Obesity in primary Sjögren's disease

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Abstract

Objective

To evaluate the prevalence of obesity in primary Sjögren's disease (SjD), and assess its association with clinical/serologic features, disease activity, damage, and sicca symptoms.

Methods

Transversal study that included 91 patients. We registered demographics, comorbidities, glandular/extra-glandular and serologic variables. We assessed the Schirmer-I test and non-stimulated salivary flow, and scored the cumulative ESSDAI, SSDDI and ESSPRI scores. We measured the body mass index (BMI), waist circumference (WC) and waist-to-hip ratio (WHR). We defined obesity as a BMI ≥30 kg/m^2. Central obesity was defined as WC >90 cm and >80 cm; or by a WHR >0.90 and >0.85, for men and women, respectively. All patients underwent bioimpedance analysis to measure body fat mass index (FMI). An elevated/high FMI was classified as obese.

Results

According to BMI, 18 patients were obese (19.7%), while 33 (36.2%) were obese according to WC, 48 (52.7%) according to WHR, and 37(40.6%) according to FMI. When we compared obese vs. non-obese patients according to BMI, the first group had a higher prevalence of anti-Ro/SSA antibodies. When we then performed the same groups comparison, but now using the WC, WHR and FMI definitions, the multivariate analysis showed an association between SSDDI and obesity.

Conclusion

According to BMI, at least 20% of patients were obese, this prevalence increased to 40% when BIA was used, with a higher prevalence found in central obesity. Obesity did not impact the symptoms and disease activity but might be associated with damage. Our results may have implications for weight reduction in these patients.

Key words

obesity, Sjögren's disease, body mass index, fat mass index, waist circumference, waist-to hip ratio

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Introduction

Obesity is an abnormal or excessive fat accumulation that presents a risk to health. Traditionally, it is defined as a body mass index (BMI) >30 kg/m^2 (1). Obesity is often related to metabolic disorders which can exacerbate cardiovascular and metabolic complications. Moreover, given the potential impacts of adiposity on inflammation due to the production of pro-inflammatory mediators, such as leptin that stimulate the inflammatory phenotype of T-cells, macrophages, and other innate immunity cells; this condition is considered a state of low-grade chronic inflammation. Therefore, obesity may play a significant role in worsening inflammation and disease progression of autoimmune rheumatic diseases (2). For instance, obese patients with systemic lupus erythematosus (SLE) have higher disease activity, more accrual damage, higher levels of inflammatory markers, and poorer patient-reported outcomes compared to overweight or normal-weight patients (2-3). Similarly, obesity has been associated with an increased risk of rheumatoid arthritis (RA), higher disease activity (particularly in ACPA+ patients) (4), a lower likelihood of achieving disease remission, and lower physical health scores, but paradoxically also with less severe erosive radiographic progression (5).

Although Sjögren's disease (SjD) has been also associated with several comorbidities, little is known about its relationship with obesity (6). In this sense, in one study in a population-based cohort, BMI was not found to be a potential risk factor for SjD compared to age- and sex-matched controls (7). Conversely, a retrospective case-control study nested within a population cohort showed that fibromyalgia, diabetes, osteoporosis, BMI, and oestrogen-only HRT use, provided a moderate predictive value for SjD (AUC of 0.67) (8). Moreover, in the UK Primary Sjögren's syndrome Registry, most patients had a normal weight or were overweight, but not obese. However, belonging to the symptom burden subgroup, taking hydroxychloroquine and immunosuppressors, being older, a higher BMI and a longer disease duration, were factors associated with a higher comorbidity and polypharmacy score (9).

Interestingly, high levels of inflammatory markers, such as C-reactive protein (CRP) and IL-6, which are common in obese individuals, are also present in SjD. Nevertheless, it is still unknown whether obesity might influence SjD's clinical course, prognosis and therapeutic management. To date, only one study has investigated the effects of obesity (defined by BMI) on the course of SjD and found that disease activity was significantly lower in the group of overweight patients (10). However, it is important to mention that although BMI remains a widely used tool, it does not distinguish between muscle and fat, which can lead to misclassification. This limitation highlights the importance of incorporating body composition analysis to achieve a more accurate understanding of obesity (1).

