positive)	29(96.66%)
Anti-dsDNA antibodies	20(66.66%)
Proteinuria	7(23.33%)

Table-V showed at the time of diagnosis 21 patients (70%) were anemic, lucopenia 2 (6.6%), thrombocytopenia 3 (10%), ESR>50- 26 (86.66%) and Proteinuria 7 (23.33%).

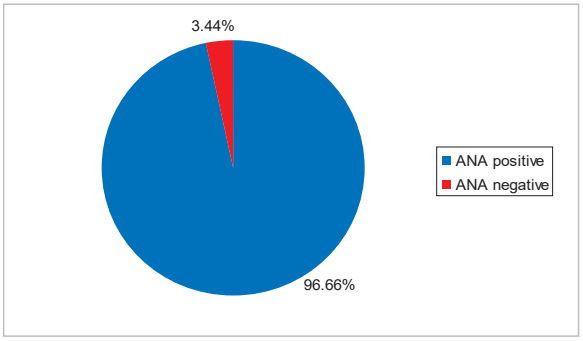


Figure-1: Distribution of SLE patients according to ANA grading.

Figure-1 showed most of the SLE patients were ANA positive (96.66%)

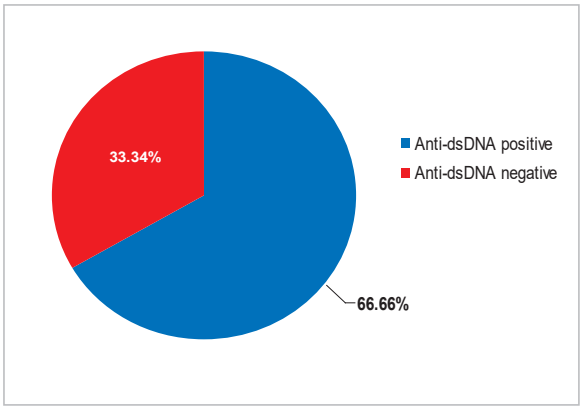


Figure-2: Distribution of SLE patients according to Anti-dsDNA antibodies grading.

Figure-2 showed the SLE patients Anti-ds DNA antibodies positive (66.66%).

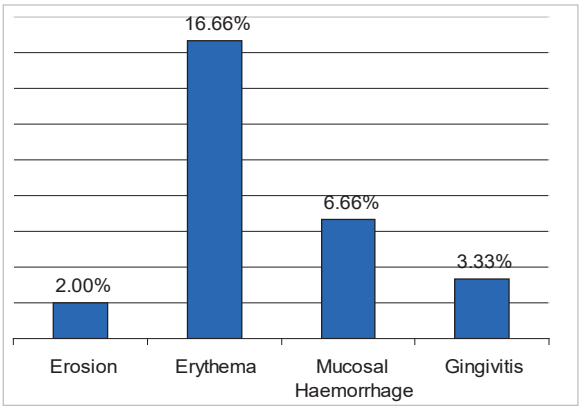


Figure-3: Different types of oral lesion in study population.

Figure-3 showed different types of oral lesion in study population. Among them erythema are the most common.

Discussion:

A total of 30 study populations, who fulfilled the American Rheumatology Association revised criteria for systemic lupus erythematosus, were selected purposively from Medical College & Hospital, Rangpur, Bangladesh. Of them, most were female with mean age was 25.93± 8.37 years and 93.33% were female and 6.6% were male. This study findings consistent with the findings of Naheed A. et al.[7] where mean age was 25.97±4.64 years with 92% patients were female and 8% were male. But differ from Parveen et al.[10] where mean age was 30.04 and male to female ratio 1:5. This figure reflect the female preponderance and the prevalence of disease in younger age population.

In this study majority patients came from the lower class family. Housewives were the highest (70%), and married persons represented 73.3% of total respondents. Out of 30 respondents 60% gave the history of photosensitivity. This result is partially accorded with the findings of Kapadia N et al.[16] but differ from Rabbani M A et al.[6] (33.0%) and Muzaffar et al. (53.3%).[14]

The classic butterfly facial rash is the most frequent skin lesion (73.33%) among the respondents. This result is nearly corresponding with Muzaffar Farhana's [14] study, which was conducted among children and Parveen et al.(70%).[10] But this result is far less than Cardinali C. et al.'s 13 finding (96%) and also differ from Patel et al.[17] (40.0%), Rabbani et al. 6 (31.0%) and Cervera et al.[24] (31.1%).

