Gastrointestinal symptoms in scleroderma patients and its influence in body mass index and quality of life

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ABSTRACT

Background: Scleroderma (SSc) gastrointestinal (GI) symptoms may affect nutritional status and patients' quality of life.
Objective: To study prevalence of GI symptoms and its relationship to nutritional profile and quality of life of patients with SSc.
Methods: Fifty two SSc patients and 51 controls were studied for BMI (body mass index), dietary recall, major GI symptoms and quality of life by SF-12 questionnaire.
Results: BMI in scleroderma patients was lower than controls (p=0.02) despite an almost similar food intake. Scleroderma patients had higher prevalence of upper gastrointestinal tract symptoms than controls (heartburn, nausea and vomiting, dysphagia and epigastric pain) that were not associated with BMI (p= 0.36) but diminished quality of life (p=0.02) .
Conclusions: SSc patients have a lower BMI than controls and higher prevalence of GI symptoms that does not affect food intake but diminishes quality of life.

Keywords: Scleroderma; Nutrition; Gastrointestinal symptoms; Quality of life

INTRODUCTION

Gastrointestinal symptoms are very common in patients with scleroderma (SSc), reported in up to 90% of the cases[1]. Although fibrosis, the hallmark of this entity, that characteristically affects the skin, the gastrointestinal tract is also involved, resulting in different degrees of dysmotility, impaired digestion, changes in nutrient absorption and secretion[1]. Symptoms are variable and their expression depends on the affected region. Esophageal dysmotility is often associated with dysphagia, gastroesophageal reflux and heartburn; involvement of small intestine with bacterial overgrowth can lead to diarrhea, flatulence and malabsorption and the involvement of the colon is a common cause of constipation[2]. Symptoms from the digestive tract appear early in the disease and are associated with a worse prognosis[3].

Dysfunction of the gastrointestinal tract may compromise not only the nutritional status of the patient but can also cause depression and loss of quality of life[4,5].

In the present study, we studied the frequency of gastrointestinal symptoms in a sample of 52 patients with scleroderma looking for an association with nutritional changes and loss of quality of life.

MATERIAL AND METHODS

This is a cross-sectional, case-control study in a sample of 52 patients with SSc, of both genders, aged 18 years or more who met the American College of Rheumatology Preliminary Classification Criteria for the diagnosis of this entity[6]. As control, we studied 51 individuals who had no SSc or other inflammatory disease and who attended the outpatient ophthalmology clinic. This study was approved by the local Committee of Ethics in Research and all participants signed informed consent form. Patients were recruited from a single Rheumatology Clinic and included according to order of arrival for consultation (convenience sample). Individuals unable to perform anthropometric measurements, pregnant women, those with renal failure and untrea-

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ted hypothyroidism were excluded. Their medical records were reviewed for demographic data, cumulative involvement of major organ systems affected by SSc according to criteria of the College American Rheumatology for organ involvement[7] and for auto antibodies profile. Anthropometric measures comprised the following steps (a) - measurement of weight: performed in a portable digital scale Marte®, with 100g divisions and a maximum of 180 kg, with subjects wearing light clothing and no shoes; (b) - height measurement: using transposable anodized stadiometer of aluminum Cardiomed® with mark division of 1 mm. For this measurement, the subject was without shoes, and lined back against the wall stadiometer; (c) – Body mass index (BMI) measurement: calculated dividing weight in kilograms by height in meters squared, according to World Health Organization, 1995[8].

A questionnaire about the presence of major gastrointestinal symptoms (heartburn, dysphagia, nausea and vomiting, epigastric pain, bloating, constipation, diarrhea, number of stools per week and use of laxatives, anorexia, story food allergies and lactose intolerance) was applied and it admitted a yes/no answer. For the quality of life evaluation the SF-12 questionnaire[9] was applied. The nutritional supply was evaluated by dietary recall that quantifies the patients's food intake in the last 24 hours that preceded the interview. These data were recorded with their respective home measures (such as: one cup, a full spoon p. ex). In some cases, where it was difficult to measure the portion (ex: small slice of cake), the portion size reported was considered by the participant, taking as a standard, the table done by Pinheiro *et al*[10], in which the foods were weighed and analyzed in the laboratory. The chemical composition of individual recalls was calculated using the Virtual Nutri Program 1.0 (*Skopein System* ®, 2004)[11]. For homemade preparations, such as pizza, lasagna, sandwiches, in order to better classify the food groups in the food pyramid, the ingredients were used according to standardized recipes proposed by Pinheiro *et al*[10] and Fisberg and Villar[12]. The relationship between dietary intake and food groups according to the Food Pyramid Adapted Guide[13,14] was established, using the method proposed by Fisberg *et al*[12].