Thus, the rationale for this study was to investigate the prevalence of obesity in a cohort of patients with primary SjD, as measured by anthropometric indices such as body mass index (BMI), waist circumference (WC), waist-to-hip ratio (WHR), as well as with a body composition variable, the fat mass index (FMI). Subsequently, to assess the association of obesity with the presence of clinical (glandular/extra-glandular) and serologic features, disease activity, damage, and symptoms (sicca/fatigue/pain) in patients with primary SjD.

Methods

This was a transversal study that included consecutive patients with primary SjD who regularly attended the Rheumatology Clinic at the Instituto Nacional de Ciencias Médicas y Nutrición, a tertiary referral hospital from Feb 2019-Jan 2020. All patients fulfilled the 2016 American College of Rheumatology/European League Against Rheumatism (ACR/EULAR) classification criteria for SjD (11). All patients were invited through direct contact. We excluded patients with any other concomitant connective tissue diseases, limb amputation, pacemaker, insulin pumps, artificial joints, pregnancy or breastfeeding.

All patients had a face-to-face interview with a rheumatologist who performed

the Schirmer-I test and non-stimulated salivary flow (NSWSF) (12). Patients also scored the EULAR Sjögren's Syndrome Patient Reported Index (ESSPRI) to assess SjD symptoms.

Patients' clinical records were carefully reviewed according to a pre-established protocol to record demographic data, age at diagnosis, duration of follow-up, and serologic data such as anti-Ro/SSA, anti/La-SSB, rheumatoid factor (RF), antinuclear antibodies (ANA), hypergammaglobulinaemia, and hypocomplementaemia. We also registered the following glandular (oral and ocular sicca symptoms, parotid enlargement) and extra-glandular manifestations: non-erosive arthritis, cutaneous vasculitis, lymphadenopathy, interstitial lung disease, renal involvement, autoimmune cytopenias and neurological involvement (polyneuropathy, mononeuropathy, cranial pars involvement, demyelination, dysautonomia). We scored the cumulative ESSDAI (European League Against Rheumatism Sjögren's Syndrome Disease Activity Index) score to assess activity during the follow up (13), and the Disease Damage Index Score (SSDDI) at the last follow-up to evaluate accrual damage (14).

We also registered the presence of some comorbidities such as hypertension, type 2 diabetes and dyslipidaemia (hypertriglyceridaemia and/or hypercholesterolaemia) from their medical charts.

Table I. Clinical and anthropometric variables of patients.

Variable	n=91
Females (%)	86 (94.5)
Age in years, mean ± SD	54.4 ± 12.8
Median years of disease (min-max)	10 (1-39)
anti-Ro/SSA, n (%)	78/90 (86.6)
anti-La/SSA, n (%)	46/90 (51.1)
Rheumatoid factor, n (%)	63/88 (71.5)
Low C3, n (%)	9 (9.8)
Low C4, n (%)	21 (23.0)
Globulins, g/dL (median, min-max)	3.6 (2.9-7)
Parotid enlargement, n (%)	37 (40.6)
Arthritis, n (%)	33 (36.2)
Vasculitis, n (%)	12 (13.1)
Pulmonary involvement, n (%)	5 (5.4)
Renal involvement, n (%)	9 (9.8)
Neurological involvement, n (%)	20 (21.9)
Haematological involvement, n (%)	24 (26.3)
Lymphadenopathies, n (%)	22 (24.1)
Schirmer-I test, n (%)	77 (84.6)
Non-stimulated salivary flow, ml/15 min (median, min-max)	0.2 (0-4)
Positive minor salivary gland biopsy, n (%)	60/70 (85.7)
Cumulative ESSDAI (median, min-max)	8 (0-44)
SSDDI (median, min-max)	2 (0-9)
ESSPRI (median, min-max)	6.4 (1-9)
Weight in kg, mean ± SD	61.7 ± 11.58
Height in cm, mean ± SD	154.8 ± 7.48
Body mass index kg/m^2, mean ± SD	24.7 ± 4.7
Waist circumference in cm, mean ± SD	86.3 ± 10.3
Hip circumference in cm, mean ± SD	100.7 ± 95
Waist-to- hip ratio	0.85 ± 0.06
Body fat mass kg, mean ± SD	34.2 ± 8.11
Body fat mass index kg/m^2, mean ± SD	8.8 ± 3.5
Fat free mass kg, mean ± SD	16.5 ± 2.4
Comorbidities, n (%)	
Type 2 diabetes mellitus	8 (8.7)
Hypertension	14 (15.3)
Dyslipidaemia	11 (12.0)

