

**Cutaneous and oral manifestations in Systemic sclerosis: A case series and review**

<sup>1</sup>Dr Shaveta Sood Assistant Professor, Department of Periodontics, Dr H S Judge Institute of Dental Sciences and Research Panjab University, Chandigarh

<sup>2</sup>Dr Aneet Mahendra, Professor, Department of Dermatology MMIMSR, Mullana, Ambala

<sup>3</sup>Dr Sanjeev Gupta, Professor and Head, Department of Dermatology MMIMSR, Mullana, Ambala

<sup>4</sup>Dr Nidhi Mittal, Pvt practice Sangrur

**Correspondence Author:** Dr Aneet Mahendra, Professor, Department of Dermatology MMIMSR, Mullana, Ambala

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**Abstract**

Systemic sclerosis (SS) is a rare autoimmune disorder characterized by connective tissue and vascular abnormalities, resulting in induration and thickening of skin and fibrosis of internal organs. Patients with systemic sclerosis often show wide range of systemic and orofacial manifestations. Its orofacial manifestations include mask like facies, restricted mouth opening, thinning of upper lip, and resorption of the mandible. The striking periodontal changes observed are gingival recession and widened periodontal ligament space as seen radiographically. SS presents great challenges to both medical and dental professionals and has a profound impact on oral health. In this article we present a case series of nine patients of progressive systemic sclerosis with significant dermatological and oral manifestations.

**Key words:** Systemic sclerosis, orofacial, periodontal ligament,

**Introduction**

The word scleroderma derives its origin from the Greek word *skleros*, meaning “hard,” and *derma*, meaning “skin.” Scleroderma is a multisystem disorder. It is divided into two variants; 1) Diffuse cutaneous systemic sclerosis and 2) Limited cutaneous systemic sclerosis on

the basis of the extent of cutaneous involvement and other clinical and immunological features.<sup>1</sup>

SS occurs four times more commonly in women, and peaks in 30 to 50 year age group.<sup>2</sup> The etiology of systemic sclerosis is still unknown. Three main pathological changes have been identified in scleroderma: endothelial damage, immunologic and inflammatory activation, and dysregulated extracellular matrix production.<sup>3</sup>

Involvement of vascular endothelial cell is believed to be the initial target of the disease. Vascular alterations may affect the small arteries and arterioles, resulting in thickening of the vessel walls and reduction of the diameter of the lumen. This further leads to occlusion and ischemia.<sup>4</sup>

The role of the immune response in early changes of scleroderma is unclear. The late response involves CD-4 T helper cells, plasma cells, and histiocytes. Sera from scleroderma patients show elevated IL-4, IL-10 and IL-13 indicative of T<sub>H</sub>2 response. The T<sub>H</sub>2 subset may contribute during fibrotic stage of scleroderma.<sup>5</sup>

There is excessive production of normal collagen mainly type I and III due to immunological stimulation of fibroblasts.<sup>6</sup> There is quantitative increase in the

amorphous ground substance, glycosaminoglycans and fibronectin, within connective tissue.<sup>7</sup>

In a few patients environmental triggers such as vinyl chloride, epoxy resins, pesticides and paint solvents, or drugs such as bleomycin, are responsible for diffuse cutaneous sclerosis.<sup>8</sup>

### **Dermatological manifestations**

The earliest manifestation is Raynaud's phenomenon (bluish discoloration of hands on exposure to cold) and is present in more than 95% of the patients. It is followed by a painful digital ischemia, digital pitted scars which may progress to ulcers, resorption of terminal phalanges and flexion contractures resulting in shortened, claw like fingers.<sup>9</sup>

Chronic, usually nonpitting, painless oedema of the hands and fingers may occur before tightening of the skin occurs.<sup>3</sup>

The hands and face are the most frequently involved. The skin develops a diffuse, hard texture which is difficult to pinch (hide bound skin). The clinical impression of thickness and toughness of the skin is enhanced because of binding down of the skin to deeper structures.<sup>10</sup>

The skin of face becomes mask-like and expressionless, with loss of the normal facial lines and then thinning of the lips and constriction of the opening of the mouth (microstomia).<sup>3</sup> There is difficulty in depressing the lower eye-lids. Small mat like telangiectasia are frequently found on the face. The sparing of pigment around hair follicle gives the skin a `salt and pepper` appearance.<sup>3</sup>

