# Effects of primary Sjögren's syndrome on female genitalia and sexual functions

M. Gözüküçük[1], E. Türkyilmaz[2], O. Küçükşahin[3], Ş. Erten[3], Y. Üstün[1], A.F. Yavuz[4]

[1]SBÜ Ankara Training and Research Hospital, Department of Obstetrics and Gynaecology, Ankara;
[2]Ministry of Health, Ankara City Hospital, Maternity Hospital, Bilkent, Ankara;
[3]Department of Rheumatology, Yıldırım Beyazıt University, Bilkent, Ankara;
[4]Department of Obstetrics and Gynaecology, Yıldırım Beyazıt University, Bilkent, Ankara, Turkey.

Murat Gözüküçük, MD
Esengül Türkyilmaz, MD
Orhan Küçükşahin, MD
Şükran Erten, MD
Yusuf Üstün, MD
Ayşe Filiz Yavuz, MD

Please address correspondence to:
Murat Gözüküçük,
Sağlık Bakanlığı Ankara Eğitim ve Araştırma Hastanesi Sakarya Mh. Ulucanlar Cd. No: 89
Altındağ, Ankara, Turkey.
E-mail: muratgozukucuk@gmail.com

ORCID ID: 0000-0002-4418-7570

Received on June 17, 2021; accepted in revised form on August 30, 2021.

Clin Exp Rheumatol 2021; 39 (Suppl. 133): S66-S72.



**Key words:** primary Sjögren's syndrome, genital atrophy, sexual dysfunction

Competing interests: none declared.

## ABSTRACT

**Objective.** *Sexual dysfunctions in patients with rheumatological diseases can negatively affect human sexual life, and thus lead to the deterioration of quality of life. This study aimed to determine the effects of primary Sjögren's syndrome (pSS) on female sexual organs and sexual functions.*

**Methods.** *A total of 68 women with pSS and 135 healthy female patients were included in the study. All the women in the study and control groups were evaluated gynaecologically, and genital findings during the examination and variables related to pSS were recorded. The women's sexual functions were evaluated with the Female Sexual Function Index (FSFI) and quality of life was evaluated using the Health Status Questionnaire-Short Form 36 (QoL-SF 36).*

**Results.** *There was no difference in terms of the ages of the patients between the pSS and control groups [50 (25-70) and 49 (23-70) years, respectively] (p=0.487). The FSFI and QoL-SF 36 scores of the pSS group were significantly lower than the control group (p<0.05). Although the age of the patients, duration of menopause, and presence of atrophy on genital examination significantly correlated with sexual dysfunction, there was no significant correlation between pSS activity-related variables and sexual dysfunction.*

**Conclusion.** *It was determined that pSS led to sexual dysfunction by causing genital atrophy and vaginal dryness in women. Moreover, mood changes associated with the disease, especially depression, were revealed to be an independent risk factor for this condition.*

## Introduction

Primary Sjögren's syndrome (pSS) is a chronic systemic rheumatic disease characterised by the lymphoplasmacytic infiltration of exocrine glands with systemic symptoms (1) and affects 0.1 to 4.8% of the population, predominantly women at a ratio of 9:1 compared to men (2). A higher incidence has been reported in perimenopausal and postmenopausal women (3). The typical symptoms of pSS are dry eyes and mouth, but in some cases, pSS can also involve the mucosa and cause an irritating sicca syndrome that can impair the patient's quality of life (QoL). Patients with pSS have to live with significant functional impairments throughout their lives and may have difficulty performing a wide variety of daily activities (4).

The prevalence of painful intercourse is high in patients with pSS (5). Genital symptoms, such as vulvar and vaginal dryness, dyspareunia, itching, genital pain, increased susceptibility to infection, and dysuria are common from the onset of pSS (6, 7). Although patients with pSS manifest with external genitalia problems and often complain of dyspareunia, the pathobiology of this symptom has not yet been clarified. Nevertheless, a possible explanation is the local inflammation of vaginal mucosa (8). In a previous study, while dyspareunia was reported in 61% of patients with pSS and vaginal dryness in 52% (7), both had the greatest impact on QoL (9).

Sexual function is a very important part of human life and closely related to QoL (10). It is known that the musculoskeletal system is frequently affected in most rheumatic diseases; however, internal organ involvement is also not rare and can affect all life activities, including social, economic, psychological and sexual functions, by causing different degrees of dysfunction. Sexual activity is affected in approximately 50% of women with pSS, with the rates of restriction and reduction in sexual intercourse being observed

to be around 50% and >80%, respectively. Furthermore, in 68% of those with sexual dysfunction, symptoms of pSS, especially vaginal dryness and dyspareunia, are reported to cause this condition (11). The aim of the current study was to determine the effects of pSS on female genitalia and to reveal the effects of variables that determine the course and burden of the disease on sexual function and QoL.

