

Primary Sjögren's Syndrome Adversely Affects the Female Sexual Function Assessed by the Female Sexual Function Index: A Case-Control Study

Çağlar YILDIZ,¹ Savaş KARAKUŞ,¹ Özlem BOZOKLU AKKAR,¹ Ali ŞAHİN,²
Birkan BOZKURT,³ Ali YANIK¹

¹Department of Gynecology and Obstetrics, Medical Faculty of Cumhuriyet University, Sivas, Turkey

²Department of Internal Medicine, Division of Rheumatology, Medical Faculty of Cumhuriyet University, Sivas, Turkey

³Department of General Surgery, Medical Faculty of Cumhuriyet University, Sivas, Turkey

ABSTRACT

Objectives: This study aims to evaluate the sexual function of females with primary Sjögren's syndrome (pSS) in comparison to healthy females by using the Female Sexual Function Index (FSFI).

Patients and methods: This case-control study included 31 female patients (mean age 46.0±10.2 years; range 30 to 68 years) with pSS and 27 healthy females (mean age 44.2±8.5 years; range 30 to 55 years) as control group. The sexual function of the participants was assessed by 19-item FSFI.

Results: Mean duration of pSS in the patient group was 35.9 months (range 3 to 264 months). Significantly higher number of pSS patients reported positive history for vaginal infection compared to controls (n=26, 83.9% vs n=7, 25.9%, respectively; p<0.001) without any difference in endocervical culture result. Cervical smear assessment revealed more inflammation and atrophy in patient group compared to control group (p=0.001). Mean FSFI total score was significantly lower in patient group than control group (18.9±9.9 vs 25.1±5.1, respectively; p=0.004). Similarly, five out of six domains of FSFI -arousal, lubrication, orgasm, satisfaction, and pain- were significantly lower in patient group. FSFI total and subscale scores, except for pain, were found to be negatively correlated with duration of pSS.

Conclusion: The pSS causes sexual dysfunction in female patients. Furthermore, as disease duration increases, female sexual function decreases. Clinical management of female patients with pSS should cover the assessment of their sexual functionality and taking the necessary precautions to maintain satisfactory quality of life and treatment outcome.

Keywords: Dyspareunia; sexual function; Sjögren's syndrome.

Primary Sjögren's syndrome (pSS) is an autoimmune, chronic-systemic disease determined by both functional and structural abnormalities of exocrine glands throughout the body.¹⁻⁵ The annual incidence of the disease in the literature is 3.9-5.3 per 100,000.⁶ Two studies from Turkey estimated the prevalence ranging from 0.21% to 0.72% depending on the classification criteria.^{7,8} pSS occurs 10 to 20 times more frequently in females over males.^{9,10}

Sjögren's syndrome-induced abnormalities of exocrine glands primarily lead to dryness of

eyes and mouth. Clinical presentation may vary from sicca symptoms of dry eyes, dry mouth to severe systemic symptoms.⁶ In addition to these, female patients with pSS often were reported to have vaginal dryness and consequent chronic dyspareunia.^{11,12} Sometimes, chronic dyspareunia may be the presenting symptom in yet undiagnosed pSS cases.¹³ However, most females diagnosed with pSS are not informed about vaginal dryness, consequent chronic dyspareunia, and sexual problems associated with the condition.⁵

Received: May 06, 2016 **Accepted:** July 18, 2016 **Published online:** February 12, 2017

Correspondence: Ali Şahin, MD. Cumhuriyet Üniversitesi Tıp Fakültesi İç Hastalıkları Anabilim Dalı, Romatoloji Bilim Dalı, 58140 Sivas, Turkey.

Tel: +90 346 - 258 09 49 e-mail: dralsahin@hotmail.com

©2017 Turkish League Against Rheumatism. All rights reserved.

Although chronic dyspareunia is a well-reported symptom in females with pSS, its impact on sexual functionality of patients has rarely been studied.¹⁴ However, it is known that there is a possible relationship between sexual well-being and overall life satisfaction in females.¹⁵ In spite of this fact, female sexual functionality is a difficult subject to talk with patients, particularly in traditional societies like Turkey. Therefore, data on the impact of pSS on female sexual functionality need to be increased to identify the effect of this chronic disease on life of women and to develop management strategies against sexual dysfunction. Therefore, in this study, we aimed to evaluate the sexual function of female patients with pSS in comparison to healthy females by using the Female Sexual Function Index (FSFI).