In 75% of patients with SS, enlarged, dilated nail fold capillaries forming "giant" or sausage-shaped loops can be seen by capillary microscopy. In some cases, cutaneous calcification may develop manifesting as Cutaneous calcinosis, which may ulcerate, extrude calcified material and reepithelialize very slowly.<sup>3</sup>

Criteria of the American college of Rheumatology for classification of progressive systemic sclerosis.<sup>11</sup>

Major
Scleroderma proximal to the metacarpophalangeal or metatarsophalangeal joints.
Minor
Sclerodactyly Digital pitted scars or loss of fingertip pulp Bibasilar pulmonary fibrosis.

Additional Raynaud's phenomenon, nailfold capillary microscopy and SS selective antibodies added to improve sensitivity of criteria. For a diagnosis of SS, a patient must fulfill either one major or two minor criteria.

### **Oral manifestations**

The mouth opening is restricted .Radial furrows appear at the angles of mouth, giving a pursed appearance, and thinning of upper lip can occur resembling a 'fish-mouth'. There is increased risk of oral ulcers and fungal infections.<sup>12</sup> The oral manifestations include xerostomia, telangectasia, increased decayed, missing and filled teeth.<sup>13,14,15</sup> Fibrosis of tongue leads to rigid tongue, making speech, and swallowing difficult.<sup>16,17</sup> Loss of lingual papillae, blanching of mucous membrane, and diffuse fibrosis of the buccal mucosa may also occur. The loss of attached gingival and gingival recession may occur due to fibrotic stricture along the mandibular mucobuccal fold. Prominent buccal mucosal crenations may also occur<sup>18</sup>. The most striking radiographic findings include widening of the periodontal ligament space especially around the posterior teeth<sup>19</sup>. Other findings include increased capillary caliber and a reduced number of capillary loops using periodontal capillaroscopy.<sup>20</sup> Facial bones may sometimes become eroded showing osseous resorption at the mandibular angles, coronoid processes and zygomatic arches.<sup>21,22</sup>

The aims of the study are:

- (1) Evaluation of dermatological and facial abnormalities.
- (2) Assessment of intraoral changes.
- (3) Assessment of osseous changes in the mandible radiologically.
- (4) To correlate dermatological and oral findings.

## **Materials and methods**

### **Participants**

Twenty nine patients with systemic sclerosis were enrolled for the study. Of 29 patients 15 had limited systemic sclerosis. Out of 14 patients of systemic sclerosis 2 were edentulous and 3 were smokers. At the end of clinical examination a total of 9 dentate patients with SS (as per the ARA criteria) were recruited of which 7 were females and 2 were males. Their age ranged from 18 to 45yrs (mean 32.7±8.7 years). Detailed history was taken and general as well as systemic examination was done. Complete blood count, chest X-ray, electrocardiogram and microscopic urinalysis were done in each case. All the patients were invited to attend the oral examination and their panoramic radiographs were taken and evaluated. On the day of oral examination the patients completed a questionnaire regarding demographic characteristics, medical history, dental visits and oral hygiene habits. The questionnaire was checked for completeness and content. Modified Rodnan Scoring (17 sites) was used to assess skin thickness. This score consists of an evaluation of patient's skin thickness rated by clinical palpation using a 0–3 scale (0=normal skin; 1=mild thickness; 2=moderate thickness; 3=severe thickness with inability to pinch the skin into a fold) for each of 17 surface anatomic areas of the body: face, anterior chest, abdomen, (right and left separately) fingers, forearms, upper arms, thighs, lower

legs, dorsum of hands and feet. These individual values are added and the sum is defined as the total skin score.<sup>23</sup>

### **Statistical analysis**

Discrete categorical data were presented as *n* (%); continuous data were given as mean±SD, range, median and interquartile range, as appropriate. Mann-Whitney *U*-test was used to test the score between two groups. Kruskal Wallis test was applied when independent variable was more than 2 groups. Proportions were compared using Chi square or Fisher's exact test whichever was applicable. All statistical tests were two-sided and minimum 95% confidence interval and *p* value <0.05 have been considered to be statistically significance. Analysis were conducted using SPSS for Windows (version 17.0; SPSS Inc., Chicago, IL, USA).