## Materials and methods

This prospective, single-centre, cross-sectional study included a total of 68 women with pSS who presented to the rheumatology outpatient clinic of a tertiary care hospital between July 2015 and June 2019 and 135 healthy females who presented to the gynaecology outpatient clinic for reasons other than sexual dysfunction and were randomised from possible controls with similar age and menopausal status to the pSS group. The study was approved by the local ethics committee, and written informed consent was obtained from all participants in compliance with the Declaration of Helsinki. The diagnosis of pSS was made according to the American-European Consensus Group criteria (12). Age, gravida, parity, body mass index (BMI), education status, smoking status, menarche age, and menopausal status and duration were recorded for all participants. In the pSS group, disease duration, serum C-reactive protein (CRP), erythrocyte sedimentation rate, anti-nuclear antibody positivity, extractable nuclear antigen antibodies panel, and salivary gland cytology were recorded. Disease-related variables (*e.g.* activity and function data), the European League Against Rheumatism (EULAR) Sjögren's Syndrome Patient Reported Index (ESSPRI), EULAR Sjögren's Syndrome Disease Activity Index (ESSDAI), Health Assessment Questionnaire (HAQ), Visual Analog Scale-Pain (VAS-Pain) and fatigue scores, and medicines used for pSS were also evaluated and recorded.

A gynaecological examination was performed in the lithotomy position in all participants in both groups by the same gynaecologist (E.T.) with at least 15 years of professional experience. The presence of atrophy was determined based on a visual subjective assessment and vaginal culture and cervico-vaginal cytology samples were also analysed and the findings were recorded. In order to determine vaginal atrophy, the shrinkage and thinning of the mucosa, loss of rugae in the vagina, and introitus stenosis were taken into consideration. The reduction of subcutaneous fat in the labia majora was evaluated as labial atrophy, and contraction in the size and even retraction of the clitoral prepuce was interpreted as clitoral atrophy. The patients' sense of vaginal dryness was questioned and recorded. Pain sensation on speculum examination was assessed using VAS (rated from 0 to 10) (13).

**Table I.** Demographic and clinical characteristics of the study groups.

| | pSS group (n=68) | Control group (n=135) | *p* |
|---|---|---|---|
| Age (years) | 50 (25-70) | 49 (23-70) | 0.487 |
| Gravida | 3 (0-10) | 3 (0-6) | **0.002** |
| Parity | 2 (0-6) | 2 (0-4) | 0.077 |
| Previous births | | | |
| C/S | 14 (20.5%) | 40 (29.6%) | 0.157 |
| VD | 54 (79.5%) | 95 (70.4%) | |
| BMI (kg/m$^2$) | 25.1 (22.4-29.3) | 24.8 (22.1-28.9) | 0.293 |
| Smoking | | | |
| Yes | 9 (13.2%) | 29 (21.4%) | 0.156 |
| No | 59 (86.8%) | 106 (78.6%) | |
| Education | | | |
| ≤0 years | 41 (60.3%) | 79 (58.5%) | 0.561 |
| >10 years | 27 (39.7%) | 56 (41.5%) | |
| Age of menarche (years) | 13 (10-19) | 13 (11-17) | 0.177 |
| Menopause | | | |
| Yes | 38 (55.9%) | 77 (57.0%) | 0.763 |
| No | 30 (44.1%) | 58 (43.0%) | |
| Duration of menopause (years) | 3.5 (1-25) | 3.6 ( 1-22) | 0.184 |
| Clitoral Atrophy | | | |
| Yes | 31 (45.6%) | 14 (10.4%) | **<0.001** |
| No | 37 (54.4%) | 121 (89.6%) | |
| Labial atrophy | | | |
| Yes | 30 (44.1%) | 13 (9.6%) | **<0.001** |
| No | 38 (55.9%) | 122 (90.4%) | |
| Vaginal atrophy | | | |
| Yes | 30 (44.1%) | 22 (16.3%) | **<0.001** |
| No | 38 (55.9%) | 113 (83.7%) | |
| Feeling of dryness in vagina | | | |
| Yes | 39 (57.4%) | 53 (39.3%) | **0.029** |
| No | 29 (42.6%) | 82 (60.7%) | |
| Cervical atrophy | | | |
| Yes | 23 (33.8%) | 22 (16.3%) | **0.003** |
| No | 45 (66.2%) | 113 (83.7%) | |
| Vaginal infection | | | |
| Yes | 14 (20.6%) | 31 (23.0%) | 0.641 |
| No | 54 (79.4%) | 104 (77.0%) | |
| Atrophy in cytology | | | |
| Yes | 20 (29.4%) | 21 (15.6%) | **0.028** |
| No | 48 (71.6%) | 114 (84.4%) | |
| Speculum pain score | 50 (0-100) | 30 (0-100) | **<0.001** |

pSS: primary Sjögren's syndrome; C/S: Cesarean section; VD: vaginal delivery; BMI: body mass index. Values given as median (min-max). All *p*-values for continuous variables were calculated from Mann Whitney U-test.

Women aged over 20 and less than 70 years were included in the study. Pregnant patients and those with known hepatic, renal, interstitial lung, gynaecological oncological diseases, psychiatric disorders, communication impairment, and rheumatologic diseases were excluded from the study. Patients receiving systemic or local estrogen therapy were not included in the sample. The Female Sexual Function Index (FSFI), Health Status Questionnaire [Short Form (SF)-36], and Hospital Depression and Anxiety Scale (HADS) were administered to the women in both groups, and their scores were recorded. The data obtained from the pSS and control groups were compared.