PATIENTS AND METHODS

This case-control study included a total of 31 female patients (mean age 46.0 ± 10.2 years; range 30 to 68 years) who had been under follow-up with diagnosis of pSS according to the American-European Consensus Group classification criteria¹⁶ and expert rheumatologist opinion in Cumhuriyet University Medical Faculty between June 2014 and June 2015, and 27 healthy females (mean age 44.2 ± 8.5 years; range 30 to 55 years) as control group. The healthy subjects were selected among hospital staff of the same ethnicity as the patients. The participants of this study had a sexual partner.

Exclusion criteria were as follows: chronic renal or hepatic impairment, presence of malignancy, smoking, other rheumatic/autoimmune disorders, medication or hormones having a potential to affect sexual functions, and history of gynecologic surgery within the past three months.

The study protocol was approved by the Institutional Ethics Committee (date 13.05.2014, no 2014-05/03) and conducted in accordance with the principles of the Helsinki Declaration and local regulations. All study participants gave written informed consents before any study-related procedures.

The following data were recorded for each study participant: sociodemographic factors, smoking status, duration of pSS (from diagnosis)

and treatments applied, concomitant diseases, fertility history including postmenopausal status, gravidity, parity, vaginal infection, endocervical culture, and cervical smear. The cervical smear findings were evaluated by a pathologist and reported semi-quantitatively using the neutrophil-lymphocyte percentage.

Sexual function of the participants was assessed by 19-item FSFI. The FSFI evaluates sexual function in six subdomains: arousal, desire, lubrication, orgasm, pain, satisfaction. Higher scores demonstrate preferable sexual function. The total score is obtained by adding the scores of six-subdomains having a range of 2-36.¹⁷ The validity and reliability of Turkish version of FSFI have been shown by Öksüz and Malhan.¹⁸

The primary outcome of the study was FSFI total and subscale scores in patient group in comparison to control group. The secondary outcome was the correlation between duration of pSS and FSFI scores of patients.

Statistical analysis

Study data were first analyzed by descriptive statistics (e.g., mean, standard deviation, range, frequency, and percentage). Parameters of patient and control groups were compared using the Student's t test for continuous variables and Mann-Whitney U test for non-parametric data (FSFI and disease duration) and chi-square test for categorical variables. Pearson correlation coefficient was calculated to measure strength of the linear relationship between duration of pSS and FSFI scores. Logistic regression analysis was performed for confounders (i.e. age). Statistical analysis was performed with IBM SPSS version 22.0 (IBM Corp., Armonk, NY, USA). Statistical level of significance was set to $p < 0.05$.

RESULTS

Mean duration of pSS in the patient group was 35.9 months (range 3 to 264 months). The most commonly used agent for the treatment of pSS was hydroxychloroquine, alone or in combination with prednisone ($n=20$, 64.5%). pSS patients did not show significant differences from healthy controls in terms of education level, smoking status, or comorbidities ($p > 0.05$ for all, Table 1).

Table 1. Sociodemographic and clinical findings of patient and control groups

	Patients with pSS (n=31)				Healthy controls (n=27)				p
	n	%	Mean±SD	Min-Max	n	%	Mean±SD	Min-Max	
Age (year)			46.0±10.2	30-68			44.2±8.5	30-55	0.087
Educational level									0.289
Low (primary-middle school)	11	35.5			5	18.5			
Medium (high school)	17	54.8			17	63.0			
High (university or higher education)	3	9.7			5	18.5			
Smoking status	8	25.8			4	14.8			0.303
Sjögren's syndrome duration (month)			35.9±47.8	3-264			N/A		N/A
Sjögren's syndrome treatment									N/A
Hydroxychloroquine	12	38.7					N/A		
Hydroxychloroquine + prednisone	8	25.8					N/A		
Prednisone	3	9.7					N/A		
Disease-modifying antirheumatic drugs	1	3.2					N/A		
Hydroxychloroquine + prednisone + disease-modifying antirheumatic drugs	6	19.4					N/A		
Biologic agents	1	3.2					N/A		
Comorbidity									0.177
None	21	67.7			19	70.4			
Hypertension	1	3.2			3	11.1			
Diabetes mellitus	0	0			2	7.4			
Hyperthyroidism	1	3.2			2	7.4			
Hypertension + diabetes mellitus	1	3.2			1	3.7			
Rheumatoid arthritis	4	12.9			0	0			
Raynaud's syndrome	2	6.5			0	0			
Familial Mediterranean fever	1	3.2			0	0			

pSS: Primary Sjögren's syndrome; SD: Standard deviation; Min: Minimum; Max: Maximum; N/A: Not applicable.