### **Clinical oral examination**

The oral examination was performed at the department of oral diagnosis and radiology and the following measurements were recorded:

- (1) Xerostomia: After ten seconds of swallowing, the patient was asked to open mouth and lift the tongue. Dryness of the mouth was graded as being (1) clinically dry, (2) not dry but showing an absence of a salivary pool at the base of lingual frenum, (3) normal with salivary pooling present.<sup>15</sup>
- (2) Maximum opening of oral aperture: With the mouth opened as widely as possible, the measuring cord was placed at the left commissure and then traced all around the vermilion border of both the lips. This gave the measurement of the circumference of the mouth.<sup>15</sup>
- (3) Interincisal distance: With the teeth in maximum intercuspation, a line was scribed on the lower teeth to represent the level of overbite. The mouth was then opened maximally, and the distance between the scribed line on the lower teeth to the incisal edge of the upper right central incisor was measured.<sup>15</sup>

(4) DMFT Index: The number of decayed, missing and filled teeth was determined through examination using a standard mouth mirror and explorer which was supplemented with full mouth radiographs. The DMFT score for each patient was assessed.<sup>24</sup>

(5) Periodontal Pocket Depth(PPD) and Clinical Attachment Level(CAL): The number of erupted teeth were recorded and a periodontal examination was performed on 6 sites of each standing tooth(mesio-buccal, mid-buccal, disto-buccal, mesio-lingual, mid-lingual, disto -lingual ) using a UNC -15 probe.<sup>25</sup>

(6) Plaque Index (PI):Plaque was scored using the index given by Silness and Loe.<sup>26</sup>

(7) Oral Hygiene Index (OHI):The oral hygiene was assessed using the index given by Greene and Vermillion.<sup>27</sup>

(8) Bleeding on probing (BOP %): The percentage of sites with bleeding on probing were assessed using periodontal probe.

(9) Tooth Mobility (TM):Tooth mobility was graded as 0(no movement with lateral pressure), 1(mild movement ,less than 1 mm lateral movement), 2(moderate movement greater than equal to 1mm lateral movement), or 3(severe ,rotational movement, depressible or lateral movement greater than 2 mm ).<sup>15</sup>

For all the patients the sum of the scores for each index was calculated and all the clinical measurements were made.

### **Radiographic examination**

Full mouth intra- oral and panoramic radiographs were taken of each patient with the use of constant exposure, positioning and film – screen combination. Views were all taken by same technician. Particular attention was paid to general bone condition, the coronoid process, the ascending ramus and the mandibular condyle shapes.

Radiographs were also assessed for changes in width of periodontal ligament.

### **Results**

The demographic variables, dental attendance and oral hygiene habits have been described in Table 1. Most (67 %) of the patients reported brushing their teeth once a day and 33 % patients had never visited the dentist earlier. Table 2 provides information on dermatological and systemic changes in patients of SSc. Most of the patients (78%) in the study had disease duration of less than 5 years. Raynaud's phenomenon, bound down skin and digital scars were seen in all the patients. Modified Rodnan Score ranged from 15-38 with an average score of 25. There was positive correlation between Modified Rodnan Score and age ( which was statistically significant. While other parameters when compared with Modified Rodnan Score were not found to be statistically significant eg duration of disease  $p=0.847$ , nos of teeth present  $p=0.876$ , plaque index  $p=0.546$ , OHI  $p=0.932$ , mean periodontal pocket depth  $p=0.185$ , mean clinical attachment level  $p=0.635$ , mean clinical attachment level  $p=0.635$ , DMFT Score  $p=0.932$ , BOP%  $p=0.379$ , mobility  $p=0.546$ , interincisal distance  $p=0.406$ , maximum oral aperture  $p=0$ ). Using Mann Whitney Test, difference between Modified Rodnan Score and other variable parameters were not found significant. Almost all patients showed generalized widening of periodontal ligament whereas resorption of the condyles was seen in 22% and only 11% showed resorption of angle of mandible.(Table 3)

