

Fatigue Have Impact on the Sexual Dysfunction in Chinese Females with Systemic Lupus Erythematosus

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Abstract

Background. systemic lupus erythematosus (SLE) might affect all aspects of life including sexual function; previous study indicated that fatigue was the risk factor of sexual dysfunction. The current study aims to investigate the effects of SLE on Chinese mainland female patients' sexual function compared with healthy subjects and to investigate the relationship among fatigue, disease parameters, depression, quality of life and sexual function in Chinese female patients with SLE.

Methods. A total of 128 female SLE patients (mean age: 43.65 ± 7.13 years) and 121 healthy female controls (mean age 43.59 ± 6.57 years) were included in this cross-sectional study. All data were collected consecutively by face-to-face questionnaires from January 2021 to December 2021. SLE patients completed questionnaires for demographic or clinical variables, the 10-cm Visual Analog Scale for pain, the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) for disease activity, the multidimensional fatigue inventory (MFI) for fatigue, the patient health questionnaire-9 (PHQ-9) for depression, the Female Sexual Function Index (FSFI) for sexual function, and the Short Form 12 health survey for quality of life. Independent sample t-test, Mann–Whitney U-test, Chi-square test, and forward stepwise binary logistic regression model were used to analyze these data.

Results. Our results showed that the prevalence of female sexual dysfunction (FSD) was 78.9% in SLE patients, which was significantly higher than the controls (56.7%) ($p < 0.05$). The results found that having child (OR: 23.04; $p = 0.000$), age (OR: 1.11; $p = 0.002$), DMARDs usage (OR: 0.04; $p = 0.004$), MFI total score (OR: 1.06; $p = 0.006$), and disease duration (OR: 1.16; $p = 0.043$) were the potential risk factors of FSD by forward stepwise binary logistic regression.

Conclusion. The present study reported that FSD was more common in Chinese SLE female patients compared to controls. Having child, age, DMARDs usage, fatigue, and disease duration had great impacts on FSD in Chinese SLE patients. Targeted and culturally sensitive interventions should be strengthened to delay the onset of FSD of this population.

Introduction

Systemic lupus erythematosus (SLE) is an autoimmune inflammatory disease that predominantly affects women between puberty and menopause [1, 2]. SLE patients can suffer from clinical manifestations including arthritis, serositis, nephritis, rashes, scars, depigmentation, skin dimpling, hair loss, or neuropsychiatric problems [3], which have great impacts on quality of life (QoL) in this population [4]. Sexual function is an important aspect of QoL and it is of great importance for SLE patients because it occurs predominantly in women with female to male ratio of 9:1 [5]. However, it is interesting to find that few SLE patients are willing to discuss their sexual problems with others, and most Chinese researchers or clinicians are reluctant to screen patients for sexual function because they don't think it's their responsibility [6, 7]. What is more, only a limited number of studies related to SLE patients' sexual

function have been conducted in China considering the conservative Chinese culture. Therefore, it is important to explore the rate and risk factors of sexual dysfunction among Chinese SLE patients.

A recent meta-analysis[8] revealed the rate of sexual dysfunction (SD) in SLE patients, ranging from 15–85.9%, which indicated the severity of the poor assessment and management of these issues. Over the past several years, only a handful of studies[9–12] used a validated tool of the Female Sexual Function Index (FSFI) to explore the relationship between SLE and female sexual dysfunction (FSD), demonstrating that SLE was associated with an increased risk of FSD in females. Tseng et al[13] have reported that 52.5% have FSD in Taiwan SLE patients. Besides, Shen et al[7] suggested that there were significant differences in impaired sexual function and relationship using a self-reported scale between Chinese SLE patients and healthy individuals. However, the rate and risk factors of FSD using the FSFI in Chinese mainland SLE patients have remained unknown.