Number of postmenopausal females in patient and control groups did not differ significantly (n=7, 22.6% vs n=5, 18.5%, respectively; p=0.703). However, gravidity and parity rates were significantly higher in patient group (Table 2). Significantly more females in patient group reported positive history for vaginal infection (n=26, 83.9% vs n=7, 25.9%, respectively; p<0.001) without any difference in endocervical culture result (Table 2). Cervical smear assessment revealed higher inflammation

and atrophy rates in patient group compared to control group (p=0.001, Table 2).

Mean FSFI total score was significantly lower in patient group than control group (18.9±9.9 vs 25.1±5.1, respectively; p=0.004). Similarly, five out of six domains of FSFI -arousal, lubrication, orgasm, satisfaction, and pain- were significantly lower in patient group (Table 3).

In the correlation analysis, FSFI total and subscale scores, except for pain, were found to be

Table 2. Fertility history of patient and control groups

	Patients with pSS (n=31)				Healthy controls (n=27)				p
	n	%	Mean±SD	Min-Max	n	%	Mean±SD	Min-Max	
Postmenopausal status	7	22.6			5	18.5			0.703
Gravidity			5.1±3.9	0-12			2.6±1.6	0-6	0.002
Parity			3.7±3.2	0-8			2.2±1.1	0-5	0.018
History of vaginal infection	26	83.9			7	25.9			<0.001
Endocervical culture									0.635
Negative	2	6.5			1	12.5			
<i>Lactobacilli</i>	12	38.7			2	25			
<i>Escherichia coli</i>	1	3.2			1	12.5			
<i>Enterococcus faecalis</i>	9	29			1	12.5			
<i>Candida albicans</i>	5	16.1			3	37.5			
<i>Streptococcus agalactiae</i>	1	3.2			0	0			
<i>Gardnerella vaginalis</i>	1	3.2			0	0			
Cervical smear									0.001
Benign cellular changes, no inflammation	7	22.6			19	70.4			
Benign cellular changes, inflammation	19	61.3			8	29.6			
Benign cellular changes, atrophy	5	16.1			0	0			

pSS: Primary Sjögren's syndrome; SD: Standard deviation; Min: Minimum; Max: Maximum.

Table 3. Female Sexual Function Index total and subscale scores in patient and control groups

	Patients with pSS (n=31)		Healthy controls (n=27)		p
	Mean±SD	Min-Max	Mean±SD	Min-Max	
FSFI total (2-36)	18.9±9.9	2-34.6	25.1±5.1	14.4-32.9	0.004
FSFI subscale score					
Desire (1.2-6)	2.6±1.3	1.2-4.8	3.2±1	1.6-6	0.059
Arousal (0-6)	2.8±1.8	0-6	3.9±1.1	1.2-5.7	0.008
Lubrication (0-6)	3.4±2	0-6	4.8±1.1	2.4-6	0.002
Orgasm (0-6)	3.2±2	0-6	4.3±1.1	1.6-6	0.013
Satisfaction (0.8-6)	3.5±1.7	0-6	4.4±1	2.4-6	0.023
Pain (0-6)	3.3±2	0-6	4.6±1.4	1.2-6	0.008

pSS: Primary Sjögren's syndrome; SD: Standard deviation; Min: Minimum; Max: Maximum; FSFI: Female Sexual Function Index.

negatively correlated with duration of pSS; in other words, as disease duration increased, FSFI scores showing female sexual function decreased (Table 4).

DISCUSSION

In this case-control study, we showed that females with pSS have significant sexual dysfunction in comparison to healthy females with varying severity depending on the duration of disease. Our study is one of the limited number of studies in the literature on the impact of pSS on the female sexual functionality assessed by a validated self-report measure, FSFI.

