Original Article

A clinical study of connective tissue diseases

Dr. Sandeep Kodali[1], Dr. L.V.N. Reddy [2], Dr. M. Lavanya [3], Dr . Kotha Sravanthi [4] Dr. N. Nagendra Chary[5]

[1]Associate Professor, Department of DVL, Mallareddy Medical College and Hospital for Women, Suraram, Quthbullapur, Jeedimetla, Hyderabad, Telangana
[2]Assistant Professor, Department of DVL, Mallareddy Institute of Medical Sciences, Suraram, Quthbullapur, Jeedimetla, Hyderabad, Telangana
[3]Assistant Professor, Department of DVL, Mallareddy Institute of Medical Sciences, Suraram, Quthbullapur, Jeedimetla, Hyderabad, Telangana
[4]Postgraduate, Department of DVL, GSL Medical College and General Hospital, Rajahmundry, East Godavari District, Andhra Pradesh
[5]Professor and HOD, Department of DVL, Hyderabad, Telangana.

Corresponding Author:
Dr. Sandeep Kodali
12-234, Adarsh Nagar, Balanagar
Hyderabad – 500037, Telangana.

Abstract:

Background: Connective tissue diseases are defined as a group of auto-immune disorders that have in common, immunological and inflammatory changes in blood vessels and connective tissues. We have undertaken this study to know about the epidemiological and clinical aspects of this disease. **Objectives**: The present study was conducted to know the occurrence of various types of connective tissue diseases, incidence in relation to gender, the age distribution and the most common symptoms and signs of connective tissue diseases. **Methods**: The present study was conducted in 40 cases of clinically diagnosed connective tissue diseases in a private hospital in Hyderabad, from April 2014 – April 2015 over a period of 12 months. A detailed history and examination was performed as per proforma. Basic and appropriate special investigations were performed; including complete haemogram, complete urine examination, renal function tests, skin biopsy and antinuclear antibody positivity test by ELISA was done in all patients.**Results**: In this study, majority of the patients (17 patients – 42.50 percent) examined were within the age group of 31 – 40 years. Majority of the patients belonged to the female gender (33 patients – 82.50 percent). Discoid Lupus Erythematosus (15 patients – 37.50 percent) was the most common disease which was observed in our study. Photosensitivity (5 patients – 2.50 percent) was the most common presentation in SLE (8 patients – 20.00 percent of all cases). The most common type of morphoea (9 patients – 22.50 percent of all cases) was the plaque type (5 patients – 55.55 cases of morphoea). Sclerosis of the skin (6 patients – 100.00 percent) was the most common finding in systemic sclerosis (15.00 percent of all the cases), followed by Reynaud's phenomenon (5 patients – 83.33 percent of cases of systemic sclerosis). Antinuclear Antibodies positivity was seen in 28 patients (70.00 percent of all the cases) of connective tissue diseases, but the positivity was highest in systemic lupus erythematosus (7 patients – 87.50 percent of the cases). **Conclusion**:. Discoid lupus Erythematous being most common presentation. Females of age group 31-40 were most frequently involved.
Key words: Connective Tissue Diseases, Discoid Lupus Erythematosus, Morphoea, Systemic Sclerosis, Dermatomyositis,.

INTRODUCTION:

Connective tissue diseases are defined as a group of acquired auto-immune disorders that have in common, of immunological and inflammatory changes in the blood vessels and connective tissues. They are protean in their manifestation wherein a plethora of external and internal factors come into play. Connective tissue diseases share many clinical and pathological features. They develop slowly over many years or present abruptly and show rapid progression and they are typically characterized by alternating periods of remissions and flares. The connective tissue diseases which include discoid lupus erythematosus (DLE), systemic lupus erythematosus (SLE), morphoea, systemic sclerosis (SSc), dermatomyositis (DM), rheumatoid arthritis (RA) and Sjogren's syndrome (SS) have certain features in common like autoimmunity, vascular abnormality, arthritis/arthralgia and skin disease. [1, 2]
With a few exceptions, there remains a paucity of good

epidemiological studies from India and South East Asia. The present study was undertaken to know the occurrence of various types of connective tissue diseases, to know the incidence of connective tissue disorders in relation to gender, to know the age distribution of connective tissue disorders, to know the most common symptoms and signs of connective tissue diseases..