ESSDAI: European League Against Rheumatism Sjögren's Syndrome Disease Activity Index; SSDDI: Disease Damage Index Score; ESSPRI: EULAR Sjögren's Syndrome Patient Reported Index.

Anthropometric assessment

Height and weight were measured while the subjects wore light clothing and no shoes. Height was measured using a wall stadiometer. Weight was determined using a corporal analysis bascule calibrated in kgs. BMI was categorised according to the World Health Organization (WHO) definitions into normal weight patients (BMI 19–24.9 kg/m^2), overweight patients (BMI 25.0–29.9 kg/m^2), and obese patients (BMI≥30 kg/m^2) (15). We also measured other anthropometric variables such as waist circumference, hip circumference, and waist-to-hip ratio as protocolised by the WHO protocol (16). Central obesity was defined as WC >90 cm and >80 cm for men and women, respectively; or by a WHR >0.90 and >0.85 for men and women, respectively.

Body composition

Bioimpedance analysis (BIA-SECA-514, Hamburgo) was used to measure body fat mass (BFM) and fat free mass (FFM). We then calculated the fat mass index (FMI) by dividing the total fat mass in kilograms by the height in meters squared. According to the BIA cut-off, FMI can be divided into four categories: low (≤4.4 kg/m^2), normal (≥4.5 kg/m^2, ≤9.2 kg/m^2), elevated (≥9.3 kg/m^2, ≤12.8 kg/m^2) and high (≥12.9 kg/m^2) for woman; low (≤1.7 kg/m^2), normal (≥1.8 kg/m^2, ≤6.1 kg/m^2), elevated (≥6.2 kg/m^2, ≤9.5 kg/m^2) and high (≥9.6 kg/m^2) for men). For this study, we defined obesity as being at the elevated or high FMI categories (17). On the other hand, we also recorded lean body mass, which is obtained by subtracting weight from fat mass. Then, we obtained the fat free mass (FFM) index by dividing the fat free mass in kilograms by the height in meters squared. According to the BIA cut-off, the FFM index can be reported as low (<15 kg/m^2 for women, <17 kg/m^2 for men) or normal (17).

This study was approved by the Institutional Biomedical Research Board of the Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico, and all patients and controls gave signed informed consent to participate.

Statistical analysis

We used descriptive statistics. Comparison between means was performed with Student's t-test. Categorical variables were analysed using the Chi square test

and logistic regression analysis with OR and 95% CI. A two-tailed $p<0.05$ was considered statistically significant. All analysis was performed using the SPSS for Windows 20.0 programme.

Results

We included 91 patients, 97.8% were women with a mean age of 54.4±12.8 years, and a median disease duration of 10 years. The general clinical/serologic characteristics and anthropometric assessment of the included patients are shown in Table I.