Systemic autoimmune diseases including pSS affect various organs and systems in the body leading to dysfunction in such organs and systems, with sexual dysfunction being one of the consequences.^{19,20} Sexual dysfunction in females with systemic autoimmune diseases is most probably multifactorial due to the chronicity,

pathophysiology, activity, and psychological impact of disease, and drugs used for the treatment.^{19,20} Among these factors, vaginal discomfort and pain may mostly contribute to sexual dysfunction in patients with pSS.²⁰

Although recent immunologic and clinical researches led to significant advances in diagnosis and management of pSS, there is rather a small number of studies on the impact of the condition on sexual functionality of females.^{1,2,21} van Nimwegen et al.¹⁴ recently studied the impact of pSS on female sexual function by a number of self-administered questionnaires including FSFI on 46 patients and 43 age-matched controls and found that females with pSS have disrupted sexual function and more sexual discomfort compared with healthy controls. In the mentioned study,¹⁴ median total FSFI scores were 20.6 and 30.3 for females with and without pSS, respectively. They also found that sexual function is affected by physical factors such as vaginal dryness, pain and fatigue, and psychological involvement of pSS. Similarly, in the present study, we found mean FSFI total scores as 18.9 and 25 in patients with pSS and age-matched healthy females, respectively ($p=0.004$), showing the impairment of sexual functionality in females with pSS. Furthermore, as in the study by van Nimwegen et al.,¹⁴ five out of six domains of FSFI -arousal, lubrication, orgasm, satisfaction, and pain- were significantly lower in patients with pSS in our study. In the study by van Nimwegen et al.,¹⁴ all subscale scores were significantly lower in females with pSS except for satisfaction score.

An important finding of the present study was that sexual functionality of patients with pSS depended on the duration of disease. In other

Table 4. Spearman correlation coefficient for relationship between duration of primary Sjögren's syndrome and Female Sexual Function Index scores

	Duration of pSS	
	r	p
FSFI total score	-0.290	0.029
FSFI subscale scores		
Desire	-0.322	0.015
Arousal	-0.304	0.022
Lubrication	-0.323	0.014
Orgasm	-0.283	0.033
Satisfaction	-0.318	0.016
Pain	-0.042	0.760

pSS: Primary Sjögren's syndrome; r: Correlation coefficient. Spearman correlation test was used; FSFI: Female Sexual Function Index.

words, as duration of pSS increased, female sexual functionality decreased.

Disease onset following menopause is a common occurrence in pSS patients.²² However, in our study, there was no difference between pSS patients and controls in terms of rate of postmenopausal females. Previous studies reported no difference in fertility, parity or reproductive success rates between pSS patients and controls.¹² However, in the present study, gravidity and parity rates were significantly higher in patients with pSS.

We also found more inflammation and atrophy in cervical smear in patients with pSS than controls, most probably due to vaginal dryness in the patients. Vaginal dryness and dyspareunia are common symptoms of females affected with pSS.²³ These gynecological symptoms lead to impaired sexual intercourse, negatively affecting pleasure, satisfaction, and sexual ability.²⁴ As in our study, Priori et al.²⁵ showed that pSS (pre- and postmenopausal) patients had impaired quality of sexual function, and FSFI was found as a valuable measure for assessing sexual function. Furthermore, Cirpan et al.²⁶ performed cervical cytology, colposcopic examination, and human papillomavirus deoxyribonucleic acid testing in females with Sjögren's syndrome, and demonstrated similar findings in Sjögren's syndrome patients and controls. However, our study showed that pSS patients had higher prevalence of inflammation and atrophy in cervical smear.

The main limitations of our study were the small sample size and cross-sectional study design that prevented us from reaching a definitive conclusion on the prevalence of sexual dysfunction among females with pSS. However, this is one of the few studies in the literature on the clinical effect of pSS on female sexual functionality, the importance of which has been well-established for females to maintain a satisfactory quality of life.^{15,19,20}

In conclusion, pSS causes sexual dysfunction in females with a severity increasing with disease duration. Clinical management of females with pSS should cover the assessment of sexual functionality of patients and taking the necessary precautions to maintain satisfactory quality of life and treatment outcome. Considering the

importance of sexual functionality in the overall health of females, both patients and physicians should be informed on the possibility of pSS-related female sexual dysfunction. The findings of this study should be confirmed by further large-scale prospective studies on the prevalence, impact on patients' quality of life, diagnosis and treatment approaches of sexual dysfunction among females with pSS. Also, further studies are required on the management of discomfort caused by sexual dysfunction in female pSS patients.

Declaration of conflicting interests

The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

Funding

The authors received no financial support for the research and/or authorship of this article.

