International Journal of Research in Dermatology
Subba DM et al. Int J Res Dermatol. 2021 Sep;7(5):702-707
http://www.ijord.com

DOI: https://dx.doi.org/10.18203/issn.2455-4529.IntJResDermatol20213347

Original Research Article

Clinical profile of cutaneous manifestations of connective tissue diseases in North-East India

Deepa Mala Subba[1], Nandakishore Thokchom[2], Linda Kongbam[2]*, Erika Salam[2], Deepa Yumnam[2]

[1]Department of Dermatology and VL, Namchi District Hospital, South Sikkim, Sikkim, India
[2]Department of Dermatology and VL, Regional Institute of Medical Sciences, Imphal, Manipur, India

Received: 04 July 2021
Accepted: 12 August 2021

***Correspondence:**
Dr. Linda Kongbam,
E-mail: lindaz_here@yahoo.co.in

ABSTRACT

Background: Connective tissue diseases (CTDs) are a heterogeneous group of autoimmune disorders having overlapping clinical features. Skin is often involved and it may be the earliest sign of the disease. This study highlighted the various cutaneous manifestations of common CTDs.
Methods: A hospital-based cross-sectional study was carried out for a period of two years in 83 patients with CTDs in dermatology OPD, RIMS, Imphal. Detailed history taking, examination and relevant serological tests were performed.
Results: The mean age was 39.78±17.29 years with female to male ratio of 4.5:1. Majority of the patients had lupus erythematosus (LE) (N=45) followed by systemic sclerosis (SSc) (N=25), rheumatoid arthritis (RA) (N=6), mixed connective tissue disease (MCTD) (N=4) and morphea (N=3). The most common presentation was raised skin lesions (45.8%) followed by Raynaud's phenomenon (36.1%), photosensitivity (27.7%), skin tightness (26.5%) and joint pain (19.3%). Among LE patients, chronic cutaneous lupus erythematosus (CCLE) was the commonest variant and localised discoid lupus erythematosus (DLE) (22.9%) was the commonest presentation followed by malar rash and annular subacute lupus erythematosus (SCLE). Skin induration, microstomia and sclerodactyly were seen in most patients of SSc. Antinuclear antibodies were positive in 89.1% of patients. Anti-dsDNA and anti-Sm antibodies were positive in 62.2% and 33.3% of LE patients, anti-Scl 70 antibody was positive in 68% of SSc patients.
Conclusions: CTDs are rare but potentially life-threatening. Proper understanding of the spectrum of cutaneous manifestations of CTDs is therefore necessary for early diagnosis and efficient management.

Keywords: Connective tissue diseases, Lupus, Systemic sclerosis, Photosensitivity, Raynaud's phenomenon, Sclerodactyly

INTRODUCTION

The CTDs are a group of polygenic disorders often heterogeneous due to autoimmune process and sometimes with overlapping clinical features. Skin is often involved and its involvement may be the earliest sign of the disease. Common CTDs showing cutaneous manifestations include LE, SSc, dermatomyositis (DM), Sjogren's syndrome, RA and MCTD.[1] The incidence and prevalence are variable. There are reports of various studies on individual connective tissue diseases.[2-23] However, comprehensive studies on the spectrum of cutaneous features of CTDs are few especially in the north-eastern part of India.

METHODS

A hospital-based cross-sectional study was conducted for a period of 24 months (October 2014 to September 2016) in the outpatient departments of dermatology, venereology and leprology and medicine, RIMS, Imphal, Manipur. Eighty three patients of all ages and both sexes with CTDs having cutaneous manifestations were included in the study.

Detailed history taking, examination and relevant laboratory investigations including serology were done. Analysis of data was done by SPSS software version 21.0 for Windows. Descriptive statistics such as mean, standard deviation (SD) and percentage were used. Ethical approval for the study was obtained from the institutional ethics committee.

RESULTS

The mean age of the patients was 39.78±17.29 years with female to male ratio of 4.5:1. The most common CTD was LE (N=45) followed by SSc (N=25), RA (N=6), MCTD (N=4) and morphea (N=3) (Figure 1).