Previous studies[9–12, 14] have found that several factors were associated with FSD in SLE patients, such as age, number of children, marital satisfaction, economic status, pain, disease duration, disease activity, certain psychological problems like depression and anxiety, functional status, and quality of life. Other factors such as higher dose of steroids also possibly result in FSD[12]. Nevertheless, only one study has included fatigue factors in this topic[12]. Fatigue is one of the most common manifestation in SLE, which is described as a subjective feeling of tiredness and a lack of energy[15]. It is a multidimensional construct, wherein a distinction can be made between physical and mental fatigue. Previous studies reported that fatigue is significantly associated with a poor quality of life in SLE[16, 17], but the association between fatigue and FSD is largely unclear. However, fatigue were closely associated with FSD in other diseases[18, 19], it is therefore for us to hypothesize that fatigue has effects on FSD in SLE patients.

Hence, the current study examines the independent association of fatigue with FSD in a Chinese population. Moreover, we aimed to investigate the effects of SLE on Chinese mainland female patients' sexual function compared with healthy subjects, in order to provide a preliminary analysis of the clinical parameters, disease activity, and psychological parameters associated with sexual function in SLE patients.

Methods

Patients

A total of 128 SLE patients were consecutively invited to participate in a single-center cross-sectional study. All data were collected consecutively by face-to-face questionnaires from January 2021 to December 2021 at the Ruijin Hospital, Shanghai Jiao Tong University School of Medicine. All patients (i) met the 2012 American College of Rheumatology diagnostic criteria[20], (ii) were aged ≥ 18 years, (iii) completed the questionnaire, (iv) they had no comorbidities (e.g., serious infections or cardiac, respiratory,

gastrointestinal, neurological, or endocrine diseases) that could influence SLE activity, (v) without any cognitive impairments and able to express their own thoughts in Mandarin freely.

Controls

A total of 121 convenience sample of women employees aged 18 years were recruited in 2020–2021. All eligible employees were distributed with an envelope containing a questionnaire composed of the FSFI, sociodemographic data, and a checklist of comorbidities by the assistant of each unit. The detailed recruitment procedure and contents of the questionnaire have been described previously.

Demographic and clinical characteristics

Demographic and clinical data included age (years), BMI, marital status, having child, education, employment status, income/person/month (yuan), health insurance, religious beliefs, residence, history of hospitalization, history of family, comorbid condition, SLE disease duration (years), VAS pain (range 0–10), and use of DMARDs, corticosteroid, and biologics were obtained by viewing medical records combined with SLE patients' self-report. At the same time, we used the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) to measure disease activity when collecting questionnaires[21].

Assessment of sexual function

Sexual function was measured by a Chinese translation of the FSFI, a 19-item self-questionnaire that evaluates the female sexual function in six domains: desire, arousal, lubrication, orgasm, satisfaction, and pain; and this tool is valid only in women who have active sexual life in the last month. The Cronbach's alpha of the Chinese version was 0.91 and this is a reliable and valid instrument for the Chinese population[22]. Women who reported having no sexual activity in the past 3 months or had a score of zero in any domain of it were considered sexually inactive and were removed from the analyses concerning the FSFI scores. Summation of the six domain scores yields a total score (range 2–36) and a total score of < 26.55 is proposed as a criterion for impaired sexual function [23].

Assessment of fatigue

Fatigue was assessed using the Chinese version of the multidimensional fatigue inventory (MFI). The MFI is a 20-item self-report instrument designed to measure fatigue. It covers the following dimensions: General Fatigue, Physical Fatigue, Mental Fatigue, Reduced Motivation and Reduced Activity. The total score of MFI-20 ranges from 20 to 80. The MFI-20 score indicates an individual's fatigue degree; a high total score indicates serious fatigue. Previous study has confirmed that the Chinese-version MFI-20 is a reliable and valid instrument for assessing fatigue, and can effectively measure the physical and mental fatigue of Chinese patients[24].

Assessment of depression

The patient health questionnaire-9 (PHQ-9) was used in the present study. The PHQ-9 was based on the diagnostic criteria for depression from the Diagnostic and Statistical Manual of Mental Disorders, 4th Edition (DSM-IV). The scores for each PHQ-9 item range from 0 (not at all), to 1 (several days), 2 (more

than half of the days), and 3 (nearly every day). A two-week recall period was used. The total score ranged from 0 to 27, with a higher score indicating greater self-reported depression. The psychometric properties of the PHQ-9 have been previously confirmed in Chinese populations[25].