MATERIAL AND METHODS

The present study was conducted on 40 patients presenting to the Dermatology OPD during period of one year i.e. April 2014 to April 2015 in a private hospital in Hyderabad, supported by clinical investigations and detailed history. (based on criteria by American College of Rheumatology), A detailed history including the age, sex, occupation, socioeconomic status, duration of the disease, present and past illness including diabetes and hypertension, personal and family history was recorded.The diagnosis was done based on clinical examination and was supported by investigations. Patients with Discoid Lupus Erythematosus, Systemic Lupus Erythematosus, Morphoea, Systemic Sclerosis and Dermatomyositis were included in the study. Routine investigations like complete haemogram, complete urine examination, random blood sugar, and blood urea and serum creatinine were done. Skin biopsy, radiological examination and serological investigations were also done. Antinuclear antibody positivity test by ELISA was done in all patients.

RESULTS & DISCUSSION

A total of 40 cases clinically diagnosed as connective tissue disease (based on ACR criteria) out of 12072 dermatological outpatients (the ratio being 1 in 301.8 patients), during study period, formed the basis of this study. A detailed clinical examination was done and the results were recorded. Among the 40 patients examined, majority were within the age group of 31 – 40 years, which was followed by 21 – 30 years age group. Majority of the patients belonged to the female gender (33 patients – 82.50 percent). The male is to female ratio was 1:4.71. This shows that there is female preponderance in connective tissue disorders

Table 1: Incidence of each connective tissue disease gender wise

Gender / Disease	Males	Females	Total	Percent	Male: female ratio
DLE	2	13	15	37.50	1:6.5
SLE	1	7	8	20.00	1:7
Morphoea	1	8	9	22.50	1:8
SSC	2	4	6	15.00	1:2
DM	1	1	2	5.00	1:1
RA	0	0	0	0	0
Sjogr-ens	0	0	0	0	0
Total	7	33	40	100.00	1:4.71

Discoid Lupus Erythematosus (15 patients – 37.50 percent) was the most common disease which was observed in our study. It was seen in 2 males (13.33 percent) and 13 females (86.67 percent). The male to female ratio here was 1:6.5. Morphoea (9 patients – 22.50 percent) was the next common disease observed in our study. It was seen in one male patient (11.11 percent) and 8 female patient (88.89 percent). The male to female ratio here was 1:8. The third most common disease observed in our study was Systemic Lupus Erythematosus (8 patients – 20.00 percent). Among them, one (12.50 percent) was a male patient while the other seven (87.50 percent) were female patients. The male to female ratio was 1:7. Another connective tissue disease, systemic sclerosis was seen in six patients (15.00 percent). Two patients (33.33 percent) were males and four patients (66.67 percent) were females. Male to Female ratio was 1:2 here. Dermatomyositis was seen in only 2 out of the 40 patients (5.00 percent) presented and examined, among all the connective tissue diseases. It was seen in one male and one female patients, the male to female ratio being 1:1.

Table 2: Incidence of connective tissue disease in each age group

Age / Disease	11 – 20 years	21 – 30 years	31 – 40 years	41 – 50 years	51 – 60 years	Total
DLE	-	2 (5.00 %)	8 (20.00 %)	2 (5.00 %)	3 (7.50 %)	15 (37.50 %)
SLE	-	3 (7.50 %)	2 (5.00 %)	2 (5.00 %)	1 (2.50 %)	8 (20.00 %)
SSc	-	2 (5.00 %)	2 (5.00 %)	2 (5.00 %)	-	6 (15.00 %)
Morphoea	1 (2.50 %)	4 (10.00 %)	3 (7.50 %)	1 (2.50 %)	-	9 (22.50 %)
DM	-	-	2 (5.00 %)	-	-	2 (5.00 %)
Total	1 (2.50%)	11(27.50 %)	17(42.50 %)	7(17.50 %)	4 (10.00 %)	40 (100.00%)

Discoid Lupus Erythematosus was most commonly seen in 31 – 40 years age group (20.00 percent), Systemic Lupus Erythematosus was most commonly seen in 21 – 30 years age (7.50 percent), Morphoea in 21 – 30 years age group (10.00 percent) and Dermatomyositis in 31 – 40 years age group (5.00 percent) whereas systemic sclerosis was seen in equally in 21 – 30, 31 – 40 and 41 – 50 years age group.

In eight patients of Systemic Lupus Erythematosus examined, 5 patients (62.50 percent) had photosensitivity and 4 patients (50.00 percent) had malar rash as the common cutaneous manifestations. Other features like Discoid rash (37.50 percent), Oral ulcers (37.50 percent), Raynaud's phenomenon (25.00 percent), facial oedema (12.50 percent) and Lupus hair (12.50 percent) were the other cutaneous manifestations seen in our study.