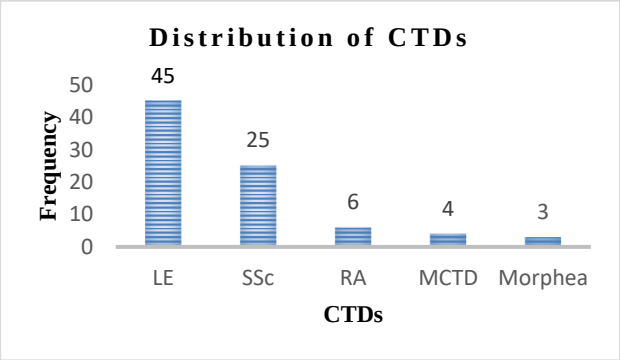

Figure 1: Distribution of CTDs.

Raised skin lesions (45.8%) was the commonest clinical presentation followed by Raynaud's phenomenon (36.1%), photosensitivity (27.7%), tightness of skin (26.5%) and joint pain (19.3 %). Other symptoms were dyspnoea, weakness and loss of appetite.

Out of 45 patients with LE, CCLE (N=23) was the commonest variant followed by ACLE (N=12), SCLE (N=9), bullous SLE (N=2) and lupus panniculitis (N=1) (Figure 2 and 3). Female to male ratio was 6.5:1. Majority of the patients presented with photosensitivity and discoid plaques (N=23 each) followed by Raynaud's phenomenon, joint pain, malar rash, alopecia, fever, oral ulcer and bullous lesions (Table 1). Most of the patients presented within a duration of 6 months. Out of 23 CCLE patients, majority (N=14) had localized plaque and 3 had scarring alopecia of scalp. Mucocutaneous, haematological and renal involvement was seen in 33.3%, 35.5% and 15.5% of LE patients respectively. Raised ESR was seen in 34.9% of patients.

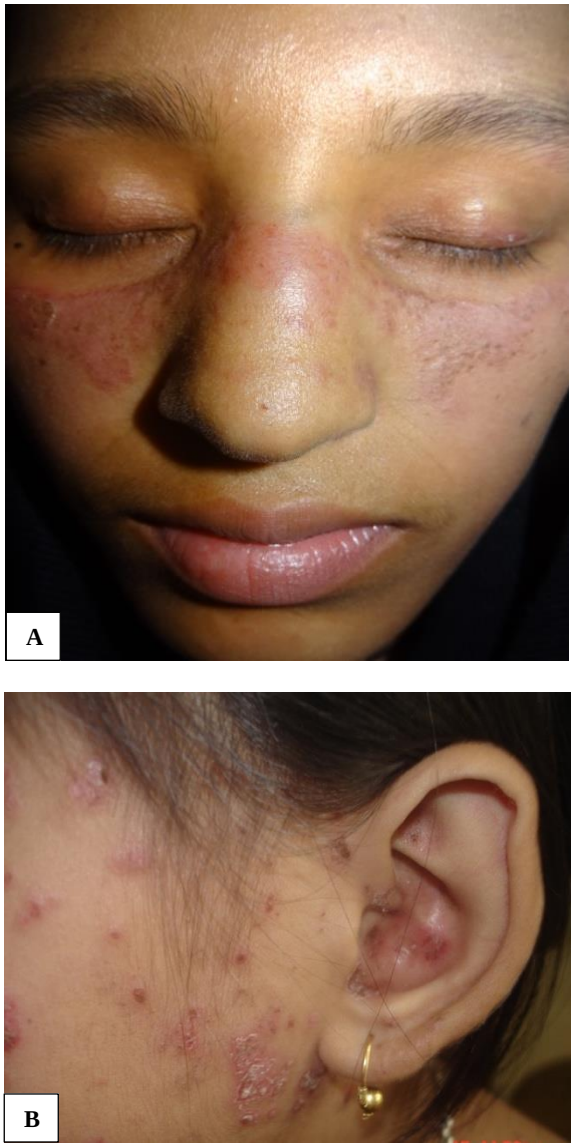

Figure 2: (A) Malar rash; (B) LE plaques on cheeks and concha in SLE.