Intra-oral assessment revealed various parameters as follows- mouth opening ( $107\pm 94$ mm), interincisal distance( $31\pm 4.76$ mm), number of teeth showing mobility( $23.84\pm 14.86$ ),bleeding on probing percentage( $30.89\pm 14.86$ ), DMFT( $13\pm 4.03$ ), PI( $2.39\pm 0.60$ ),OHI( $3.62\pm 0.62$ ), full mouth

PPD( $5.9\pm 0.6\text{mm}$ ) and clinical attachment level( $6.1\pm 0.60\text{mm}$ ). (Table 4)

## **Discussion**

The present case series has revealed some oral features associated with SS and their association with dermatological findings. According to our study the mean age of occurrence of SS was  $35.33\pm 8$  years and the ratio of female: male is 7:2 which are in accordance to the study by Anbiaee et al.<sup>28</sup>

In the present case study mask like facies, raynaud's phenomenon, digital scars, thinned out lips were present in all the patients and the findings were similar to Nagy et al<sup>29</sup>. In a study of 21 patients with SS, Marmary et al<sup>14</sup> found that 80% of SS patients were unable to open mouth beyond 40mm. The inter-incisal distance was also found to be significantly reduced in most of the patients with SS Nagy et al<sup>29</sup>. In the present study the mouth opening was restricted to a mean interincisal distance of  $32\text{ mm} \pm 4.8\text{ mm}$ . Limitation of mouth opening and reduced movement of the cheeks and tongue usually leads to poor dental hygiene. Maintenance of oral hygiene may be difficult due to patient's inability to grip and manipulate a tooth brush or other oral hygiene aids.

In our study xerostomia was present in 33%, as compared to an incidence of 44% and 70% found by Nagy et al<sup>29</sup> and Wood et al<sup>15</sup> respectively. Xerostomia can result in increased susceptibility to dental caries, Candida infections and periodontal disease. Decayed, missing, and filled surfaces, mobile teeth, and periodontal disease are more prevalent in patients with systemic sclerosis.

Radiographically, the striking feature of this disease is the widening of the periodontal ligament space in absence of significant periodontal disease. Siefert<sup>30</sup>, White<sup>19</sup> and others have reported that this is an inconsistent finding in all patients with systemic sclerosis; however this was contradicted by Marmary<sup>14</sup>, who observed widening in all

21 patients examined. Widening of periodontal ligament was seen in all the 9 cases in our study (6 patients had generalized widening while 3 had localized widening). Gonzales and Coleman<sup>31</sup> suggested increased collagen synthesis in the PDL leads to increase in the bulk of the ligament. This is accommodated at the expense of alveolar bone, causing an increase in the width of the PDL space.

Taveras<sup>32</sup> reported the first documented case of osteolysis of the mandibular angle and condyle in adult patients with scleroderma. The exact etiology of the osteolysis is unknown, but there are three proposed theories: 1) tightening of the facial skin may exert excessive pressure on the mandible and induce the bone loss; 2) the vasculopathy associated with this disease may diminish the blood supply to the mandible resulting in bone ischemia and necrosis; and 3) atrophy of the muscle of mastication may lead to bone necrosis.

Amongst the present cases resorption of mandibular condyles is present in only 2 patients. 1 patient showed resorption of the angle of mandible. Duration of disease did not seem to have an affect on the mandibular resorption. There are conflicting reports on the correlation between progression or duration of systemic sclerosis and severity of bone resorption. Wood and Lee<sup>15</sup> in a study of 31 women with systemic sclerosis found that 29% had resorption of the mandible, and all these patients demonstrated greater restriction in mouth opening and more widespread organ involvement, while Marmary et al<sup>14</sup>, found no correlation between bone resorption at the angle of the mandible, widening of periodontal ligament, age, duration of disease and medication/ clinical or laboratory findings.

All the patients had inadequate oral hygiene and high level of periodontal destruction. However, interestingly patients with SS experienced lesser BOP % irrespective of

deeper full mouth PPD. This could be due to obliterative microvasculopathy found in SS as reported by Lee et al<sup>33</sup>.

**Management-** Patients with limited range of mouth opening can benefit from oral exercises and stretching of the facial skin and oral musculature may help to maintain oral opening, oral health and mastication. Use of increasing number of tongue blades between the posterior teeth to stretch the facial tissues is an effective technique to increase mouth opening. Other recommended aids are eating a balanced diet and using electric toothbrush and anti-bacterial mouthwashes. Rarely, patients may benefit from bilateral commissurotomy to increase the width of their mouth. Instructions and reinforcement of oral hygiene, along with frequent dental checkups are necessary for the maintenance of oral health.