Table 3: Incidence of Cutaneous manifestations of SLE

S.no.	Cutaneous manifestation	No. of cases	Percentage
1	Malar rash	4	50.00
2	Discoid rash	3	37.50
3	Photosensitivity	5	62.50
4	Oral ulcers	3	37.50
5	Raynaud's phenomenon	2	25.00
6	Facial oedema	1	12.50
7	Lupus Hair	1	12.50

Table 4: Incidence of different types of Morphoea

S.no.	Type of morphoea	No. Of cases	Percentage
1	Plaque	5	55.55
2	Linear	2	22.22
3	Guttate	1	11.11
4	Pansclerotic	1	11.11
Total		9	100 (of total cases)

Out of the 9 cases of morphoea seen, 5 cases (55.55 percent) were of the plaque type, 2 cases (22.22 percent) were of the linear type and one each of guttate (11.11 percent) and pan sclerotic (11.11 percent) type.

Table 5: Incidence of Reynaud's phenomenon in LE and SSC

s. No.	Connective tissue disease	No. Of cases seen	No. Of cases		Percent
			Giving history of raynaud's phenomenon	Presenting history of raynaud's phenomenon	
1	DLE	15	1	0	6.66
2	SLE	8	2	1	25.00
3	SSc	6	5	2	83.33

Reynaud's phenomenon was seen in one patient (6.66 percent) of Discoid Lupus Erythematosus, two patients (25.00 percent) of Systemic Lupus Erythematosus and five patients (83.33 percent) of Systemic Sclerosis.

In 6 patients of systemic sclerosis examined, sclerosis of the skin was the most common cutaneous feature (100.00 percent), followed by Reynaud's phenomenon (83.33percent) and Sclerodactyly (66.66 percent). Other cutaneous findings seen in patients in systemic sclerosis in our study were Pigmentary changes (50.00 percent), characteristic facies (pinched nose, loss of lines of expressions, microstomia and purse-string appearance of mouth) of systemic sclerosis (50.00 percent), stellate scars (33.33 percent) and gangrene of digits (33.33 percent).

Table 6: Incidence of cutaneous manifestations of SSC in the 6 patients studied

S. No.	Cutaneous manifestations	No. Of cases	Percentages
1	Sclerosis of skin	6	100.00
2	Reynaud's phenomenon	5	83.33
3	Sclerodactyly	4	66.66
4	Characteristic facies	3	50.00
5	Pigmentary changes	3	50.00
6	Stellate scars	2	33.33
7	Gangrene of digits	2	33.33

Table 7: Incidence of anti nuclear antibody positivity in each disease studied

S. No.	Type of connective tissue disease	No. Of cases seen	No. Of cases positive with ana	Percentage
1	DLE	15	10	66.66
2	SLE	8	7	87.50
3	Morphoea	9	5	55.55
4	SSC	6	5	83.33
5	DM	2	1	50.00
6	RA	-	-	-
7	SS	-	-	-
	Total	40	28	70.00

ANA positivity was seen in 70.00 percent of all the cases of connective tissue diseases. Highest percentage of Anti-Nuclear Antibody positivity was seen in Systemic Lupus Erythematosus (87.50 percent), followed by Systemic sclerosis (83.33 percent), Discoid Lupus Erythematosus (66.66 percent), Morphoea (55.55 percent) and Dermatomyositis (50.00 percent).

Complete blood picture, which was done in all the patients, showed mild to moderate anemia, with microcytic and hypochromic to normocytic hypochromic red blood in 32 patients (80.00 percent). Erythrocyte Sedimentation Rate was raised in 36 patients (90.00 percent of all the patients). Complete Urine Examination showed mild proteinuria in 15 patients (37.50 percent). Blood sugar was raised in 2 patients (5.00 percent of all cases). Blood sugar and serum creatinine were normal in all the patients. Antinuclear antibody positivity test by ELISA was done in all patients but was positive only in 28.00 patients (70.00 percent). Histopathology of skin in discoid lupus erythematosus showed hyperkeratosis with follicular plugging, thinning and