Out of 28 scleroderma patients, SSc accounted for 25 and morphea 3 patients. Female to male ratio was 3.1:1. Raynaud's phenomenon was present in all SSc patients. Majority of the patients had sclerodactyly (N=19) followed by skin induration and microstomia (N=18 each) (Figure 4). Other clinical findings are listed in Table 2. Pulmonary function test and HRCT showed restrictive pattern of lung disease in 3 patients of systemic sclerosis. Out of three morphea patients, 2 had plaque type and one had linear morphea (Figure 5).

Majority of RA patients (N=6) belonged to the age group of 41-50 years. Rheumatoid vasculitis was seen in 4 patients and rheumatoid nodules in 2 patients.

In patients of MCTD, SLE and polymyositis (N=2) was the most common association, followed by one each of SLE with SSc and SLE with RA.

ANA positivity was seen in 89.1% of patients. Serological findings in each type of CTDs are given in Table 3.

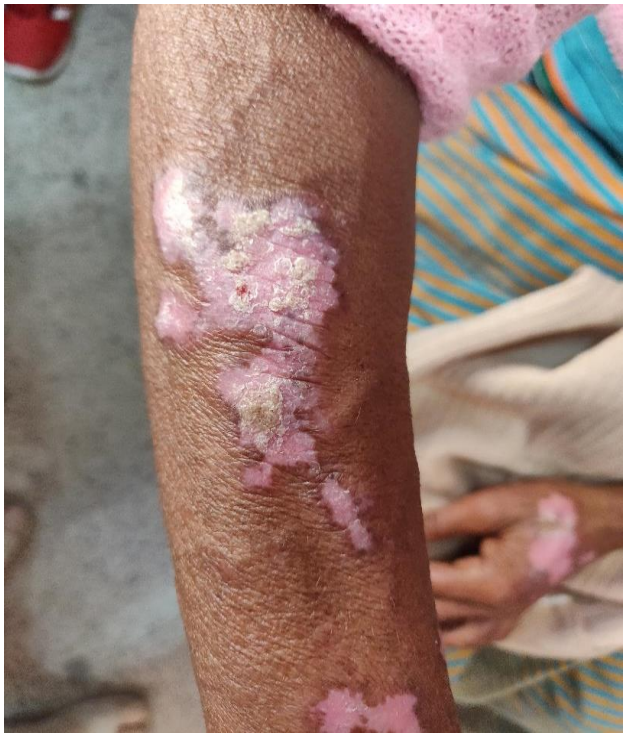

Figure 3: Discoid lupus erythematosus.

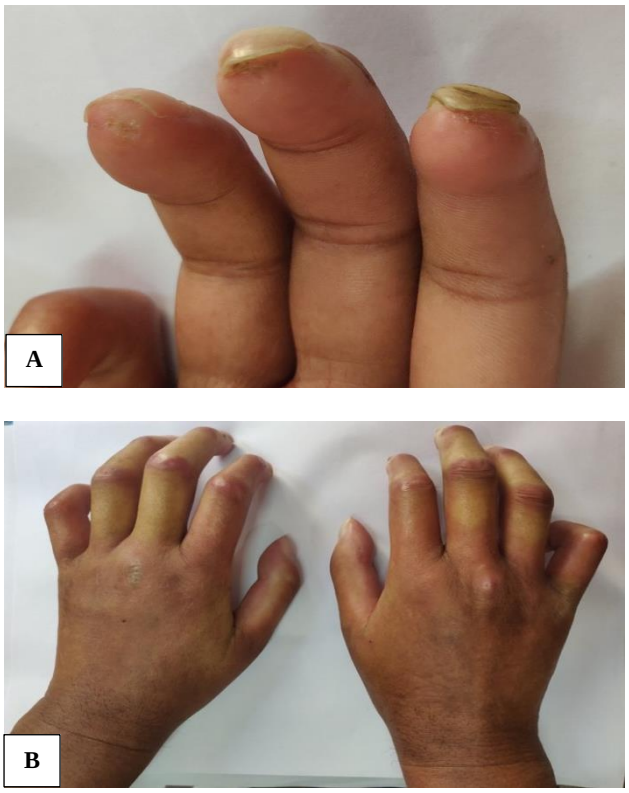

Figure 4: (A) Digital pitted scars; (B) sclerodactyly with calcinosis cutis in SSc.