As controls, we analyzed 51 patients from the same geographical area that attended to the Outpatient clinic for ophthalmologic consultation (refraction) and gynecological routine examination.

Data were grouped into frequency tables. Nominal data were calculated as percentages. For numerical parametric data, the central tendency measure was calculated using the mean and standard deviation; the median and interquartile ranges (IQR) were used for non parametric data.

Correlation studies were done by Spearman tests. Tests of association of nominal data were made by unpaired t test (parametric sample) and Mann Whitney (non parametric sample), when two samples were compared. One way ANOVA and Kruskal Wallis tests were used to compare more than two samples. Tests of association of nominal data were made by Fisher tests and chi-square. The significance was adopted at 5%.

Calculations were made with the aid of the software Graph Pad Prism version 5.0.

RESULTS

A) DESCRIPTIVE ANALYSIS OF THE STUDY POPULATION

In the sample of 52 patients with scleroderma there were 17/52 (32.7%) cases of diffuse scleroderma, 27/52 (51.9%) of limited scleroderma, 7/52 (13.5%) of overlap and 1/52 (1.9%) of scleroderma sine scleroderma. The clinical and auto antibody profile of this population can be seen in Table I.

Demographic data, associated diseases, life habits of scleroderma patients and controls as well as the pairing of the samples can be seen in Table II.

COMPARATIVE ANALYSIS OF BMI, FOOD INTAKE AND GASTROINTESTINAL SYMPTOMS AND QUALITY OF LIFE AMONG PATIENTS WITH SSC AND CONTROLS

The BMI of scleroderma patients ranged from 13.97 to 42.19 kg/m2 (mean 25.77 ± 5.41 kg/m2) and it was lower than those of controls whose BMI ranged from 19.1 to 46.29 kg/m2 (mean 28.29 ± 5.99 kg/m2), p = 0.028, unpaired t test.

The comparison between BMI of scleroderma patients and controls for nutritional groups can be appreciated in Figure 1.

Comparison of BMI in different forms of scleroderma (limited, diffuse and overlapping) showed no difference (p = 0.76; one way ANOVA)

The dietary recall of SSc patients and controls can be seen in Table III, which shows that except for the amount of fat and calcium (that was higher in the SSc group) and micronutrients (folate and vitamin B12),

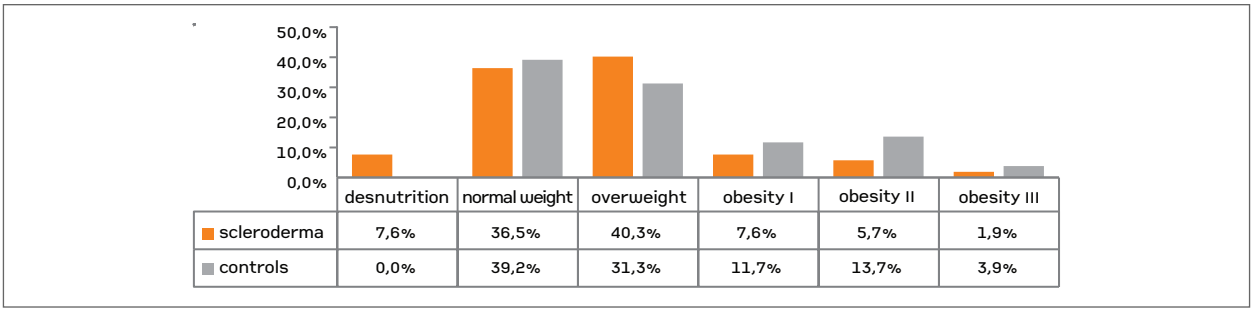

FIGURE 1. Distribution of body mass index in patients with scleroderma and control (expressed in percentage)
NOTE: BMI below 18.5 - malnutrition; BMI between 18.5 and 24.9 - normal weight;
BMI between 25.0 and 29.9 - overweight; BMI between 30.0 and 34.9 - grade I obesity;
BMI between 35.0 and 39.9 - grade II obesity; BMI 40.0 and above - morbid obesity.