Anthropometric assessment

According to BMI, we found normal weight in 45 patients (49.4%), low weight in 3 patients (6.6%), overweight in 25 (27.4%), and obesity in 18 patients (19.7%). On the other hand, 33 patients (36.2%) were obese according to the WC, while 48 (52.7%) were obese according to the WHR.

We then compared the patients with obesity (n=18) *versus* the remaining ones according to their BMI (Table II). We found no differences in demographics, disease duration, glandular and extra-glandular features, cumulative ESSDAI, SSDDI, and ESSPRI scores. However, obese patients had a higher prevalence of anti-Ro/SSA antibodies (90.4% *vs*. 66.7%) and were more likely to have hypertension (25% *vs*. 6.7%).

When we compared obese *versus* non-obese patients according to their WC (Table III), they were similar in terms of demographic variables and serology, but the obese patients had a longer disease duration (13 *vs*. 9 years) and a higher cumulative ESSDAI score (12 *vs*. 6.5 points). They were also more likely to have parotid gland enlargement (58.1% *vs*. 34.5%), and higher globulin levels (3.9 *vs*. 3.5 g/dL). Again, obese patients were more likely to have hypertension. In logistic regression analysis, including all the variables that were significant at the univariate analysis, the variables that remained associated with obesity were disease duration (OR 1.06 95% CI 0.99-1.1, p=0.05) and the SSDDI score (OR 1.36, 95% CI 1.04–1.7, p=0.02).

In the same vein, when we compared obese patients with their counterpart according to the WHR (Table IV), the obese group included more women (100% *vs*. 88.4%), had higher SSDDI scores (3 *vs*. 2 points), more parotid gland enlargement (51.2% *vs*. 38.3%), and a positive Schirmer's test (93% *vs*. 77.1%). In the logistic regression analysis, including all the variables that were significant at the univariate analysis, again only the SSDDI remained associated (OR 1.31, 95% CI 1.01–1.69, p=0.03).

Body composition assessment

According to the bioimpedance, 7 patients had low FMI, 47 had normal FMI, 24 had increased FMI and 13 had high FMI. We considered the presence of obesity in 37 patients (increased + high FMI), thus our prevalence of obesity reached 40.6%.

We then compared the patients with low/normal FMI (n=54) with the group with high/increased FMI (n=37) (Table V). Patients with obesity were more likely to have parotid gland enlargement (54.1% *vs*. 31.4%), neurological involvement (35.1 *vs*. 13.0%), higher cumulative ESSDAI scores (11 *vs*. 7 points), higher SSDDI scores (3 *vs*. 2 points), and higher globulin levels (3.8 *vs*. 3.6 g/dL). These patients were also more likely to have hypertension (24.3% *vs*. 9.3%). In the logistic regression analysis that included all the variables that were significant at the univariate analysis, the variable that was again associated with obesity was the SSDDI score (OR 1.50, 95% CI 1.1–1.9, p=0.005).

When we analysed the domains of the SSDDI, we observed a higher prevalence of neurological damage in obese patients (32.4% *vs*. 9.3%). The lymphoproliferative domain only had a statistical tendency (8.1 *vs*. 0%, p=0.06).

Finally, as a sensitivity analysis, we evaluated the patients according to their fat free mass index, 16 had low and 75 normal values. When we compared these groups (data not shown), all variables were similar in the groups, except for parotid enlargement, which occurred less frequently in the low FFM index group (12.5% *vs*. 46.7%, p=0.01, OR 0.16, 95 CI 0.03–0.16).

Table II. Obesity according to body mass index.