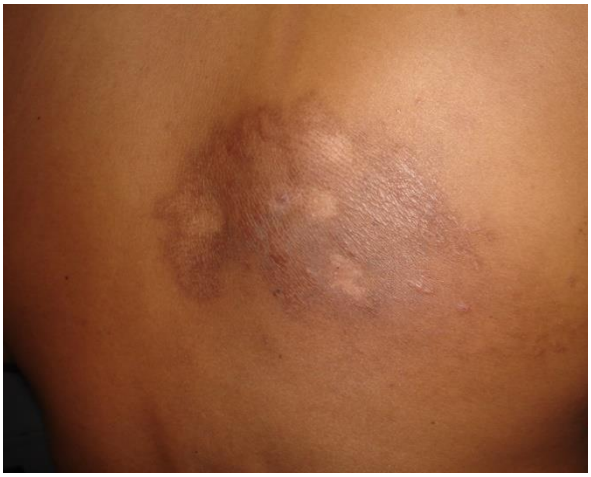

Figure 5: Plaque morphea.

Table 1: Clinical features in LE (N=45).

Sr. No.	Clinical features	Frequency	Percentage
1.	Photosensitivity	23	51.1
2.	Discoid plaques	23	51.1
3.	Raynaud's phenomenon	20	44.4
4.	Joint pain	16	35.5
5.	Malar rash	12	26.6
6.	Alopecia	9	20
7.	Fever	5	11.1
8.	Oral ulcer	5	11.1
9.	Bullous lesions	2	4.4

Table 2: Clinical features in SSc (N=25).

Sr. No.	Clinical features	Frequency	Percentage
1.	Raynaud's phenomenon	25	100
2.	Sclerodactyly	19	76
3.	Skin induration	18	72
4.	Microstomia	18	72
5.	Decreased forehead wrinkling	14	56
6.	Positive Ingram sign	13	52
7.	Radial furrow	13	52
8.	Digital pitting	13	52
9.	Parrot beaking of nose	12	48
10.	Mask-like face	12	48
11.	Digital ulcers	12	48
12.	"Salt and pepper" pigmentation	11	44
13.	Bulbous fingers	10	40
14.	Atrophy of fingers	9	36
15.	Telangiectasia	7	28
16.	Calcinosis cutis	2	8

Table 3: Serology in different types of CTDs.

Sr. No.	CTD	Antibodies	Frequency	Percentage
1.	LE (N=45)	ANA	42	93.3
		Anti-ds DNA	28	62.2
		Anti-Sm	15	33.3
		Anti-Ro/SSA	5	11.1
		Anti-centromere	5	11.1
		Anti-U1RNP	5	11.1
		Anti-La/SSB	4	8.8
		Anti-Scl-70	1	2.2
2.	SSc (N=25)	ANA	25	100
		Anti-Scl 70	17	68
		Anti-dsDNA	9	36
		Anti-centromere	3	12
3.	RA (N=6)	Anti-dsDNA	3	50
		Anti-CCP	3	50
		ANA	1	16.6
		Anti-Sm	1	16.6
		Anti-U1RNP	1	16.6
4.	MCTD (N=4)	ANA	4	100
		Anti-U1RNP	4	100
		Anti-Ro/SSA	2	50
		Anti-Scl-70	1	25
		Anti-Sm	1	25

DISCUSSION

The mean age of presentation in the study group was 39.78±17.29 years and this finding is similar to other studies.[3-5]

In the present study, LE (54.2%) was the most common CTD followed by SSc, RA, MCTD and morphea. Female to male ratio in patients with LE was 13:1, most commonly in the age group of 21-30 years. Kosaraju et al also reported female to male ratio of 15:1 and this increased frequency of SLE among females was thought to be due to hormonal effects.[6] CCLE was the commonest variant followed by ACLE, SCLE, bullous SLE and lupus panniculitis which is similar to other studies.[2,7] The commonest symptom was photosensitivity followed by joint pain, malar rash, fever and oral ulcer in the present study. Durosaro et al and Moghadam-Kia et al reported discoid rash whereas Jallouli et al reported arthritis as the most common clinical presentation (54.8%).[2,7,8]