### **Conclusions**

Oral changes in SS though very common are often overlooked by the dermatologists. In cases of SS, periodontal ligament widening usually follows but may even precede extensive cutaneous involvement helping in early diagnosis of SS. Equal emphasis should be laid on oral changes as is routinely done for systemic complaints. Along with medical treatment, regular oral monitoring should be done by performing clinical and radiological examinations, so as to follow the course of the disease and prevent poor oral hygiene and loss of teeth.

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<b>Table 1.</b>	<b>Demographic Characteristics</b>	
a. Age	35.33± 7.9	
b. Sex	Female	7
	Male	2
c. Disease duration	4.44	

(yrs)		
d. Occupation	Housewife	4
	Student	1
	Worker	4
e. Education	illiterate	1
	up to 10 <sup>th</sup> std	5
	10 <sup>th</sup> std and above	3
f. Last dental visit	never	1
	<1 time	4
	1-3 times	4
g. Brushing	occasionally	2
	1 time daily	6
	≥ 2 times daily	1

<b>Table 2.</b>	<b>Cutaneous findings</b>	<b>Number affected</b>
<b>A</b>	Raynaud's phenomenon	9
<b>B</b>	Hide bound skin	9
<b>C</b>	Digital ulcers	9
<b>D</b>	Sclerodactly	9
<b>E</b>	Pitted scars	9
<b>F</b>	Calcinosis cutis	2
<b>G</b>	Pigmentation	4
<b>H</b>	Modified Rodnan Score	25
❖	<b>Extra oral findings</b>	<b>Number affected</b>
<b>A</b>	Mask like facies	9
<b>B</b>	Thinned out lips	9
<b>C</b>	Beak shaped nose	5
<b>D</b>	Microstomia	9
<b>E</b>	Radial furrows	3
<b>F</b>	Mat like talengestacia	3
<b>G</b>	Xerostomia	3
<b>H</b>	Xeropthlamia	4

<b>I</b>	Difficulty in retracting lower eye lids	4
❖	<b>Systemic Complications</b>	<b>Number affected</b>
<b>A</b>	GIT	8
<b>B</b>	Respiratory	6
<b>C</b>	Renal	3
<b>D</b>	Musculoskeletal	4
<b>E</b>	Cardiac	2

<b>Table 3. Radiographic changes</b>		
<b>A</b>	Generalized widening of PDL	6
<b>B</b>	Localized widening of PDL	3
<b>C</b>	Resorption of condyles	2
<b>D</b>	Resorption of angle of mandible	1



Table 4. Rodnan's score and Intra-oral findings

	N		Mean	Std. Deviation	Minimum	Maximum	Percentiles		
	Valid	Missing					25	50	75
<b>Rodnan's score</b>	9	0	37.22	7.579	24	49	32.50	37.00	43.00
<b>nos of teeth present</b>	9	0	28.67	2.062	26	32	27.50	28.00	30.50
<b>plaque index(PI)</b>	9	0	2.4633	.62103	1.23	3.45	2.2100	2.3500	2.9100
<b>OHI</b>	9	0	3.6233	.62913	2.76	4.90	3.2500	3.5000	3.9700
<b>mean periodontal pocket depth</b>	9	0	5.9900	.65102	4.78	6.78	5.5950	5.9000	6.6050
<b>mean clinical attachment level</b>	9	0	6.1078	.60811	4.98	6.90	5.6550	6.1000	6.6400
<b>DMFT SCORE</b>	9	0	13.00	4.031	5	17	10.00	14.00	16.00
<b>BOP%</b>	9	0	30.894%	9.2617%	20.5%	45.6%	21.000%	30.600%	38.400%
<b>Mobility</b>	9	0	23.844%	14.8632%	2.1%	43.2%	11.700%	23.400%	39.450%
<b>interincisal distance</b>	9	0	31.89	4.762	27	41	28.00	31.00	35.50
<b>maximum oral aperture</b>	9	0	107.94	8.052	97	124	100.75	108.50	112.00