Variable	Non obese n=73	Obese n=18	*p*-value
Females, (%)	69 (94.5)	17 (94.4)	0.99
Age, mean ± SD	53.3±13.3	58.3 ±10.2	0.25
Disease duration in years, mean ± SD	9.5 (1-39)	12 (1-20)	0.45
Cumulative ESSDAI (median, min-max)	7.5 (0-44)	9 (0-28)	0.64
SSDDI score (median, min-max)	2 (0-9)	3 (1-8)	0.47
ESSPRI score (median, min-max)	6 (1-9)	7.3 (2.6-9.6)	0.16
Schirmer's-I test (%)	61 (83.6)	16 (88.8)	0.79
Non-stimulated salivary flow ml/15 min (median, min-max)	0.1 (0-4)	0.25 (0-4)	0.30
Positive minor salivary gland biopsy, n (%)	46/56 (82.1)	14/14 (100)	0.19
anti-Ro/SSA, n (%)	66/72 (91.6)	12 (66.6)	0.01
anti-La/SSB, n (%)	40/72 (55.6)	6 (33.3)	0.11
Rheumatoid factor, n (%)	51/71 (71.8)	12/17 (70.5)	0.83
Globulins, mg/dL, mean(min-max)	3.7 (2-9.7)	3.5 (2.8-5.8)	0.69
Low C3, n (%)	7 (9.6)	2 (11.1)	1.0
Low C4, n (%)	18 (24.6)	3 (16.6)	0.47
Parotid enlargement, n (%)	30 (41.0)	7 (38.8)	0.48
Lymphadenopathies, n (%)	17 (23.2)	5 (27.7)	0.79
Arthritis, n (%)	26 (35.6)	7 (38.8)	0.87
Vasculitis, n (%)	11 (15.0)	1 (5.5)	0.27
Pulmonary involvement, n (%)	3 (4.1)	2 (11.1)	0.57
Renal involvement, n (%)	7 (9.5)	2 (11.1)	0.87
Neurological involvement (%)	14 (19.1)	6 (33.3)	0.22
Comorbidities, n (%)			
Hypertension, n (%)	8 (11.0)	6 (33.3)	0.01
Type 2 diabetes, n (%)	8 (11.0)	0 (0)	0.14
Dyslipidaemia, n (%)	8 (11.0)	3 (16.7)	0.50

ESSDAI: European League Against Rheumatism Sjögren's Syndrome Disease Activity Index; SSDDI: Disease Damage Index Score; ESSPRI: EULAR Sjögren's Syndrome Patient Reported Index.

Table III. Obesity according to waist circumference.

Variable	Non obese n=58	Obese n=33	*p*-value
Females, n (%)	55 (94.8)	31 (93.9)	0.85
Age in years, mean ± SD	52.1 ± 12.8	56.7 ± 11.6	0.85
Disease duration in years, (median, min-max)	9 (1-28)	13 (3-39)	0.004
Cumulative ESSDAI (median, min-max)	6.5 (0-30)	12 (0-44)	0.006
SSDDI score (median, min-max)	2 (0-8)	3 (2-9)	0.004
ESSPRI score (median, min-max)	6.4 (1-9.6)	6.4 (2.3-9)	0.57
Schirmer's-I test, (%)	47 (81)	30 (90.9)	0.40
Non-stimulated salivary flow ml/15 min (median, min-max)	0.15 (0-3)	0.2 (0-4)	0.91
Positive minor salivary gland biopsy, n (%)	37/45 (82.2)	23/25 (92.2)	0.22
anti-Ro/SSA, n (%)	51/57 (89.4)	27 (81.8)	0.34
anti-La/SSB, n (%)	30/57 (52.6)	16 (48.5)	0.70
Rheumatoid factor, n (%)	38/56 (67.8)	25/32 (80.2)	0.58
Globulins mg/dL (median, min-max)	3.5 (2.3-8.8)	3.9 (2-9.7)	0.04
Low C3, n (%)	4 (6.9)	5 (15.2)	0.20
Low C4, n (%)	13 (22.4)	8 (24.2)	0.80
Parotid enlargement, n (%)	19 (32.7)	18 (54.5	0.03
Lymphadenopathies, n (%)	11 (19.0)	11 (35.3)	0.18
Arthritis, n (%)	20 (34.5)	13 (39.4)	0.68
Vasculitis, n (%)	8 (13.8)	4 (12.1)	1
Pulmonary involvement, n (%)	3 (5.2)	2 (6.1)	1
Renal involvement, n (%)	3 (5.2)	6 (18.2)	0.06
Neurological involvement (%)	10 (17.2)	10 (30.3)	0.19
Comorbidities			
Hypertension, n (%)	5 (8.6)	9 (27.2)	0.01
Type 2 diabetes, n (%)	4 (6.8)	4 (12.1)	0.99
Dyslipidaemia, n (%)	7 (12.0)	4 (12.1)	0.39