Raynaud's phenomenon was seen in 49.1% of SLE patients in a study by Heimovski et al whereas only 13% had Raynaud's phenomenon in this study.[10]

Mucocutaneous, haematological and renal involvement were seen in 33.3%, 35.5% and 15.5% of LE patients respectively in this study; similar to Agrawal et al.[3] However, another study showed less prevalence of mucocutaneous manifestations.[6]

Majority of CCLE patients had localised lesion (60.8%) mostly on face and 13% had scarring alopecia of scalp. These findings were similar to other studies.[2,11,14] No specific association between scarring alopecia and SLE had been reported.[12]

Anti-Sm antibodies were positive in more than half of LE patients (55.5%) in this study while another study reported in only 39.2%.[8] Anti-Sm antibody had been reported to be associated with Raynaud's phenomenon and malar rash.[8,15] Presence of anti-dsDNA antibodies was the hallmark of SLE, however, only 35.5% positivity was seen in this study.[6] Three out of seven patients of lupus nephritis were positive for anti-dsDNA antibodies. Anti-dsDNA antibody was strongly associated with renal involvement in patients with lupus.[6] Inflammation in SLE, in contrast to inflammation in other rheumatic diseases, was characterized by elevated ESR.[6] Raised ESR was seen in 34.9% of patients in this study.

Female preponderance was observed in SSc with female to male ratio of 3.1:1; similar to earlier studies.[16-19] However, a higher female to male ratio have also been reported by Pradhan et al (10:1) and Flower et al (26:1).[13,20] The mean age of presentation was 45.08±19.5 years which was similar to other studies.[21,22] In the present study, only one patient presented at 10 years of age. In a study conducted in Eastern India, 9 out of 46 patients were children.[21]

Raynaud's phenomenon was seen in all patients of SSc and majority had sclerodactyly (76%) which was similar to studies from different parts of India.[17,18,21-24] Cutaneous sclerosis was found in most patients in the present study and similar findings have been reported by other authors (range: 90-98.5%).[21-24] Fingertip ulceration was noted in 48% of patients which was also similar to that of previous studies (range: 37-63%).[18,21,22] In this study, "salt and pepper" pigmentation was seen in 44% of patients. Other authors had reported diffuse hyperpigmentation and depigmentation at site of scars as other pigmentary changes.[22,24]

In this study, mat-like telangeictasia was seen most commonly on face. In another study, periungual region was the most common site of telangiectasia.[22] Microstomia was noted in only 21.2% of patients in this study whereas Purnima et al and Sharma et al reported in 60% and 55.5% respectively.[22,24] Calcinosis cutis was found in 2 patients as similar to other studies.[18,21]

Anterior chest wall thickening in 40% of SSc patients have been reported in a study.[23] None had anterior chest wall thickening in this study. However, pulmonary function abnormality and HRCT showed restrictive pattern of lung disease in 3 patients. Thus, pulmonary fibrosis may not always be associated with chest skin tightening. Gastrointestinal symptoms were not seen in any patient in the present study whereas others have reported symptoms of oesophageal reflux and dysphagia.[18,20,22] ANA positivity was seen in 96% of SSc patients which was similar to other studies.[17,21,22,24] In this study, anti-Scl 70 antibodies were positive in 68% of patients whereas another study reported in 35%.[24]

In this study, out of 6 cases of RA, 4 patients had rheumatoid vasculitis and 2 had rheumatoid nodules. Other studies also showed similar findings Bartels et al however, reported a low prevalence of rheumatoid vasculitis.[26-28] None of the patients were positive for Rh factor in this study. However, Cojocaru et al reported Rh factor positivity in all RA patients.[27]

In MCTD, the commonest association was SLE and polymyositis (N=2) followed by SLE and RA (N=1) and SLE and Sjogren's syndrome (N=1). Gurman et al found scleroderma existing with various other CTDs such as dermatomyositis or polymyositis, Sjogren's syndrome, RA and SLE.[29] SLE with polymyositis has been reported by Maazoun et al in a case series of 6 patients.[31] None of the patients of MCTD in this study had interstitial lung disease; whereas Vegh et al reported interstitial lung disease in 53.6%.[30] All the patients were positive for ANA and U1RNP antibodies in this study.