The sexual functions of the women participating in the study were evaluated in six subdomains, namely arousal, desire, lubrication, orgasm, pain, and satisfaction, using the validated Turkish version of FSFI originally developed by Rosen *et al*. (14, 15). Higher scores in this scale demonstrate preferable sexual function. The total score is obtained by adding the scores of six subdomains and ranges from 2 to 36.

Disability was assessed with HAQ (16), QoL with the Short Form-36 (SF-36) Physical and Mental Health Summary Scales of (17, 18), and anxiety and depression with HADS (HADS-A and HADS-D, respectively) (19, 20).

At enrolment, ESSDAI (21), CDAI (22), and DAS-28 (23) were completed by the clinician, and their values were calculated according to the standard formula. All assessment were undertaken by the same clinician. VAS-Pain was evaluated based on a physician global assessment scale of 0 to 100, and all the patients completed ESSPRI (24) (mean score of 0–10 in numerical scales questioning pain, fatigue and dryness features, including oral, ocular, and global dryness).

Statistical analysis was performed using the Statistical Package for the Social Sciences, version 22 (SPSS Inc., Chicago, IL, USA). Data were presented as mean ± standard deviation or median (minimum-maximum) values and as numbers or percentages where appropriate. The homogeneity of variances between the groups was evaluated with the Levene test, and the distribution of continuous variables was evaluated using the Shapiro-Wilk and Kolmogorov-Smirnov tests. According to the results of the normality test, differences between independent groups were analysed with the Mann-Whitney U-test or Student's t-test. For the scale scores, non-parametric tests were chosen without testing the assumption of normal distribution. The chi-square and/or Fisher's exact test was used to compare groups in terms of the categories of variables. Correlations between variables were obtained using the Spearman or Pearson correlation coefficient and summarised with rho's and relevant *p*-values. A total FSFI score of <23 was defined as sexual dysfunction (25), and the patients in the pSS group were further divided into two subgroups according to their FSFI scores to perform statistical comparisons between these subgroups. A multivariate linear regression analysis was performed, and the correlation of sexual function with other parameters was examined.

To define the risk factors of the outcome variable (FSFI score), the multiple logistic regression analysis was conducted, and the adjusted odds ratios (OR) were calculated together with their confidence intervals (CI). All covariates with missing data in less than 20% of observations and a *p*-value of <0.25 in univariate testing were consid-

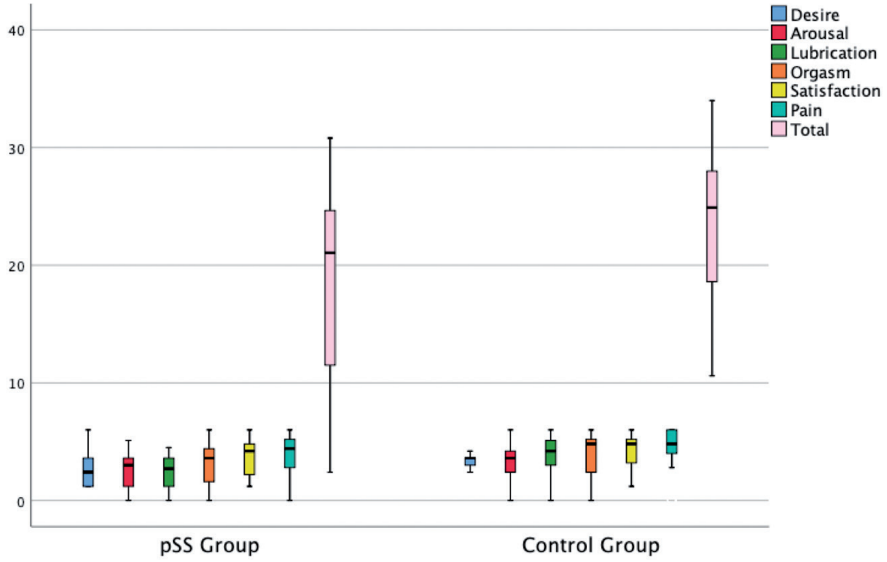


**Fig. 1.** FSFI (Female Sexual Function Index) scores of the study groups ($p<0.05$).

**Table II.** SF-36 quality of life and HADS scores of the study groups.

| | pSS group (n = 68) | Control group (n = 135) | *p* |
|---|---|---|---|
| Quality of life score (SF-36) | | | |
| Physical functioning | 70 (15-100) | 90 (0-100) | **<0.001** |
| Physical role challenge | 50 (0-100) | 100 (0-100) | **<0.001** |
| Emotional role difficulty | 66.6 (0-100) | 100 (0-100) | **0.012** |
| Energy/vitality | 50 (5-90) | 65 (5-100) | **0.001** |
| Mental health | 64 (8-96) | 68 (12-92) | 0.074 |
| Social functionality | 75 (0-100) | 75 (12.5-100) | **0.027** |
| Bodily pain | 55 (0-100) | 70 (22.5-100) | **<0.001** |
| General perception of health | 45 (5-95) | 65 (10-100) | **<0.001** |
| Hospital depression/anxiety scale | | | |
| Depression score | 6 (1-19) | 6 (0-19) | 0.299 |
| Anxiety score | 6 (0-17) | 4 (0-14) | **0.001** |

pSS: primary Sjögren's syndrome; SF-36: Short Form-36.
Values given as median (min-max).
All *p*-values for continuous variables were calculated from Mann Whitney U test.