REFERENCES

1. Luciano N, Valentini V, Calabrò A, Elefante E, Vitale A, Baldini C, et al. One year in review 2015: Sjögren's syndrome. *Clin Exp Rheumatol* 2015;33:259-71.
2. Maslinska M, Przygodzka M, Kwiatkowska B, Sikorska-Siudek K. Sjögren's syndrome: still not fully understood disease. *Rheumatol Int* 2015;35:233-41.
3. Cornec D, Jamin C, Pers JO. Sjögren's syndrome: where do we stand, and where shall we go? *J Autoimmun* 2014;51:109-14.
4. Konttinen YT, Porola P, Konttinen L, Laine M, Poduval P. Immunohistopathology of Sjögren's syndrome. *Autoimmun Rev* 2006;6:16-20.
5. Schoofs N. Caring for women living with Sjögren's syndrome. *J Obstet Gynecol Neonatal Nurs* 2003;32:589-93.
6. Patel R, Shahane A. The epidemiology of Sjögren's syndrome. *Clin Epidemiol* 2014;6:247-55.
7. Birlik M, Akar S, Gurler O, Sari I, Birlik B, Sarioglu S, et al. Prevalence of primary Sjögren's syndrome in Turkey: a population-based epidemiological study. *Int J Clin Pract* 2009;63:954-61.
8. Kabasakal Y, Kitapcioglu G, Turk T, Oder G, Durusoy R, Mete N, et al. The prevalence of Sjögren's syndrome in adult women. *Scand J Rheumatol* 2006;35:379-83.
9. Brandt JE, Priori R, Valesini G, Fairweather D. Sex differences in Sjögren's syndrome: a comprehensive review of immune mechanisms. *Biol Sex Differ* 2015;6:19.

10. Reksten TR, Jonsson MV. Sjögren's syndrome: an update on epidemiology and current insights on pathophysiology. *Oral Maxillofac Surg Clin North Am* 2014;26:1-12.
11. Lehrer S, Bogursky E, Yemini M, Kase NG, Birkenfeld A. Gynecologic manifestations of Sjögren's syndrome. *Am J Obstet Gynecol* 1994;170:835-7.
12. 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.
13. Mulherin DM, 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.
14. van Nimwegen JF, Arends S, van Zuiden GS, Vissink A, Kroese FG, Bootsma H. The impact of primary Sjögren's syndrome on female sexual function. *Rheumatology (Oxford)* 2015;54:1286-93.
15. Stephenson KR, Meston CM. The conditional importance of sex: exploring the association between sexual well-being and life satisfaction. *J Sex Marital Ther* 2015;41:25-38.
16. Vitali C, Bombardieri S, Jonsson R, Moutsopoulos HM, Alexander EL, Carsons SE, 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.
17. Rosen R, Brown C, Heiman J, Leiblum S, Meston C, Shabsigh R, et al. The Female Sexual Function Index (FSFI): a multidimensional self-report instrument for the assessment of female sexual function. *J Sex Marital Ther* 2000;26:191-208.
18. Öksüz E, Malhan S (2005) The validity and reliability of Turkish version of Female Sexual Function Index-FSFI Sendrom 2005;17:54-60.
19. Araujo DB, Borba EF, Abdo CH, Souza Lde A, Goldenstein-Schainberg C, Chahade WH, et al. Sexual function in rheumatic diseases. *Acta Reumatol Port* 2010;35:16-23. [Abstract]
20. Tristano AG. The impact of rheumatic diseases on sexual function. *Rheumatol Int* 2009;29:853-60.
21. Sada PR, Isenberg D, Ciurtin C. Biologic treatment in Sjögren's syndrome. *Rheumatology (Oxford)* 2015;54:219-30.
22. Mavragani CP, Fragoulis GE, Moutsopoulos HM. Endocrine alterations in primary Sjogren's syndrome: an overview. *J Autoimmun* 2012;39:354-8.
23. Marchesoni D, Mozzanega B, De Sandre P, Romagnolo C, Gambari PF, Maggino T. Gynaecological aspects of primary Sjogren's syndrome. *Eur J Obstet Gynecol Reprod Biol* 1995;63:49-53.
24. 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.
25. Priori R, Minniti A, Derme M, Antonazzo B, Brancatisano F, Ghirini S, et al. Quality of Sexual Life in Women with Primary Sjögren Syndrome. *J Rheumatol* 2015;42:1427-31.
26. Cirpan T, Guliyeva A, Onder G, Terek MC, Ozsaran A, Kabasakal Y, et al. Comparison of human papillomavirus testing and cervical cytology with colposcopic examination and biopsy in cervical cancer screening in a cohort of patients with Sjogren's syndrome. *Eur J Gynaecol Oncol* 2007;28:302-6.