CONCLUSION

CTDs can present with various specific and non-specific cutaneous lesions and can be the earliest sign of the disease. LE remains the commonest CTDs in this part of the country and necessitates detailed laboratory investigations for prognosis and follow up. Evaluation of pulmonary involvement in SSc is also of paramount importance. A comprehensive knowledge of the spectrum of cutaneous manifestations of CTDs is imperative for early diagnosis and efficient management of the patients to minimize systemic complications.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the institutional ethics committee

REFERENCES

1. Jacobe HT, Sontheimer RD. Autoantibodies encountered in patients with autoimmune connective tissue diseases. In: Bolognia JL, Jorizzo JL, eds. Dermatology. 3rd ed. China: Elsevier Saunders; 2012: 603-4.
2. Durosaro O, Davis MD, Reed KB, Rohlinger AL. Incidence of cutaneous lupus erythematosus, 1965-2005: a population-based study. Arch Dermatol. 2009;145(3):249-53.
3. Agrawal SR, Tiewsoh I, Rajput A, Jain A. A cross-sectional hospital based study of clinical and immunological profile of systemic lupus erythematosus patients from central rural India. Indian J Allergy Asthma Immunol. 2013;27(1):33-7.
4. Makol A, Crowson CS, Wetter DA, Sokumbi O, Matteson EL, Warrington KJ. Vasculitis associated with rheumatoid arthritis: a case control study. Rheumatology. 2014;53(5):890-9.
5. Font J, Cervera R, Espinosa G, Pallares G, Casals MR, Jimenez 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;57(8):456-9.
6. Kosaraju K, Shenoy S, Suchithra U. A cross-sectional hospital-based study of autoantibody profile and clinical manifestations of systemic lupus erythematosus in south Indian patients. Indian J Microbiol. 2010;28(3):245-7.
7. Moghadam-Kia S, Chilek K, Gaines E, Costner M, Rose ME, Okawa J, et al. Cross-sectional analysis of a collaborative web-based database for lupus erythematosus associated skin lesions: 114 prospectively enrolled patients. Arch Dermatol. 2009;145(3):255-60.
8. Jallouli M, Frigui M, Hmida MB, Marzouk S, Kaddour N, Bahloul Z. Clinical and immunological manifestations of systemic lupus erythematosus: a study on 146 south Tunisian patients. Saudi J Kidney Dis Transpl. 2008;19(6):1001-8.
9. Merola JF, Prystowsky SD, Iversen C, Puerta JA, Norton T, Tsao P, et al. Association of discoid lupus with other clinical manifestations among patients with systemic lupus erythematosus. J Am Acad Dermatol. 2013;69(1):19-24.
10. Heimovski FE, Simioni, Skare TL. Systemic lupus erythematosus and Raynaud's phenomenon. An Bras Dermatol. 2015;90(6):837-40.
11. Santiago-Casas Y, Vila LM, McGwin G, Cantor RS, Petri M, Golman RR, et al. Association of discoid lupus with clinical manifestations and damage accrual in profile: a multiethnic lupus COHORT. Arthritis Care Res. 2012;64(5):704–12.
12. Das NK, Dutta RN, Sengupta SR. Skin lesions in lupus erythematosus: a marker of systemic involvement. Indian J Dermatol. 2011;56(5):537-40.
13. Pradhan V, Rajadhyaksha A, Nadkar M, Pandit P, Surve P, Lecerf M, et al. Clinical and autoimmune profile of scleroderma patients from western India. Int J Rheumatol. 2014;2014:983781.
14. Dickey BZ, Holland KE, Drolet BA, Galbraith SS, Lyon VB, Siegel DH, et al. Demographic and clinical characteristics of cutaneous lupus erythematosus at a paediatric dermatology referral centre. Br J Dermatol. 2013;169(2):428-33.