flattening of stratum malphighii, hydrophic degeneration of basal cells, individual cell necrosis of basal cell with colloid body formation with squamatization of basal cells and dyskeratosis in epidermis, whereas dermis showed patchy lymphocytic infiltrate admixed with plasma cells arranged along dermo epidermal junction, around hair follicles and sebaceous gland which was associated with characteristic pilo sebaceous atrophy, hyalinization, edema, fibrinoid change, interstitial mucin deposition especially just below the epidermis and pigmentary incontinence (melanin within melanophages in upper dermis), and vasodilatation and slight extravasation of red blood cells. Histopathology of skin in morphoea and systemic sclerosis in general showed normal epidermis with homogenous appearance of collagen in upper dermis, thickened loosely packed more hypo cellular deeply eosinophilic collagen in lower dermis, glands(especially the eccrine) are atrophic and appear to lie higher in the dermis with few or no adipocytes surrounding them, the inflammatory infiltrate is less and most of the subcutaneous fat is replaced by newly formed collagen, the blood vessels are few, often with a fibrotic wall and narrow lumen. Differences between morphoea and systemic sclerosis was vascular changes were more prominent and presence of aggregates of calcium in systemic sclerosis. Histopathology of dermatomyositis showed hyperkeratosis, epidermal atrophy, vacuolar degeneration of basal keratinocyte, with thickened basement membrane associated with thickened with sparse, superficial, patchy, or band-like peri vascular, lymphocytic infiltration along it whereas dermis was edematous, pale, with mucin deposits and pigmentary

DISCUSSION:

The incidence of connective tissue diseases was 40 patients in 12072 patients, the ratio coming to one for every 301.8 dermatology outpatients.

Among the 40 patients of connective tissue diseases studied, 17 cases (42.50 percent) fell in the age group of 31 – 40 years. Female preponderance was seen in this study with a male to female ratio of 1:4.71. Among the 40 patients included in this study, 33 patients (82.50 percent) were females, and 7 (17.50 percent) were males. Among all the connective tissue diseases studied, discoid lupus erythematosus was the most common 15 cases (37.50 percent) followed by 9 cases (22.50 percent) of Morphoea. No cases of Sjogren's syndrome or Rheumatoid arthritis attended during this period of study.

A study was done by Almeida et al,[3] on connective tissue diseases, a total of 120 patients were enrolled. There was a predominance of females numbered 104 (86.66percent). The average age group involved was 36–58 years. Cases of systemic lupus erythematosus (50.83 percent) outnumbered all the other connective tissue diseases, which is in concordance with our study. Other diseases seen in the study by Almeida et al were Rheumatoid arthritis (34.16 percent of all cases), systemic sclerosis (13.33 percent of all the cases), mixed connective tissue disorder (0.83 percent) and polymyositis (0.83 percent). Cutaneous lesions were detected in 50 patients (41.66 percent), dyspnea in 47 patients (39.16 percent) and alopecia in 55 patients (45.83 percent).

In a study on 14 patients of SLE by Dhabhai R et al.[4], there were 10 female and 4 male patients. Female predominance was seen with a male to female ratio of 1:2.5. Photosensitivity was the most common feature followed by malar rash. This was in concordance with our study. ANA test was positive in 87.50 percent of the cases.

In a study by Sharma VK et al, [5]skin sclerosis (100.00 percent) was the most common finding followed by Reynaud's phenomenon (92.9 percent), Pigmentation (91.00 percent) and Sclerodactyly (64.6percent). Other cutaneous findings found in this study were fingertip ulceration (58.6 percent), restricted mouth opening (55.5 percent) and gangrene of digits (6.7 percent). In a study by Ghosh SK, 46 patients of systemic sclerosis were included in the study, where male is to female ratio was 1:8.2. Reynaud's phenomenon (84.8 percent) and dyspigmentation (86.9 percent) were the most common symptoms seen. Sclerodactyly (82.6 percent), difficulty in opening the mouth (82.6 percent), fingertip ulceration and scarring (63 percent) patients and digital gangrene (4.3 percent) were the other clinical findings in these patients. ANA was positive in 78.2% patients. In the present study, out of 6 patients of systemic sclerosis examined, sclerosis of the skin was the most common cutaneous feature (100.00 percent), followed by Reynaud's phenomenon (83.33 percent) and Sclerodactyly (66.66 percent). Other cutaneous findings seen in patients in systemic sclerosis in our study were pigmentary changes (50.00 percent), characteristic facies (pinched nose, loss of lines of expressions, microstomia and purse-string appearance of mouth) of systemic sclerosis (50.00 percent), stellate scars (33.33 percent) and gangrene of digits (33.33 percent). ANA test was positive in 83.33 percent.