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Discussion

The link between obesity and some autoimmune rheumatic diseases has been previously recognised. For instance, a Mendelian randomisation study found that BMI is a risk factor for asthma, rheumatoid arthritis, psoriasis and type 1 diabetes (18). Moreover, the prospective cohorts of the Nurses' Health Study I and II also found a risk of seropositive and seronegative RA in obese women (19). In the context of SjD, only one study has investigated this association and found no association with BMI when comparing SjD patients with age- and sex-matched controls (7).

On the other hand, BMI is by far the most widely used and standardised tool among body fat-induced health risk assessment tools. Using this index, previous studies in primary SjD in Caucasian population have shown that most patients are not obese (9, 20-22) and have an average BMI of 24.8-25.4 (20). Herein, 19.7% of our patients were obese using the BMI definition. This percentage could be consistent with the high prevalence of obesity in our country, which is 40.2% in women and 30.5% in men, in individuals older than 20 years (23). Nevertheless, BMI has limitations in the inability to distinguish body fat mass from lean body mass and reflect body fat distribution. For example, individuals with high muscle mass may be categorised as overweight, while those with a high percentage of body fat but low muscle mass may be considered normal weight (24).

Moreover, central obesity is characterised by an increase in WC and visceral fat deposition. The WC has demonstrated a reasonable ability to approximate the volume of visceral adipose tissue (24). Indeed, an increased WC is a risk factor for metabolic syndrome in the general population and in RA (25). In a study that included 20 patients with primary SjD, 7 had normal WC, 4 had a moderately increased WC, and 9 had a greatly increased WC, being the mean value 0.85 (22). Herein, using this index we observed obesity in 36.2% of the patients. Likewise, WHR is another anthropometric proxy of abdominal obesity. Both WHR and WC predict cardiovascular events and death more accurately than the BMI (23). In our study, using the WHR definition, the prevalence of obesity increased to 52.7%.

More recently, there are some other indirect techniques such as BIA to quantify body fat. In addition to body fat percentage, FMI is a useful tool for identifying obesity because it is independent of lean mass and adjusts for height differences. Al Khayyat *et al*. reported that FMI among 28 post-menopausal women with SjD was 9.07 kg/m^2, and 10.31 kg/m^2 for age and gender matched controls, respectively (19). In another study in SjD, the mean FMI was 8.5 kg/m^2 (22). Herein, we observed that 40% of our patients were obese according to this index.

Regarding the presence of comorbidities, obese patients (according to all definitions) were more likely to have hypertension. No differences were found regarding the presence of type 2 diabetes and dyslipidaemia. In contrast, a study in German population that compared obese and non-obese SjD patients (primary and associated) according to BMI, found that type 2 diabetes and hypertension were significantly more frequent in the obese group (10).

A second aim of our study was to identify the clinical and serological variables of SjD associated with obesity. When we used BMI, we were only able to identify anti-Ro/SSA antibodies as a risk factor for obesity. In contrast, when using other anthropometric proxies for abdominal obesity, the globulin levels and parotid gland enlargement were associated but only in the univariate analysis. Interestingly, parotid gland enlargement was less common in patients with low lean body mass. In the same vein, a previous study in SjD population (both primary and associated) found no significant differences in extra-glandular manifestations, such as skin conditions, neuromuscular manifestations, cryoglobulinaemia, renal involvement, pulmonary manifestations, or polyarthritis among patients with or without obesity according to BMI (10).