TABLE I. CLINICAL AND AUTO ANTIBODIES PROFILE OF 52 PATIENTS WITH SCLERODERMA

Clinical Data	N	%
Raynaud	46/50	92.0%
Digital necrosis	8/50	16.0%
Telangiectasias	21/46	45.6%
Rodnam (score)	0 to 43 (mean 17.37±8.25)	
Esophageal involvement	29/49	59.1%
Colon involvement	1/52	1.9%
Pneumonitis	22/49	44.8%
Myocarditis	2/48	4.1%
Pulmonary Hypertension	11/50	22.0%
Myositis	10/48	20.8%
Arthritis	16/50	32.0%
Autoantibodies profile		
Antinuclear antibody	45/51	88.2%
Anti centromere	12/49	24.4%
Anti Scl-70	4/48	8.3%
Anti Ro	7/41	17.0%
Anti La	4/23	17.39%

food consumption is equal in the two groups.

Data obtained from comparison between clinical symptoms related to gastrointestinal tract in patients and controls are in Table IV, where it can be seen that high GI symptoms are most common in patients with scleroderma.

In 40/52 (76.9%) SSc patients, symptoms from high gastrointestinal tract were found (heartburn, nausea, vomiting, dysphagia and epigastric pain) and in 22/52 (42.3%) those from low gastrointestinal tract were present (flatulence, diarrhea, constipation). Comparing the BMI of SSc patients with gastrointestinal symptoms (mean 25.5 ± 5.6) with those with no symptoms (mean 27.9 ± 1.5) no difference was found (p=0.36; unpaired test).

When studying the quality of life, the median SF-12 value in SSc patients was 83.90 (IQR 72.5 to 97.5) and controls 98.00 (IQR 76-98.7) with p=0.004. (Mann Whitney). Comparing the quality of life in individuals with and without gastrointestinal symptoms the SF--12 have a mean value of 81.24 ± 15.20 in those with symptoms *vs* 93.30 ± 7.30 in those without symptoms (p=0.02; unpaired t test). However no correlation was

TABLE II. PAIRING DATA OF 52 SCLERODERMA PATIENTS AND 51 CONTROLS

	Scleroderma N=52	Control N=51	P
Gender (male/female)	4/52	4/51	1.0
Mean age (years)	50.7±12.9	51.0±14.7	0.91
Tobacco exposure	24/52= 46.1%	21/51=26%	0.55
Ethnic background	28 caucasians and 24 afro-descendants	30 caucasians and 21 afro-descendants	0.69
Diabetes mellitus	13/52 =25%	11/51=21.5%	0.81

TABLE III. COMPARATIVE ANALYSIS OF FOOD CONSUMPTION AMONG PATIENTS WITH SCLERODERMA AND CONTROLS

	Scleroderma n=52	Control n=51	P
Kilocalories (mean)	1703±730.3	1500±610.1	0.13 (*)
Carbohidrate (median- g)	211.1; IQR de 150.9 a 305.1	186.1; IQR de 133.0 a 252.0	0.20 (**)
Protein (median-g)	61.02; IQR de 43.9 a 75.7	60.45; IQR de 43.05 a 93.41	0.51 (**)
Lipids (median g)	58.1; IQR de 38.4 a 82.7	40.6; IQR de 22.8 a 61.33	0.01 (**)
Saturated fat (median- g.)	15.56; IQR de 9.48 a 19.8	13.6; IQR de 7.4 a 18.8	0.16 (**)
Monounsaturated fat (median-g)	11.29; IQR de 6.62 a 15.54	13.9; IQR de 8.0 a 22.5	0.09 (**)
Polyunsaturated fat (median g)	5.81; IQR de 2.84 a 8.81	6.48; IQR 4.2 a 10.5	0.21 (**)
Cholesterol (median- mg)	156.9 IQR de 102.6 a 236.7	132.6; IQR de 74.4 a 238.3	0.45 (**)
Sodium (median- mg)	1723; IQR de 1021 a 2261	1347; IQR de 828.7 a 2220.0	0.46 (**)
Calcium (median- mg)	599.0±315.9	455.4±263.0	0.014 (**)
Iron (median- mg)	9.48; IQR de 6.71 a 13.43	11.07; IQR de 7.93 a 14.34	0.12 (**)
Vitamin B12 (median -µg)	0.89; IQR de 0.26 a 2.50	2.05; IQR de 1.30 a 4.51	0.0008 (**)
Vitamin A (median- µg)	312.1; IQR de 190.5 a 561.4	249.9; IQR de 105.1 a 525.3	0.38 (**)
Folate (median- µg)	133.4; IQR de 83.2 a 246.7	230.0; IQR 188.7 a 374.1	<0.0001

*unpaired t teste; **Mann Whitney; IQR=interquartile range

found between BMI values and the SF-12 (r=-003; 95%CI=0.30 to 0.24; p=0.80; Spearman test).