ered as criteria for the inclusion of variables in the final multiple regression model. These data were only retained if the *p*-value was <0.05 or they provided significant confounding evidence (>10% change in effect size) and variables that needed to be adjusted, such as age. Highly collinear covariates (defined based on a correlation coefficient of >0.6) were not included together in the final multivariate model. The goodness of model fit was assessed with the Hosmer-Lemeshow test (26). A *p*-value of less than 0.05 was considered statistically significant for all statistical analyses.

## Results

The median age of the 68 patients with pSS was 50 (25–70) years, and that of the 135 healthy controls was 49 (23–70) years ($p$=0.487). Age, parity, previous births, BMI, smoking and education status did not differ between the two groups ($p$>0.05). The number of postmenopausal patients and duration of menopause were similar in both groups [menopausal 38 (55.9%) *vs*. 77 (57%), premenopausal 30 (44.1%) *vs*. 58 (43%), duration 3.5 (1–25) *vs*. 3.6 (1–22)] ($p$>0.05). Clitoral, labial and vaginal atrophy, speculum pain score, and atrophy in cytology were significantly higher in the pSS group ($p$<0.05). The clinical and demographic characteristics of the patients and healthy controls are listed in Table I. The FSFI (Fig. 1) and QoL-SF 36 scores of the pSS group were significantly lower than those of the control group ($p$<0.05). The HADS-D scores were similar in the two groups, while the HADS-A scores were significantly higher in the pSS group (Table II).

Lubrication, pain, and total FSFI scores were significantly lower in the premenopausal women with pSS than in the premenopausal women in the control group ($p$<0.05). In addition, the postmenopausal women with pSS were found to have lower scores in all FSFI domains except pain compared to those in the control group ($p$<0.05). The subgroup analysis of the pSS group showed that the patients with sexual dysfunction were older [52 (34–75) *vs*. 49 (27–55), $p$<0.001] and had a longer duration

**Table III.** Demographic data, disease-related variables and medical treatments used in women with pSS according to the presence of sexual dysfunction.

| | pSS with sexual dysfunction (Total FSFI scores <23) (n=43) | pSS without sexual dysfunction (Total FSFI scores ≥23) (n=2 5) | *p* |
|---|---|---|---|
| Age (years) | 52 (34-70) | 49.5 (27-55) | **<0.001** |
| Gravida | 4 (2-10) | 3 (0-7) | **0.005** |
| Parity | 3 (1-6) | 2 (0-5) | **0.007** |
| Duration of disease (years) | 4 (1-16) | 4 (1-15) | **0**.191 |
| Presence of menopause n (%) | 31 (72) | 7 (28) | **0.001** |
| Duration of menopause (years) | 4 (1-25) | 1 (1-5) | **<0.001** |
| CRP (mg/l) | 4 (3-21.9) | 5.8 (2.4-28) | 0.197 |
| ESR (mm/h) | 28 (5-75) | 26 (2-98) | 0.632 |
| Pain$^{VAS}$(cm) | 50 (0-100) | 40 (0-90) | 0.201 |
| HAQ | 0.3 (0-1.2) | 0.3 (0-0.8) | 0.857 |
| ESSPRI | 3.3 (1.4-8.3) | 4 (1.4-9) | 0.499 |
| ESSDAI | 11 (2-28) | 9 (2-31) | 0.254 |
| ANA positivity n (%) | 28 (65.1) | 17 (68) | 0.959 |
| Minor salivary gland cytology (grade) | 3 (0-4) | 3 (0-4) | 0.686 |
| Serology n (%) | | | |
| Negative | 11 (25.6) | 6 (24) | |
| SS-A/Ro positive | 22 (51.2) | 16 (64) | 0.335 |
| SS-B/La positive | 5 (11.6) | 0 (0) | |
| SS-A/Ro and SS-B/La positive | 5 (11.6) | 3 (12) | |
| Medical treatments n (%) | | | |
| Hydroxychloroquine | 24 (55.8) | 10 (40) | |
| Hydroxychloroquine+Corticosteroid | 7 (16.3) | 9 (36) | 0.228 |
| Hydroxychloroquine+MTX | 10 (23.3) | 5 (20) | |
| MTX | 2 (4.6) | 1 (4) | |

pSS: primary Sjögren's syndrome; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; VAS: Visual Analogue Scale; HAQ: Health Assessment Questionnaire; ESSPRI: European League Against Rheumatism (EULAR) Sjögren's Syndrome Patient Reported Index; ESSDAI: EULAR Sjögren's Syndrome Disease Activity Index; SS-A: anti-Sjögren's syndrome related antigen A autoantibodies; SS-B: anti-Sjögren's syndrome related antigen B autoantibodies; MTX: methotrexate. Values given as median (min-max). All *p*-values for continuous variables were calculated using the Mann-Whitney U test.