In a study by Das S et al., [7] out of 24 patients, dermatomyositis was seen in 4 patients (16.66 percent), whereas in our study, dermatomyositis was seen in only 2 patients (5.00 percent).

CONCLUSION:

It can be concluded from this study that connective tissue diseases are common, among them discoid lupus erythematosus is the most common disease followed by morphoea, systemic lupus erythematosus, systemic sclerosis and dermatomyositis. Connective tissue diseases are more common in female sex. The incidence of connective tissue diseases is more common between 31 to 40 years of age. The present study provides a snapshot of the spectrum of cutaneous manifestations of connective tissue diseases in small sample of South Indian population.

REFERENCES:

1. Goodfield MJD, Jones SI, Veale DJ. The Connective Tissue Diseases. In: Burns T, Breathnach S, Cox N, Griffiths C, editors. Rook's Textbook of Dermatology. 7th ed. Blackwell Publishing Company; 2004.p. 56.1 – 56.129.
2. Gurmohan Singh, Gurpreet Singh, Harji Kaur, Pandey SS. Systemic collagen disorders. In: Valia RG, Valia AR editors. IADVL Textbook and atlas of Dermatology. 2nd ed. Bhalani Publishing House, 2013. P. 908.
3. Almeida Mdo S, Bértolo MB, Da Silva BB, De Deus Filho A, Almeida MM, Veras FF et al. Epidemiological study on connective tissue diseases in Brazil. Trop Doct 2005 Oct;35(4):206–9.
4. Dhabhai R, Kalla G, Singhi MK, Ghiya BC,

Kachhawa D. Dexamethasone-cyclophosphamide pulse therapy in systemic lupus erythematosus. Indian J Dermatol Venereol Leprol 2005; 71:9–13.
5. 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;72:416–20.
6. 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;57:201–5.
7. Das S, Giri PP, Roy AK. Dexamethasone - cyclophosphamide pulse in collagen vascular diseases: An observation. Indian Dermatol Online J 2011;2:10-2

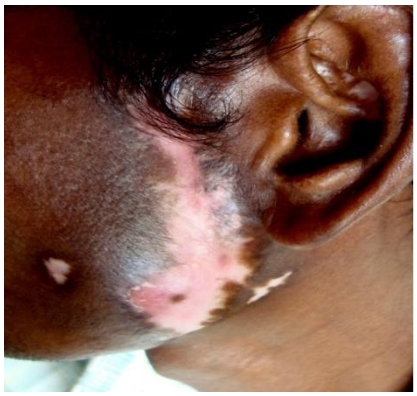

Figure 1: Discoid rash over the characteristic areas – earlobe, mandibular area.

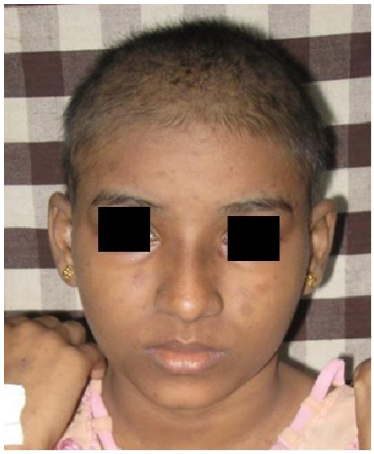

Figure 2 (a) – Rash over the malar area in a case of systemic lupus erythematosus

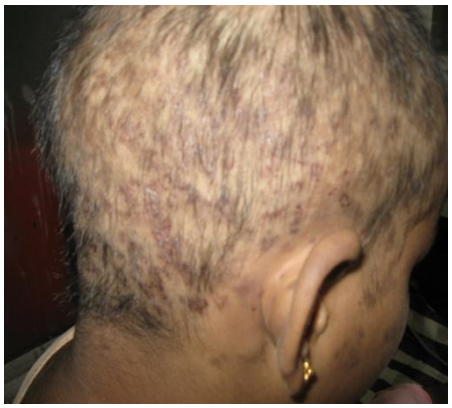

Figure 2 (b): Scarring alopecia over the scalp seen in systemic lupus erythematosus

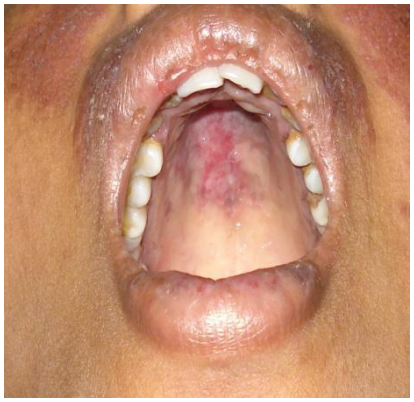

Figure 2 (c) – Oral ulcers seen in Systemic Lupus Erythematosus.