Assessment of quality of life

The 12-item short-form health survey questionnaire (SF-12)[26] is a generic QoL questionnaire that consists of 12 items that can be divided into 8 domains: physical functioning (PF), role limitations due to physical problems (RP), bodily pain (BP), general health perceptions (GHP), vitality, social functioning (SF), role limitations due to emotional problems (RE), and general mental health (GMH). The scores for the physical and mental composite summaries (PCS and MCS) were subsequently calculated based on the above domains. The scores in each domain could range from 0 to 100, and higher scores indicated better QoL.

Statistical analysis

Statistical analysis was performed using the IBM SPSS version 20.0 software. For continuously and normally distributed variables, we used mean \pm standard deviation and independent samples t-test group to recognize differences between groups. For non-normally distributed data, we used median and interquartile range while group differences were assessed by Mann-Whitney U test. For categorical variables, we used frequencies (%) and the group differences were measured by Chi-square test. All the significant variables that were shown in the independent sample were included into the backward stepwise binary logistic regression model. Statistical significance was considered when $p < 0.05$ (two-sided).

Results

Patient characteristics

Table 1 shows the socio-demographic data of patients and controls. A total of 128 SLE patients and 121 healthy women were included. There were no significant differences between the baselines in two groups such as age, BMI, marital status, having child, educational, employment status, average monthly income, health insurance, religious beliefs and residence ($p > 0.05$). Figure 1 shows the subscale and total scores of FSFI between SLE and control groups. There were statistically significant differences between two groups including the subscale score of FSFI and the total score ($p < 0.05$).

Table 1
Demographic characteristics in SLE patients and health controls.

Variables	SLE patients (n = 128)	Health controls (n = 121)	<i>P</i>
Age, years	43.65 ± 7.13	43.59 ± 6.57	0.944
BMI, kg/m ²	23.12 ± 4.15	23.06 ± 3.35	0.902
Marital status			0.784
Single/Divorced/Widowed	31 (24.2)	28 (23.1)	
Married	97 (75.8)	93 (76.9)	
Having child, yes	92 (71.8)	88 (72.7)	0.787
Education			0.992
Primary and below	25 (19.5)	23 (19.0)	
Secondary	30 (23.4)	29 (24.0)	
Graduate and above	73 (57.1)	69 (57.0)	
Employment status			0.379
Unemployed	64 (50.0)	71 (57.8)	
Employed	64 (50.0)	50 (42.2)	
Income/person/month			0.678
≤ 3000 Yuan	2 (1.6)	2 (1.7)	
1000–3000 yuan	28 (21.9)	24 (19.8)	
3000–5000 yuan	35 (27.3)	33 (27.3)	
≥ 5000 yuan	63 (49.2)	62 (51.2)	
Health insurance, yes	109 (85.2)	102 (84.3)	0.756
Religious beliefs, yes	17 (13.3)	11 (9.1)	0.262
Residence			0.145
Urban	114 (89.1)	100 (82.6)	
Rural	14 (10.9)	21 (17.4)	
Data are presented as mean ± SD or number (%); SLE: Systemic Lupus Erythematosus; BMI: Body mass index.			

Differences between non-FSD patients and FSD patients in SLE

Table 2 represents the differences between SLE patients with or without FSD. Obviously, patients with FSD had older age, longer disease duration, higher disease activity, higher depression level, higher fatigue level from both the total and subscale scores in MFI questionnaire, and lower level of quality of life, with a trend toward higher rate of unmarried, having child, and DMARDs usage. ($p < 0.05$).

Table 2

The comparison between SLE patients with and without sexual dysfunction concerning the demographic and clinic characteristics, and the different indices.