**Table IV.** Gynaecologic examination findings, HAD-S and Quality of Life (SF-36) scores according to the presence of sexual dysfunction in women with pSS.

| | pSS with Sexual Dysfunction (Total FSFI scores <23) (n=43) | pSS with no Sexual Dysfunction (Total FSFI scores ≥23) (n=25 ) | *p* |
|---|---|---|---|
| Clitoral atrophy n (%) | 23 (53.5%) | 8 (32%) | 0.086 |
| Labial atrophy n (%) | 22 (51.2%) | 8 (32%) | 0.125 |
| Vaginal atrophy n (%) | 23 (53.5%) | 7 (28%) | **0.041** |
| Feeling of dryness in vagina n (%) | 27 (62.8%) | 12 (48%) | 0.234 |
| Cervical atrophy n (%) | 19 (46.3%) | 2 (9.1%) | **0.003** |
| Atrophy in cervico-vaginal cytology n (%) | 10 (23.8%) | 1 (4%) | **0.034** |
| Speculum pain score | 50 (0-100) | 40 (0-90) | 0.201 |
| Hospital Depression/Anxiety Scale | | | |
| Depression Score | 7 (3-9) | 6 (3-9) | **0.003** |
| Anxiety Score | 7 (4-9) | 5 (4-10) | **0.007** |
| Quality of Life Score (SF-36) | | | |
| Physical functioning | 70 (15-100) | 85 (45-100) | **0.010** |
| Physical role challenge | 25 (0-100) | 75 (0-100) | 0.069 |
| Emotional role difficulty | 66.6 (0-100) | 100 (0-100) | 0.066 |
| Energy/vitality | 50 (5-90) | 50 (20-85) | 0.292 |
| Mental health | 60 (8-96) | 72 (24-92) | **0.020** |
| Social functionality | 62.5 (0-100) | 75 (25-100) | 0.103 |
| Bodily pain | 52.5 (0-100) | 55 (12.5-100) | 0.403 |
| General perception of health | 45 (5-90) | 45 (5-95) | 0.975 |

pSS: primary Sjögren's syndrome; HAD-S: Hospital Anxiety and Depression Scales; SF-36: Short Form 36; FSFI: Female Sexual Function Index.
Values given as median (min-max). All *p*-values for continuous variables were calculated from Mann Whitney U-test.

**Table V.** Pearson's correlation analysis of the FSFI scores with age and gynaecological examination findings.

| | Desire | Arousal | Lubrication | Orgasm | Satisfaction | Pain | FSFI Total Score |
|---|---|---|---|---|---|---|---|
| Age | -0.552* | -0.627* | -0.656** | -0.634* | -0.748** | -0.514* | -.0717** |
| Duration of menopause | -0.677** | -0.666** | -0.504* | -0.657** | -0.701** | -0.475* | -0.702** |
| Clitoral atrophy | -0.520* | -0.429* | -0.392* | -0.513* | -0.586* | -0.170 | -0.484* |
| Labial atrophy | -0.520* | -0.429* | -0.392* | -0.513* | -0.586* | -0.294 | -0.484* |
| Vaginal atrophy | -0.520* | -0.659** | -0.562* | -0.634* | -0.725** | -0.170* | -0.679** |
| Feeling of dryness in vagina | -0.117* | -0.143* | -0.401* | -0.151 | -0.320 | -0.330 | -0.228 |
| Cervical atrophy | -0.568* | -0.667** | -0.571* | -0.639* | -0.741* | -0.624* | -0.742** |
| Speculum pain score | -0.450* | -0.452* | -0.223 | -0.405* | -0.431* | -0.514* | -0.495* |
| Atrophy in cytology | -0.397* | -0.221* | -0.104* | -0.223* | -0.422* | -0.157 | -0.284 |

FSFI: Female Sexual Function Index.
*$p$<0.05; **$p$<0.001.

**Table VI.** Logistic regression analysis demonstrating predictors of sexual dysfunction within all (pSS and control) patients.

| | B | S.E. | df | OR (95% CI) | $p$ |
|---|---|---|---|---|---|
| Age | 0.010 | 0.024 | 1 | 1.011 (0.964-1.059) | 0.661 |
| Parity | 0.554 | 0.177 | 1 | 1.741 (1.231-2.462) | 0.002 |
| Menopause status | -1.221 | 0.322 | 1 | 3.392 (1.803-6.380) | <0.001 |
| Anxiety | 0.135 | 0.046 | 1 | 1.144 (1.046-1.253) | 0.003 |
| Presence of pSS | 0.724 | 0.344 | 1 | 2.062 (1.051-4.045) | 0.048 |

OR: odds ratio; 95% CI: 95% confidence interval.