Present study showed that 10(33.3%) patients, had oral lesions. It is supported by the findings of Rasheed A. et al.[8] (31.2%) and parveen et al.[10] (34%). Different percentage of prevalence of oral ulcers were also seen by Kole and Ghosh,[3] and Malaviya et al.[18]

Maculopapular rashes and SCLE were noted in 20% and 3.3% of the cases respectively in this study which were similar to Kole and Ghosh[3] (23.46%,5.18%) and Rasheed A. et al.[8]

Raynaud's phenomenon was a less common skin manifestation in SLE i.e. 6.6%, while higher figures were seen by Kole and Ghosh[3] and Malaviya et al.[18] This variation may be attributable to diverse environmental conditions.

In this Study it was found that 53% respondents have non-scarring alopecia.This result is partially supported by Parveen et al. 10 (47.o%), Yell JA et a1.[15] (40.0%), but differ from the findings of Rabbani MA et al.[6] (22.0%) , Kapadia N et al.[16] and Akter and Khan(37.0%).[19]

Current study revealed that out of all patients 40% have specific LE lesion only, both type of lesions have 60% patients. Only non-specific lesion scored 0%. This result is largely differ from Zecevic RD et al.[12] Evidence of DLE rash (10%) of current study were similar with Parveen et al. (10.0%), but differ from Rabbani et al.[6] (15.0%) Kapadia N at el.[16] and Rasheed A. et al. (20.8%).[8]

Current study revealed that among the respondents 20% had palmar erythema, 6.6% had Raynaud's phenomenon, 13.3% had hyper pigmentation, 3.3% had leg ulcers, 3.3% had livodo reticularis, but this results are differ from some other studies.

Hyperpigmentation was noted in 4(13.3%) of our study which was consonance with Rabbani et al. 6 while it was lower in a study by Tuffanelli and Dubois[20] (8.4%). This difference may be due to excessive exposure to sunlight in our country and a general tendency to postinflammatory melanosis.

The incidence of ANA-negative SLE was similar (3.44%) as compared to 4-13% reported previously.[21] Anti dsDNA antibodies were elevated in 66.66% of our patients similar to literature.[22] ANA was positive in 96.66% similar to what was reported previously.[23,24]

Conclusion:

Skin manifestations in SLE are significant clues in diagnosis that can give valuable information regarding diagnosis (SLE-specific), as well as, disease activity (SLE-nonspecific skin manifestations are associated with disease activity). Skin manifestations are responsible for increased morbidity also. However, there is a need for large multicentered, randomized trials to know the more precise figures in our population.

References:

1. McCauliffe DP. Cutaneous lupus erythematosus. Semin Cutan Med Surg. 2001 Mar;20(1):14-26. doi: 10.1053/sder.2001.23091. 2. Font J, Bosch X, Ingelmo M, Herrero C, Bielsa I, Mascary JM. Acquired ichthyosis in a patient with systemic lupus erythematosus. Arch Dermatol. 1990 Jun;126(6):829.
3. Kole AK, Ghosh A. Cutaneous manifestations of systemic lupus erythematosus in a tertiary referral center. Indian J Dermatol. 2009;54(2):132-6. doi: 10.4103/0019-5154.53189.
4. Kumar P, Clark M, editors. Kumar and Clark Clinical Medicine. Oxford: Elsevier saunders; 2005. P.574-7.
5. Mok CC, Lau CS. Pathogenesis of systemic lupus erythematosus. J Clin Pathol. [serial online] 2003; 56 [cites 2009 January 5] [10 screens] Available from URL: http://www.-pubmedcentral .nih.gov/articlerender.fcgi?artid = 176998 &tool =pmcentrez.
6. Rabbani MA, Shah SM, Ahmed A. Cutaneous manifestations of systemic lupus erythematosus in Pakistani patients. J Pak Med Assoc. 2003 Nov;53(11):539-41.
7. Naheed A, Shaheen JA, Khalid M. Cutaneous manifestations of sysmemic lupus erythematosus - An experience from Bahawal-Victoria Hospital, Bahawalpur. Journal of Pakist Association of Dermatologists.2014; 24 (1): 15-20.
8. Rasheed A, Rasul S, Hameed A. Prevalence of usual and unusual skin manifestations of sysmemic lupus erythematosus in a tertiary care hospital. Journal of Pakistan Association of Dermatologists.2016; 26 (2):118-122.
9. Bhattarai S, Agrawal S et al. Spectrum of cutaneous manifestations in lupus erythematosus-a dermatologist perstective. Health Renaissance, January – April 2012;Vol 10 (No. 1);8-11.
10. Parveen N, Das DK et al. Cutaneous manifestation of systemic lupus erythematosus. J Medicine 2007; 8: 44-48.
11. Caeiro F, Michielson FM, Bernstein R, Hughes GR, Ansell BM. Systemic lupus erythematosus in childhood. Ann Rheum Dis. 1981 Aug;40(4):325-31. doi: 10.1136/ard.40.4.325.
12. Zecević RD, Vojvodić D, Ristić B, Pavlović MD, Stefanović D, Karadaglić D. Skin lesions--an indicator of disease activity in systemic lupus erythematosus? Lupus. 2001; 10(5):364-7. doi: 10.1191/096120301675962535.
13. Cardinali C, Caproni M, Bernacchi E, Amato L, Fabbri P. The spectrum of cutaneous manifestations in lupus erythematosus--the Italian experience. Lupus. 2000;9(6):417-23. doi: 10.1191/096120300678828569.
14. Muzaffar Farhana. Cutaneous manifestations of systemic lupus erythematosus in Pakistani children.J Pakistan Assoc Derma 2004 sep;14(3). 110-3.
15. Yell JA, Mbuagbaw J, Burge SM. Cutaneous manifestations of systemic lupus erythematosus. Br J Dermatol. 1996 Sep;135(3):355-62.
16. Kapadia N, Haroon TS. Cutaneous manifestations of systemic lupus erythematosus: study from Lahore, Pakistan. Int J Dermatol. 1996 Jun;35(6):408-9. doi: 10.1111/j.1365-4362.1996.tb03021.x.
17. Patel P, Werth V. Cutaneous lupus erythematosus: a review. Dermatol Clin. 2002 Jul;20(3):373-85, v. doi: 10.1016/s0733-8635(02)00016-5.
18. Malaviya AN, Singh RR, Singh YN, Kapoor SK, Kumar A. Prevalence of systemic lupus erythematosus in India. Lupus. 1993 Apr;2(2):115-8. doi: 10.1177/096120339300200209.
19. Akhter J, Khan MA. SLE in Pakistan. specialist. 1992;9:25-7.
20. Tuffanelli DL, Dubois EL. Cutaneous manifestations of SLE. Arch Dermatol 1964;8:377-86.doi: 10.1001/archderm.1964.01600040005001.

21. Noz KC. ANA-negative SLE. Br J Dermatol.1993;129:345-6.
22. McCarty GA. Autoantibodies and their relation to rheumatic diseases. Med Clin North Am. 1986 Mar;70(2):237-61. doi: 10.1016/s0025-7125(16)30952-x.
23. Font J, Cervera R, Espinosa G, Pallarйs L, Ramos-Casals M, Jimйnez S, et al. Systemic lupus erythematosus (SLE) in childhood: analysis of clinical and immunological findings in 34 patients and comparison with SLE characteristics in adults. Ann Rheum Dis. 1998 Aug;57(8):456-9. doi: 10.1136/ard.57.8.456.
24. Cervera R, Khamashta MA, Font J, Sebastiani GD, Gil A, Lavilla P,et al. Systemic lupus erythematosus: clinical and immunologic patterns of disease expression in a cohort of 1,000 patients. The European Working Party on Systemic Lupus Erythematosus. Medicine (Baltimore). 1993 Mar;72(2): 113-24.