Variables	With sexual dysfunction (n = 101)	Without sexual dysfunction (n = 27)	P
Age, years	40.90 ± 13.50	36.37 ± 6.84	0.018*
BMI, kg/m ²	23.14 ± 4.28	23.02 ± 3.69	0.896
Marital status			0.001**
Single/Divorced/Widowed	30 (29.7)	1 (3.7)	
Married	70 (70.3)	26 (96.3)	
Having child, yes	68 (67.3)	24 (88.9)	0.027*
Education			0.804
Primary and below	20 (19.8)	4 (14.8)	
Secondary	29 (28.7)	9 (33.3)	
Graduate and above	52 (51.5)	14 (51.9)	
Employment status			0.279
Unemployed	53 (52.5)	11 (40.7)	
Employed	48 (47.5)	16 (59.3)	
Income/person/month			0.798
≤ 1000 Yuan	2 (2.0)	0 (0)	
1000–3000 yuan	23 (22.8)	5 (18.5)	
3000–5000 yuan	28 (27.7)	7 (25.9)	
≥ 5000 yuan	48 (47.5)	15 (55.6)	
Health insurance, yes	86 (85.1)	23 (85.2)	0.996
Religious beliefs, yes	13 (12.9)	4 (14.8)	0.792
History of hospitalization, yes	81 (80.2)	20 (74.1)	0.488
History of family, yes	14 (13.9)	1 (3.7)	0.145
Comorbid condition, yes	62 (61.4)	12 (44.4)	0.113
Residence			0.974
Urban	90 (89.1)	24 (88.9)	

Variables	With sexual dysfunction (n = 101)	Without sexual dysfunction (n = 27)	<i>P</i>
Rural	11 (10.9)	3 (11.1)	
SLE disease duration, years	6.39 ± 7.22	3.80 ± 2.77	0.005**
VAS pain (range 0–10)	2.00 ± 1.50	1.67 ± 1.14	0.286
SLEDAI	6.28 ± 7.88	2.78 ± 3.64	0.001**
DMARDs usage, yes	73 (72.3)	26 (96.3)	0.008**
Corticosteroid usage, yes	84 (83.2)	23 (85.2)	0.802
Biologics usage, yes	18 (17.8)	8 (29.6)	0.176
Depression, PHQ9	5.27 ± 4.88	2.81 ± 4.54	0.020*
Fatigue, MFI			
General fatigue	12.12 ± 3.09	10.67 ± 3.36	0.035*
Physical fatigue	12.37 ± 3.53	10.67 ± 2.98	0.024*
Mental fatigue	10.42 ± 3.67	8.12 ± 3.54	0.005**
Reduced motivation	9.35 ± 2.87	8.56 ± 3.30	0.220
Reduced activity	11.67 ± 3.03	9.96 ± 4.00	0.046*
Total score	56.43 ± 13.05	48.04 ± 13.51	0.004**
Quality of life, SF-12			
PCS	44.11 ± 8.85	47.48 ± 7.91	0.075
MCS	45.96 ± 5.77	46.39 ± 4.82	0.720
Total score	90.06 ± 9.29	93.87 ± 8.07	0.046*
Data are presented as mean ± SD or number (%); SLE: Systemic Lupus Erythematosus; BMI: Body Mass Index; VAS: Visual Analog Scale; SLEDAI: Systemic Lupus Erythematosus Disease Activity Index; DMARDs: Disease-Modifying Anti-rheumatic Drugs; PDD: Perceived Devaluation-Discrimination; PHQ-9: Patient Health Questionnaire-9; MFI: Multiple Fatigue Inventory; SF-12: Short Form 12 health survey; PCS: physical components summary; MCS: mental components summary. * <i>P</i> < 0.05; ** <i>P</i> < 0.01.			

Determinants of FSD in SLE patients

As shown in Table 3, stepwise logistic regression analyses were used to identify a model to predict SLE patients who would have FSD. The results indicated that having child (OR: 23.04; *p* < 0.000), age (OR: 1.11;

$p = 0.002$), DMARDs usage (OR: 0.04; $p = 0.004$), MFI total score (OR: 1.06; $p = 0.006$), and disease duration (OR: 1.16; $p = 0.043$) were the potential risk factors of FSD in SLE.

Table 3
Result of analysis of forward stepwise ordered logit regression models in SLE patients.

Variables	B	S.E	P	OR (95%CI)
Having child	3.14	0.89	0.000**	23.04 (4.01, 132.40)
Age	0.11	0.04	0.002*	1.11 (1.04, 1.19)
DMARDs usage	-3.28	1.16	0.004**	0.04 (0.01, 0.36)
MFI total score	0.06	0.02	0.006**	1.06 (1.02, 1.10)
Disease duration	0.15	0.07	0.043*	1.16 (1.00, 1.34)

SLE: Systemic Lupus Erythematosus; DMARDs: Disease-Modifying Anti-rheumatic Drugs; MFI: Multiple Fatigue Inventory; OR: odds ratio; CI: confidence interval. * $P < 0.05$; ** $P < 0.01$.