**Table VII.** Logistic regression analysis demonstrating predictors of sexual dysfunction within patients with pSS.

| | B | S.E. | df | OR (95% CI) | $p$ |
|---|---|---|---|---|---|
| Age | 0.211 | 0.075 | 1 | 1.235 (1.067-1.430) | 0.005 |
| Parity | 0.815 | 0.383 | 1 | 2.260 (1.066-4.790) | 0.033 |
| Depression Score | 0.916 | 0.302 | 1 | 2.499 (1.384-4.513) | 0.002 |

OR: odds ratio; 95% CI: 95% confidence interval.
Analyses adjusted for menopausal status, anxiety, age at diagnosis, and atrophy at smear.

of menopause [4 (1–25) *vs*. 1 (1–5), $p$<0.001] compared to those without sexual dysfunction. The depression and anxiety scores were also significantly higher among the women with sexual dysfunction in the pSS group ($p$<0.05). Serology, salivary gland cytology and treatment methods were not different in pSS patients with sexual dysfunction compared to those without sexual dysfunction ($p$>0.05). Table III presents the data on the demographic, disease-related and medical treatment characteristics of the pSS subgroups formed according to sexual dysfunction status, and Table IV shows the genital examination findings, HADS and QoL (SF-36) scores of these subgroups.

According to the Pearson correlation analysis conducted to investigate the relationship between the FSFI score and other data, gynaecological examination findings had a strong and significant correlation with all the domain scores of FSFI (Table V), but there was no significant correlation between any of the disease-related variables and sexual function. In addition, the QoL SF-36 measures in eight domains had no significant correlation with any of the FSFI domains. Similarly, the HADS-A and HADS-D scores did not have a significant correlation with sexual function. Clitoral, labial and vaginal atrophy, speculum pain score, and atrophy in cytology were significantly correlated with age, duration of menopause, and pSS ($p$<0.05).

In the multivariate logistic regression analysis, the presence of pSS was found to be independently associated with sexual disorder (OR 2.062 95% CI 1.051–4.045 $p$=0.048) (Table VI). Among the women with pSS, there was an independent significant relationship between sexual disorder and age, parity, and depression score (Table VII).

## Discussion

In the course of pSS, gynaecological concerns, especially vaginal dryness and dyspareunia are frequent in female patients, and some studies on this topic have revealed varying but high prevalence (7, 11, 27). Although a high prevalence of gynaecological symptoms in pSS is reported in the literature, there are only limited data on their impact on sexual ability and activity. In the current study, the women with pSS had significantly lower FSFI scores in all domains compared to the healthy controls, and the gynaecological evaluation of the patients showed that vaginal, labial, clitoral and cervical atrophy and speculum pain scores were significantly higher among the women with pSS. The most common cause of genitourinary atrophy in women has been shown to be estrogen deficiency or infections (28). Increased vaginal dryness in women with pSS may be related to not only the underlying autoimmune effect of the disease on vascular supply to the vagina [autoimmune epithelitis with periepithelial lymphocytic infiltration and clonal lymphocytic expansion (1)] but also the stress of chronic disease reducing vaginal moisture (29). Furthermore, in a recent study, lower estrogen exposure and lower cumulative menstrual cycle duration were shown in women with pSS (30). The association between vulvovaginal atrophy and avoiding intimacy, loss of libido, and dyspareunia has also been previously reported (31, 32). Similarly, in the current study, the

detection of genital atrophy on gynaecological examination and cytology indicates a significant correlation of pSS with all areas of sexual dysfunction. In addition, the exclusion of vaginal infections that may cause pain based on a culture analysis and the lack of a significant difference between the two groups suggest that the decrease in the FSFI domain scores is due to atrophy.

In our study, the presence of pSS was significantly associated with sexual dysfunction independently, and age and the depression score also seemed to affect the quality of sexual life in women with pSS. This shows that vaginal dryness and dyspareunia can be seen in women with pSS even at a very early age and pSS may increase sexual dysfunction in women as age progresses; thus, in patients with chronic diseases, diminished sexual activity can also be a result of reduced pleasure and interest in sexual activity due to disease-related problems, especially depression (33, 34).

Different variables are used in pSS to determine the activity and course of the disease and to monitor the effectiveness of drug therapy. The correlation of these variables with sexual functions and genital changes has not yet been fully established (27). In our study, no relationship was found between disease activity, medications used, and most domains of QoL and sexual dysfunction. In patients with pSS, genitourinary complaints and sexual dysfunction can be seen even if the disease does not progress further, or it may even be the first presentation sign of the disease (35).

Fatigue has been reported in up to 70% of patients with pSS, and its pathophysiology is unknown and probably involves more than one factor (36, 37). In pSS, fatigue is often chronic and persistent (38) and known to be associated with lower levels of physical activity and greater functional impairment (39, 40). Fatigue causing physical dysfunction is also one of the leading causes of sexual dysfunction in rheumatological diseases affecting QoL (41). Our study revealed that except the correlation between the physical functioning score and the total FSFI score, there was no other correlation between the remaining SF-36 scores and FSFI domains. This suggests that sexual function may be affected in patients with pSS experience physical problems.

Although the clinician performing the gynaecological examination had sufficient experience and a cervical cytology test was performed to confirm the findings, the decision of atrophy was based on a subjective assessment, which can be considered as a limitation of our study. Sexual function is frequently and severely affected in patients with fibromyalgia (42), and there are conflicting data concerning the association between fibromyalgia and Sjögren's syndrome (43). Another limitation of this study is that we did not evaluate the presence of fibromyalgia in patients with pSS.