15. Li J, Leng X, Li Z, Ye Z, Li C, Li X, et al. Chinese SLE treatment and research group registry: III. Association of autoantibodies with clinical manifestations in Chinese patients with systemic lupus erythematosus. J Immunol Res. 2014;25:1-6.
16. Wang J, Assassi S, Guo G, Tu W, Wu W, Yang L, et al. Clinical and serological features of systemic sclerosis in a Chinese COHORT. Clin Rheumatol. 2013;32(5):617-21.
17. Chularojanamontri L, Sethabutra P, Kulthanan K, Manapajon A. Dermatology life quality index in Thai patients with systemic sclerosis: a cross-sectional study. Indian J Dermatol Venereol Leprol. 2011;77(6):683-7.
18. Shanavas N, Das AK. Profile of systemic sclerosis and associated renal involvement. Arch Med Health Sci. 2015;3(2):209-14.
19. Basel ME, Khalil N. Disease characteristics of systemic sclerosis among Egyptian patients. Kasr El Ainy Med J. 2015;21(2):41-6.
20. Flower C, Nwankwo C. Systemic sclerosis in an Afro-Caribbean population: a review of demographic and clinical features. West Indian Med J. 2008;57(2):118-21.
21. Ghosh SK, Bandyopadhyay D, Saha I, Barua JK. Mucocutaneous and demographic features of systemic sclerosis: a profile of 46 patients from Eastern India. Indian J Dermatol. 2012;57(3):201-5.
22. Sharma VK, Trilokraj T, Khaitan BK, Krishna SM. Profile of systemic sclerosis in a tertiary care center in north India. Indian J Dermatol Venereol Leprol. 2006;72(6):416-20.
23. Deepa AS, Rachel RP, Ramchandran P, Devaraj U, Arnold SA, Shobha V, et al. Pulmonary involvement in systemic sclerosis: a clinical profile. Lung India. 2016;33(2):144-7.
24. Purnima G, Bhavani VG, Kumar TSP, Dhankar SU. Profile of systemic sclerosis in tertiary care centre, Vijayawada. IOSR. 2016;15:24-8.
25. Letenberger J, Cayce RL, Haley RW, Huet BA, Bergstresser PR, Jacobe HT. Morphea subtypes are distinct autoimmune syndromes: a review of 245 adults and pediatric cases. Arch Dermatol 2009;145:545-50.
26. Bartels C, Bell C, Rosenthal A, Shinki K, Bridges A. Decline in rheumatoid vasculitis prevalence among US veterans: a retrospective cross-sectional study. Arthritis Rheum. 2009;60(9):2553-7.
27. Cojocaru M, Cojocaru IM, Silosi I, Doina C. Extra-articular manifestations in rheumatoid arthritis. J Clin Med. 2010;5(4):286-91.
28. Watts RA, Mooney J, Lane SE, Scott DG. Rheumatoid vasculitis: becoming extinct? Rheumatology. 2004;43(7):920-3.
29. Gurman AB, Moscovici YB. Scleroderma overlap syndrome. Isr Med Assoc J. 2011;13(1):14-20.
30. Vegh J, Szilasi M, Soos G, Devenyi K, Dezso B, Soltesz P, et al. Interstitial lung disease in mixed connective tissue disease. Orv Hetil. 2005;146:2435-43.
31. Maazoun F, Frikha F, Snoussi M, Kaddour N, Masmoudi H, Bahloul Z. Systemic lupus erythematosus myositis overlap syndrome: report of 6 cases. Clin Pract. 2011;1(4):89.
32. Szodoray P, Hajas A, Kardos L, Dezso B, Soos G, Zold E, et al. Distinct phenotypes in mixed connective tissue disease: subgroups and survival. Lupus. 2012;21(13):1412-22.

Cite this article as: Subba DM, Thokchom N, Kongbam L, Salam E, Yumnam D. Clinical profile of cutaneous manifestations of connective tissue diseases in North-East India. Int J Res Dermatol 2021;7:702-7.