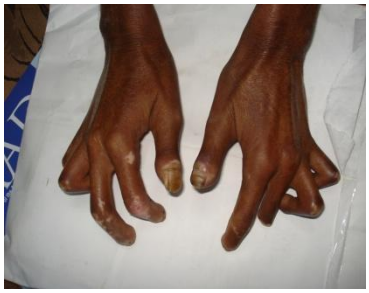

Figure 3 (a) – A case of systemic sclerosis showing sclerodactyly, resorption/loss of terminal phalanges of the fingers.

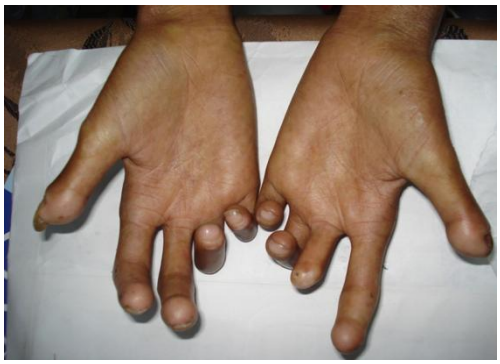

Figure 3 (b) – A case of systemic sclerosis showing sclerodactyly, resorption/loss of terminal phalanges of the fingers and stellate scars.

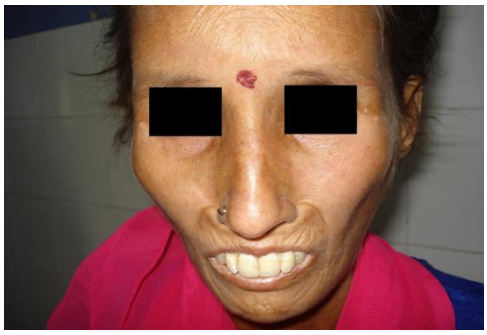

Figure 3 (c) – A case of systemic sclerosis showing loss of lines of expression (smoothening) over the face, small nose, microstomia and purse-string like appearance of the mouth

Cite this article as: Sandeep Kodali, Reddy LVN, Lavanya M, Kotha Seavanthi, Nagendra Chary. A study of connective tissue diseases. MRIMS J Health Sciences 2015;3(2):150-155.

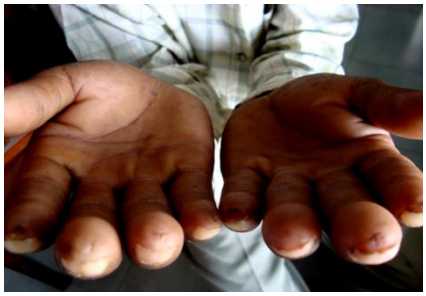

Figure 3 (d) – A case of systemic sclerosis showing stellate scars over the tips of the fingers.

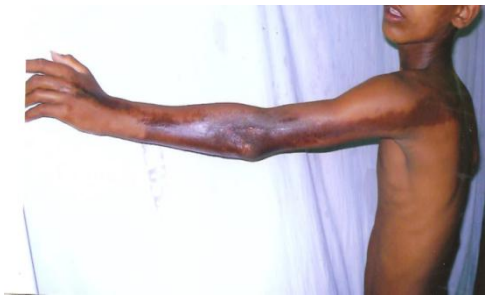

Figure 4 (a) – Linear morphoea involving left upper arm

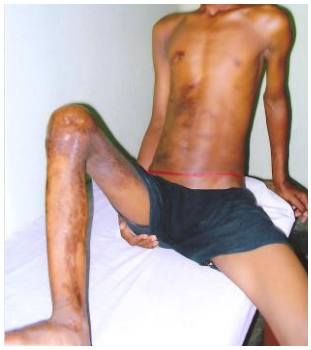

Figure 4 (b) – Pansclerotic type of morphoea

Source of Support: Nil. **Conflict of Interest:** None.
Acknowledgement: : Authors wish to thank Dr. Raghurama Rao Gandikota, Professor and HOD, Department of DVL, GSL Medical College and General Hospital, Rajahmundry, for being a great source of inspiration, and Dr. Mythri Priyadarshini Kodali, for being a constant source of support.