Sexual functions should be questioned to determine sexual dysfunction in all patients with rheumatologic diseases, although this is not an easy process since sexual health is often neglected. In conclusion, the findings of the current study clearly showed that pSS caused sexual dysfunction in women. Since sexual dysfunction is often associated with genitourinary atrophy, dyspareunia and psychological changes due to disease, this dysfunction should also be evaluated in patients with pSS, and medication should be considered, if necessary, for the management of vaginal dryness, dyspareunia, and depression.

## References


1. PARISIS D, CHIVASSO C, PERRET J, SHAHNAWAZ SOYFOO M, DELPORTE C: Current state of knowledge on primary Sjögren's syndrome, an autoimmune exocrinopathy. *Clin Med* 2020; 9: 2299.
2. HACKETT KL, NEWTON JL, FRITH J *et al*.: Impaired functional status in primary Sjögren's syndrome. *Arthritis Care Res* 2012; 62: 1760-4.
3. BINARD A, DEVAUCHELLE-PENSEC V, FAUTREL B, JOUSSE S, YOUINOU P, SARAUX A: Epidemiology of Sjögren's syndrome: Where are we now? *Clin Exp Rheumatol* 2007; 25: 1-4.
4. MAVRAGANI CP, MOUTSOPOULOS HM: The geoepidemiology of Sjögren's syndrome. *Autoimmun Rev* 2010; 9: A305-A310.
5. MULHERIN MD, SHEERAN TP, KUMARARATNE DS, SPECULAND B, LUESLEY D, SITUNAYAKE RD: Sjögren's syndrome in women presenting with chronic dyspareunia. *Br J Obstet Gynaecol* 1997; 104: 1019-23.
6. LEHRER S, BOGURSKY E, YEMINI M, KASE NG, BIRKENFELD A: Gynecologic manifestations of Sjögren's syndrome. *Am J Obstet Gynecol* 1994; 17: 835-7.
7. MARCHESONI D, MOZZANEGA B, DE SANDRE P, ROMAGNOLO C, GAMBARI PF, MAGGINO T: Gynaecological aspects of primary Sjögren's syndrome. *Eur J Obstet Gynecol Reprod Biol* 1995; 63: 49-53.
8. SKOPOULI FN, PAPANIKOLAOU S, MALAMOU-MITSI V, PAPANIKOLAOU N, MOUTSOPOULOS HM: Obstetric and gynaecological profile in patients with primary Sjögren's syndrome. *Ann Rheum Dis* 1994; 53: 569-73.
9. BELENGUER R, RAMOS-CASALS M, BRITO-ZERON P *et al*.: Influence of clinical and immunological parameters on the health-related quality of life of patients with primary Sjögren's syndrome. *Clin Exp Rheumatol* 2005; 23: 351-6.
10. STEPHENSON KR, MESTON CM: The conditional importance of sex: exploring the association between sexual wellbeing and life satisfaction. *J Sex Marital Ther* 2015; 41: 25-38.
11. MADDALI BONGI S, DEL ROSSO A, ORLANDI M, MATUCCI-CERINIC M: Gynaecological symptoms and sexual disability in women with primary Sjögren's syndrome and sicca syndrome. *Clin Exp Rheumatol* 2013; 31: 683-90.
12. VITALI C, BOMBARDIERI S, JONSSON R *et al*.: Classification criteria for Sjögren's syndrome: a revised version of the European criteria proposed by the American-European Consensus Group. *Ann Rheum Dis* 2002; 61: 554-8.
13. HILDEN M, SIDENIUS K, LANGHOFF-ROOS J, WIJMA B, SCHEI B: Women's experiences of the gynecologic examination: factors associated with discomfort. *Acta Obstet Gynecol Scand* 2003; 82: 1030-6.
14. ROSEN R, BROWN C, HEIMAN J *et al*.: The Female Sexual Dysfunction Index (FSFI): a multidimensional self-report instrument for the assessment of female sexual function. *J Sex Marital Ther* 2000; 26: 191-208.
15. ÖKSÜZ E, MALHAN S: Prevalence and risk factors for female sexual dysfunction in Turkish women. *J Urol* 2006; 175: 654-8.
16. DALTROY LH, LARSON MG, ROBERTS NW, LIANG MH: A modification of the Health Assessment Questionnaire for the spondyloarthropathies. *J Rheumatol* 1990; 17: 946-50.
17. SULLIVAN M, KARLSSON J: The Swedish SF-36 Health Survey III. Evaluation of criterion-based validity: results from normative population. *J Clin Epidemiol* 1998; 51: 1105-13.
18. PERSSON LO, KARLSSON J, BENGTSSON C, STEEN B, SULLIVAN M: The Swedish SF-36 Health Survey II. Evaluation of clinical validity: results from population studies of elderly and women in Gothenborg. *J Clin Epidemiol* 1998; 51: 1095-103.
19. ZIGMOND AS, SNAITH RP: The hospital anxiety and depression scale. *Acta Psychiatr Scand* 1983; 67: 361-70.
20. AYDEMIR O, GUVENIR T, KUEY L, KULTUR S: Validity and reliability of Turkish version of hospital anxiety and depression scale. *Turk Psikiyatri Derg* 1997; 8: 280-7.
21. SEROR R, BOOTSMA H, SARAUX A *et al*.: EULAR Sjögren's Task Force. Defining disease activity states and clinically meaningful