In our cohort we found no differences in the cumulative ESSDAI score between the obese and non-obese groups, neither according to the anthropometric

Table IV. Obesity according to waist hip ratio.

Variable	Non obese n=48	Obese n=43	*p*-value
Female, n (%)	48 (100)	38 (88.4)	0.02
Age in years, mean± SD	53.7 ± 13.9	56.8 ± 12.4	0.25
Disease duration y years (median, min-max)	9 (1-39)	12 (1-24)	0.08
Cumulative ESSDAI (median, min-max)	6 (0-22)	9 (0-44)	0.12
SSDDI score (median, min-max)	2 (0-6)	3 (0-9)	0.05
ESSPRI score (median, min-max)	5.0 (1.3-9)	6.1 (1-9.6)	0.33
Schirmer's-I test (%)	37 (77.1)	40 (93.0)	0.02
Non-stimulated salivary flow ml/15 min (median, min-max)	0.2 (0-4)	0.1 (0-4)	0.09
Positive minor salivary gland biopsy, n (%)	32/37 (86.4)	28/33 (84.8)	0.84
anti-Ro/SSA, n (%)	42 (87.5)	36/42 (85.7)	0.80
anti-La/SSB, n (%)	24 (50)	22/42 (52.4)	0.82
Rheumatoid factor, n (%)	32/45 (71.1)	31 (72.1)	0.24
Globulins mg/dL (median, min-max)	3.5 (2.3-7)	3.9 (2-97)	0.15
Low C3, n (%)	5 (10.4)	4 (9.3)	1.0
Low C4, n (%)	10 (20.8)	11 (25.6)	0.62
Parotid enlargement, n (%)	15 (31.3)	22 (51.2)	0.05
Lymphadenopathies, n (%)	9 (18.8)	13 (30.2)	0.32
Arthritis, n (%)	17 (35.4)	16 (37.2)	1.0
Vasculitis, n (%)	4 (8.3)	8 (18.6)	0.14
Pulmonary involvement, n (%)	2 (4.2)	3 (6.9)	0.99
Renal involvement, n (%)	4 (8.3)	5 (11.6)	0.59
Neurological involvement (%)	10 (21.2)	10 (23.8)	0.80
Haematological involvement, n (%)	11 (23.4)	13 (30.7)	0.42
Comorbidities			
Hypertension, n (%)	6 (12.5)	8 (18.6)	0.44
Type 2 diabetes, n (%)	3 (6.3)	5 (11.6)	0.30
Dyslipidaemia, n (%)	4 (8.3)	7 (16.3)	0.24

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Table V. Obesity according to fat mass index.