DISCUSSION

The results of the present study show that patients with SSc have a high prevalence of gastrointestinal symptoms and such symptoms are associated with their quality of life. In this sample the symptoms were mostly from the higher gastrointestinal tract as had been detected by Wielosz Xi[15] that found high GI symptoms in 74% of their patients versus only 30% for low GI tract.

The study of BMI showed that around 8% of SSc patients were malnourished, while 36% had normal weight and 40% were overweight. Obesity grade 1,2,3 were less common and appeared in smaller proportion than in the control population. The data obtained follow the pattern observed by Krause *et al*[16] in German patients with SSc. These authors found 13.7% of malnutrition, 55.6% of normal weight and obesity grade 1 in 25.8% of their patients. Interestingly, despite the difference found for BMI, nutritional support did not vary much between SSc patients and controls except for lipids and calcium intake that was higher and B12 vitamin and folic acid which was lower in the SSc group. Lundberg *et al*[17] studying 30 patients with scleroderma also found that the food intake of these patients was similar to that of the normal population. Thus, it is not possible to attribute the difference in the BMI to change in food consumption, despite the high prevalence of observed gastrointestinal symptoms. It is possible that metabolic disorders and disturbances in

TABLE IV. COMPARATIVE STUDY OF GASTROINTESTINAL COMPLAINTS IN PATIENTS WITH SCLERODERMA AND CONTROLS

	Scleroderma n=52		Controls n=51		
	N	%	N	%	P
Heartburn	28	53.8	11	21.5	0.0007(*)
Nausea	20	38.4	10	19.6	0.024 (*)
Vomiting	10	19.2	2	3.9	0.015 (*)
Chewing difficulty	19	36.5	11	21.5%	0.094 (*)
Dysphagia	19	36.5	1	1.9	<0.0001 (**)
Episgastric pain	21	40.3	12	23.5	0.066 (*)
Flatulence	22	42.3	16	31.3	0.25 (*)
Constipation	21	40.3	11	21.5	0.19 (*)
Diarrhoea	6	11.5	2	3.9	0.26 (**)
Food allergy	4	7.6	3	5.88	1.0 (**)
Lactose intolerance	2	3.8	1	1.9	1.0 (**)
Anorexia	17	32.7	2	3.9	0.0002 (**)
Frequent use of laxatives	2	3.8	1	1.9	1.0(**)
Evacuations (number/week)	1-21 Median 7		1-28 Median 7		0.17(***)

*Qui=quadrado; **teste de Fisher; ***Mann Whitney

absorption can explain this finding. A minority of patients complained of diarrhea but subclinical malabsorption cannot be excluded. According to Bures *et al*[18] half of patients with scleroderma and intestinal bacterial overgrowth may not present clinically relevant complaints. Krause *et al*[16] attributed the malnutrition seen in SSc patients to the chronic inflammatory process and noted that it was closely linked to mortality. The same was observed Hesselstrand *et al*[19]. The role of adipokines although accepted as an element that establishes a link between inflammation and nutritional status in patients with systemic lupus erythematosus and rheumatoid arthritis, is little studied in SSc. It is known that adiponectin, an adipokine with anti-inflammatory properties made in subcutaneous and visceral fat tissue, which regulates the metabolism of glucose and fatty acids, have been found to be decreased in scleroderma. This decrease was associated with greater thickening of skin and lung fibrosis[20].

The gastrointestinal tract is probably the third most affected site in SSc patients, followed by skin and by Raynaud[21]. It happens in all forms of scleroderma[21]. In our sample it was not possible to associate the occurrence of gastrointestinal symptoms to changes in BMI, although the small number of patients included did not allow the analysis for specific gastrointestinal symptoms. A multicenter Canadian[22] involving 586 patients with scleroderma found that the risk of malnutrition was associated with specific gastrointestinal symptoms mainly with loss of appetite, flatulence, nausea, diarrhea and constipation.

Although gastrointestinal symptoms did not explain changes in BMI in the present study, these were linked to significant loss of quality of life. The association between gastrointestinal complaints and lessened quality of life has been studied by Omair *et al*[4] that compared the life quality of patients with scleroderma and gastrointestinal involvement with other rheumatic patients. Depressive symptoms were also more common in symptomatic patients[5].

Limitations of this study are the nutritional assessment made by BMI, which does not allow distinction of muscle mass from adipose tissue, and the gastrointestinal tract exploration based on clinical symptoms that does not exclude asymptomatic minor involvements.

In conclusion we noted a high prevalence of gastrointestinal symptoms in this SSc population which diminished the quality of life but did not explain the lower BMI than controls. Weight changes also could not be explained by lower food consumption. Further studies are needed do understand this phenomenon in more details.

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