improvement in primary Sjögren's syndrome with EULAR primary Sjögren's syndrome disease activity (ESSDAI) and patient-reported indexes (ESSPRI). *Ann Rheum Dis* 2016; 75: 382-9.
22. ALETAHA D, NELL VP, STAMM T *et al*.: Acute phase reactants add little to composite disease activity indices for rheumatoid arthritis: validation of a clinical activity score. *Arthritis Res Ther* 2005; 7: 796-806.
23. FRANSEN J, VAN RIEL LCM: DAS remission cut points. *Clin Exp Rheumatol* 2006; 24 (Suppl. 43): S29-32.
24. SEROR R, RAVAUD P, MARIETTE X *et al*.: EULAR Sjögren's Task Force. EULAR Sjögren's Syndrome Patient Reported Index (ESSPRI): development of a consensus patient index for primary Sjögren's syndrome. *Ann Rheum Dis* 2011; 70: 968-72.
25. CLAYTON AH, SEGRAVES RT, LEIBLUM S *et al*.: Reliability and validity of the Sexual Interest and Desire Inventory-Female (SIDI-F), a scale designed to measure severity of female hypoactive sexual desire disorder. *J Sex Marital Ther* 2006; 32: 115-35.
26. HOSMER DW, LEMESHOW S: Applied Logistic Regression, Second Edition, John Wiley & Sons, New York, 2000.
27. PRIORI R, MINNITI A, DERME M *et al*.: Quality of sexual life in women with primary Sjögren syndrome. *J Rheumatol* 2015; 42: 1427-31.
28. CALLEJA-AGIUS J, BRINCAT MP: Urogenital atrophy. *Climacteric* 2009; 12: 279-85.
29. D'CRUZ DP, KHAMASHTA MA, HUGHES GR: Systemic lupus erythematous. *Lancet* 2007; 369: 587-96.
30. MCCOY SS, SAMPENE E, BAER AN: Sjögren's Syndrome is associated with reduced lifetime sex hormone exposure: a case-control study. *Arthritis Care Res* 2020; 72: 1315-22.
31. NAPPI RE, PALACIOS S: Impact of vulvo-vaginal atrophy on sexual health and quality of life at postmenopause. *Climacteric* 2014; 17: 3-9.
32. SIMON JA, NAPPI RE, KINGSBERG SA, MAAMARI R, BROWN V: Clarifying Vaginal Atrophy's Impact on Sex and Relationships (CLOSER) survey: emotional and physical impact of vaginal discomfort on North American postmenopausal women and their partners. *Menopause* 2014; 21: 137-42.
33. REES J, O'BOYLE C, MACDONAGH R: Quality of life: impact of chronic illness on the partner. *J R Soc Med* 2001; 94: 563-6.
34. VAN BERLO WT, VAN DE WIEL HB, TAAL E, RASKER JJ, WEIJMAR SCHULTZ WCM, VAN RIJSWIJK MH: Sexual functioning of people with rheumatoid arthritis: a multicenter study. *Clin Rheumatol* 2007; 26: 30-8.
35. SELLIER S, COURVILLE P, JOLY P: Dyspareunia and Sjögren's syndrome. *Ann Dermatol Venereol* 2006; 133: 17-20.
36. NG W-F, BOWMAN SJ: Primary Sjögren's syndrome: too dry and too tired. *Rheumatology* (Oxford) 2010; 49: 844-53.
37. MIYAMOTO ST, LENDREM DW, NGW-F, HACKETT KL, VALIM V: Managing fatigue in patients with primary Sjögren's syndrome: challenges and solutions. *Open Access Rheumatol* 2019; 11: 77-88.
38. HALDORSEN K, BJELLAND I, BOLSTAD AI, JONSSON R, BRUN JG: A five-year prospective study of fatigue in primary Sjögren's syndrome. *Arthritis Res Ther* 2011; 13: R167.
39. WOUTERS EJM, VAN LEEUWEN N, BOSSEMA ER *et al*.: Physical activity and physical activity cognitions are potential factors maintaining fatigue in patients with primary Sjögren's syndrome. *Ann Rheum Dis* 2012; 71: 668-73.
40. HACKETT KL, NEWTON JL, FRITH J *et al*.: Impaired functional status in primary Sjögren's syndrome. *Arthritis Care Res* 2012; 64: 1760-4.
41. TRISTANO AG: The impact of rheumatic diseases on sexual function. *Rheumatol Int* 2009; 29: 853-60.
42. ORELLANA C, CASADO E, MASIP M, GALISTEO C, GRATACÓS J, LARROSA M: Sexual dysfunction in fibromyalgia patients. *Clin Exp Rheumatol* 2008; 26: 663-6.
43. PRIORI R, IANNUCCELLI C, ALESSANDRI C *et al*.: Fatigue in Sjögren's syndrome: relationship with fibromyalgia, clinical and biologic features. *Clin Exp Rheumatol* 2010; 28 (Suppl. 63): S82-6.