Variable	Non obese n=54	Obese n=37	*p*-value
Female, n (%)	52 (96.3)	34 (91.9)	0.36
Age in years, mean± SD	52.9 ± 13.4	57.1± 12.2	0.18
Disease duration y years (median, min-max)	9 (1-39)	12 (1-28)	0.06
Cumulative ESSDA score (median, min-max)	7 (0-30)	11 (0-44)	0.03
SSDDI score (median, min-max)	2 (0-6)	3 (1-9)	0.01
ESSPRI score (median, min-max)	5.8 (1-9)	7.1 (2.3-9.6)	0.08
Schirmer's-I test (median, min-max)	43 (79.6)	34 (91.9)	0.25
Non-stimulated salivary flow ml/15 min (median, min-max)	0.1 (0-3)	0.2 (0-4)	0.46
Positive minor salivary gland biopsy, n (%)	35/41 (85.3)	29 (78.3)	0.92
anti-Ro/SSA, n (%)	48/53 (90.6)	30 (81.1)	0.22
anti-La/SSB, n (%)	30/53 (56.6)	16 (43.2)	0.12
Rheumatoid factor, n (%)	35/52 (67.3)	28/36 (77.7)	0.54
Globulins mg/dL, (median, min-max)	3.6 (2.3-8.8)	3.8 (2.0-9.7)	0.05
Low C3, n (%)	6 (11.1)	3 (8.1)	0.63
Low C4, n (%)	13 (34.1)	8 (21.6)	0.78
Parotid enlargement, n (%)	17 (31.5)	20 (54.1)	0.03
Lymphadenopathies, n (%)	10 (18.5)	12 (32.4)	0.12
Arthritis, n (%)	21 (38.9)	12 (32.4)	0.48
Vasculitis, n (%)	6 (11.1)	6 (16.2)	0.34
Pulmonary involvement, n (%)	2 (3.7)	3 (8.1)	0.64
Renal involvement, n (%)	4 (7.4)	5 (13.5)	0.36
Neurological involvement, n (%)	7 (13.0)	13 (35.1)	0.01
Haematological involvement, n (%)	11 (21.2)	13 (35.1)	0.14
Comorbidities			
Hypertension, n (%)	5 (9.3)	9 (24.3)	0.05
Type 2 diabetes, n (%)	6 (11.1)	2 (5.4)	0.35
Dyslipidaemia, n (%)	6 (11.1)	5 (13.5)	0.79

ESSDA: European League Against Rheumatism Sjögren's Syndrome Disease Activity Index; EULAR Sjögren's Syndrome Patient Reported Index; SSDDI: Disease Damage Index Score; ESSPRI: EULAR Sjögren's Syndrome Patient Reported Index.

or body composition definitions. Nevertheless, in the study of Mezei *et al*. the ESSDAI of the obese group was lower than the ESSDAI of the non-obese group (2 *vs*. 4, $p<0.001$) (10). The authors explained this finding as an 'obesity paradox' that might be partly explained by the differences in comorbidities and the use of statins among the groups. In disagreement, in RA, overweight and/or obese patients have higher disease activity, and lower chances of achieving and maintaining minimal disease activity (3). Moreover, we did not find differences regarding the ESSPRI among obese and non-obese patients. In contrast, in SLE patients obese patients experience more pain and fatigue (3).

Notwithstanding, we observed an association between obesity and the SSDDI score (higher score in the obese groups according to different definitions), being the neurological damage the one that drove this association. This finding could be bidirectional, first partly explained by the fact that obesity might be a risk factor for the development of damage through chronic inflammation, for example through an IL-17-mediated inflammatory response (a phenomenon that has been described in multiple sclerosis and RA) (1); or because the development of damage leads to impaired functionality and mobility, which in turn causes obesity. Indeed, controversial results have been described on the association between obesity and the development of damage in SLE (26-27).

Our study has the following limitations. First, its transversal design limited the interpretation of our results and prevented us from establishing causality. Second, we might have a selection bias as patients were recruited from a tertiary reference centre. Third, we did not assess the relationship between obesity and treatment response. Obese patients may have different pharmacokinetic clearance and distribution that may influence treatment response. For instance, BMI has a negative effect on response to TNF inhibitors in patients with inflammatory arthritis, whereas this was not the case for tocilizumab, abatacept rituximab, IL-17 and IL-23 inhibitors (28). We also did not evaluate the use of statins that might have

a pleiotropic effect in this population; however, we have a low prevalence of dyslipidaemia. Finally, bioimpedance methods may be influenced by age, sex, ethnicity, and health conditions (29). Nevertheless, our study is the first to examine the prevalence of obesity defined by both anthropometric and body composition, and its association with some SjD variables.

Conclusion

Obesity was present in at least 20% of our patients according to BMI, but the prevalence increased to 40% when BIA was used, with a higher prevalence found in central obesity. Obesity might be associated with the development of damage, although causality is still unknown. Prospective studies with larger multiethnic cohorts are needed to understand this association. However, the current results could have implications for weight reduction in these patients. Thus, a healthier lifestyle should be recommended.

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