Discussion

As is known to us, this is the first study investigating the prevalence and potential risk factors (e.g. fatigue, depression, disease activity) of FSD using the FSFI in SLE patients from mainland China. The prevalence of FSD in our SLE patients was 78.9%, higher than that reported in other studies using the FSFI (García M et al. reported 45.9%[10], Cheng J et al. 52.6%[13], and Serna-Peña G et al. 28%[11]), which could be explained by the existence of conservative Asian culture and the different participants included in different studies with either Chinese or Western cohorts. All of these findings highlighted that FSD should be included as part of the routine care for detection and management. Previous studies[10–14] have reported that many reasons may lead to FSD such as demographic characteristics, psychological problems, disease activity and drug usage etc. Our univariate analysis of demographic, clinical, and psychological factors was consistent with previous studies showing that SLE patients with FSD was related to age, having child, marital status, disease duration, disease activity, DMARDs usage, and depression.

In our study, except demographic, psychological and clinical factors that may lead to FSD, we also included fatigue which was rarely reported[12]. Fatigue is a complex and multi-faceted phenomenon, defined as a feeling of physical tiredness and lack of energy[15]. Fatigue is important because it is a very common symptom of SLE, and significantly impairs patients' quality of life[17]. Therefore, it would be interesting to assess the effects of fatigue using the Multidimensional Fatigue Inventory (MFI-20) on FSD in SLE. The results of our univariate analysis indicated that both total and almost subscale scores (except reduced motivation) in MFI questionnaire were associated with FSD, which was in accordance with the study by Pinto B et al[12] stating that fatigue had a significant effect on FSD. Furthermore, this

study revealed SLE patients with poor quality of life tended to suffer from FSD. This study is the first to examine the quality of life and its impact on FSD in Chinese SLE patients.

To identify which variables were most significantly correlated with FSD, a stepwise logistic regression analysis was used. Only independent variables individually associated with FSD with a P -value < 0.05 were entered into a stepwise logistic regression model. We found that having child, age, DMARDs usage, MFI total score, and disease duration were significantly associated with the FSD in SLE, which indicated that older age, not using DMARDs, higher fatigue level, and longer disease duration were independent risk factors for FSD in SLE.

There are, however, additional important shortcomings in this study that need to be addressed. First, the sample size was relatively small and the single-center study design might mean that results were not necessarily generalizable to a broader population. Another limitation of this study was the majority of patients were outpatients, therefore, our sample was not representative of the Chinese RA population. Second, previous study[7] has reported that body-image disturbance is associated with an impaired partner relationship in women with SLE, however, this emotional aspect was not measured in this study. Finally, no causal conclusions could be inferred because the study was cross-sectional in design. Further prospective studies with expanded sample sizes should be conducted to support the development of effective interventions to improve sexual function of SLE patients.

In conclusion, SLE considerably impaired sexual function compared to controls in the present study. Older age, not using DMARDs, higher fatigue level, and longer disease duration had great impacts on FSD in Chinese mainland SLE patients. Measuring sexual function should be considered a vital part of the comprehensive evaluation of the health status of SLE patients. Targeted and culturally sensitive interventions should be strengthened to delay the onset of FSD of this population.

Declarations

Ethics approval and consent to participate

The study was approved by the Ethics Committee of the Ruijin Hospital, Shanghai Jiao Tong University School of Medicine. Written informed consents were obtained from all participants in the study, in compliance with the Helsinki Declaration.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and/or analyzed during the current study available from the corresponding author on reasonable request.

Conflict of interest

The authors declared that they have no competing interests.

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Authors' contributions

Lijuan Zhang, Beiwen Wu, and Junna Ye contributed to the concept and design of the study. Lijuan Zhang and Junna Ye contributed to the acquisition and interpretation of data and drafting the article. All authors read and approved the final version of the article.

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Figures



Figure 1

Comparison of the subscale and total scores of FSFI in SLE patients and controls.