

Fatigue of systemic lupus erythematosus in China: contributors and effects on the quality of life

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Objective: Fatigue is a very common symptom of systemic lupus erythematosus (SLE), which significantly impairs patients' quality of life. The purpose of this study is to evaluate contributors of fatigue and effects of fatigue on the quality of life in Chinese SLE patients.

Methods: A survey of 119 SLE patients using the Fatigue Severity Scale (FSS) to assess the severity of fatigue was carried out. SLE patients completed the Systemic Lupus Erythematosus Disease Activity Index, the Hospital Anxiety and Depression Scale, the Short Form 36 health survey and the Pittsburgh Sleep Quality Index. Meanwhile, 105 healthy individuals completed FSS, the Hospital Anxiety and Depression Scale and Short Form 36 health survey. We used chi-squared analysis, independent samples *t*-tests and logistic regression models to analyze data.

Results: Our results found that the FSS score of patients with SLE was higher than that of healthy controls. The disease duration, anxiety, depression, subjective sleep quality and sleep disorders significantly correlated with fatigue in SLE patients. Moreover, logistic regression models showed depression and sleep disorders as predictors of fatigue. In SLE patients, fatigued patients had lower quality of life than those who were non-fatigued.

Conclusion: This is the first time to explore contributors of fatigue and the influence of fatigue on SLE patients' quality of life in China. Our study showed that depression and sleep disorders were predictors of fatigue, and fatigue seriously damaged SLE patients' quality of life. The results indicate that it is necessary to conduct holistic assessment and effective intervention, such as systemic psychiatric screening, psychological care and practical sleep guidance, to relieve symptoms of fatigue and finally improve their quality of life in SLE patients.

Keywords: systemic lupus erythematosus, fatigue, quality of life, depression, sleep disorders

Background

Systemic lupus erythematosus (SLE) is a chronic, progressive and recurrent autoimmune disease, which may cause inflammation activity and damage in any of the organs, often resulting in decreased physical, emotional and social abilities, and depression, pain, fatigue and so on.^{1,2} Moreover, fatigue, as a common symptom, affects more than 90% of SLE patients.^{3,4} Previous studies reported that fatigue had a negative impact on work performance, family responsibility and social activities,^{4,5} which can seriously affect the quality of life in SLE patients.^{6,7} Therefore, it is very important to identify factors leading to fatigue and improve their quality of life in SLE patients.

Due to the complexity of study on SLE fatigue mechanism and the lack of a unified conclusion, we explore the factors related to SLE fatigue through cross-sectional studies. Studies indicate that fatigue in SLE is associated with anxiety, depression, pain and body mass index (BMI).^{8,9} The correlation between fatigue scoring and depression is higher in the SLE population than other medical conditions such as Lyme disease or multiple sclerosis.^{10,11} Jump et al¹² find the importance of pain in predicting fatigue

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levels in SLE patients. Data from a multiethnic SLE cohort study show that 28% of the patients are obese, with a BMI of 30 kg/m² and above, and that this is associated with more severe fatigue.¹¹ Physical inactivity, lack of social support and sleep disorders are also associated with fatigue in SLE patients.^{13,14} But the cause of fatigue is still unclear. For example, the association between fatigue and disease activity in SLE is still controversial.¹⁵

Although patients with SLE suffer from severe fatigue, only few studies related to fatigue of SLE patients have been conducted in China. The purpose of our study is 1) to explore contributing factors of fatigue in SLE patients and 2) to evaluate the impact of fatigue on the quality of life in Chinese SLE patients.

Methods

Participants

Patients were recruited from the Second Affiliated Hospital of Nantong University between November 2016 and November 2017. A total of 125 SLE patients from outpatients or inpatients of the rheumatology department and 110 healthy individuals based on patients' gender and age from those attending for an annual examination were invited to participate in a cross-sectional study, and 119 (95.2% of the patients) and 105 (95.5% of the healthy individuals) of them were eventually included in the present research, as six SLE patients and five healthy individuals were reluctant to spend time filling out questionnaires. All patients fulfilled the 1997 American College of Rheumatology revised criteria for the classification of SLE.¹⁶ Patients were excluded on the basis of the following: 1) they had comorbidities (for instance, malignancy, cardiopathy, respiratory or endocrine diseases) that could affect fatigue and 2) they did not complete questionnaires. Healthy subjects were excluded if they had a history of or if they are currently diagnosed with other systemic or neurological diseases. This research was approved by the Ethics Committee of the Second Affiliated Hospital of Nantong University, and the written informed consents were acquired from all participants based on the Declaration of Helsinki.

Demographic and clinical characteristics

Demographic and clinical data included gender, age (years), BMI, marital status, education level (years), employment status, income/person/year, personal health insurance, tobacco and alcohol usage and exercise. The disease duration (years) and use of hormones 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.¹⁶

Measures of clinical variables

Fatigue Severity Scale (FSS): The FSS questionnaire was used to assess the severity of fatigue. The FSS contained nine items formulated as statements on the fatigue experience itself (item 3), what caused fatigue (item 2) and how fatigue affected daily life (seven items). People were instructed to assign a score between 1 (completely disagree) and 7 (completely agree) to each of 9 FSS items. The average of scores of the nine items was the overall score, and higher scores demonstrated more severe fatigue. The FSS has been proved to have reliability, high sensitivity and internal consistency in fatigue assessment.¹⁷ We used a cutoff score ≥ 4 to define fatigue cases based on data in the literature demonstrating that the FSS score ≥ 4 reliably differentiated subjects with fatigue from the controls.^{17–19}

The Hospital Anxiety and Depression Scale (HADS): We used the HADS to assess psychological status. The seven-item subscales were used to assess anxiety and depression scores ranging from 0 to 21, and the higher the score, the more serious the mood disorder.²⁰

The Pittsburgh Sleep Quality Index (PSQI): We used the PSQI to assess sleep quality. It had 19 questions including seven aspects (subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disorders, use of hypnotics and daytime dysfunction), and each part's score from 0 (score of no difficulty) to 3 (score of severe difficulty) was summed to get a total score from 0 to 21.²¹

The Short Form 36 health survey (SF-36): We used the SF-36 to assess quality of life. It evaluated eight aspects (physical functioning (PF), role limitations due to physical problems (RP), bodily pain (BP), general health perception (GH), energy/vitality (VT), social function (SF), role limitations due to emotional problems (RE), and mental health (MH)), and the score range was 0–100, with the higher score demonstrating the better health status. The score of Z-transformed and normalized domain was divided into the Physical Components Summary (PCS) score and the Mental Components Summary (MCS) score.²²

Data collection

These written questionnaires were finished by patients with the physician present or by the physician enquiring patients linked questions (an interview-led questionnaire) in the clinical

surrounding. After finishing data collection, the results were calculated by nurses. Two research assistants double-checked original data and then added the results to a computer database.

Statistical analysis

Descriptive analyses were performed as number (percentage) or mean (\pm SD) according to type and distribution of measured variables. The differences on the basis of categorical variables and continuous variables that were investigated in SLE patients who were divided into non-fatigued patients and fatigued patients were measured with the chi-squared analyses and *t*-tests, respectively, as well as the differences between the SLE patients and healthy individuals. All variables significantly related to fatigue by univariate tests were included into logistic regression models with the dichotomous fatigue assessed by the FSS as the dependent variable. We used independent sample *t*-test based on continuous variables to assess groups (non-fatigued patients or fatigued patients) differences on the quality of life. We considered that

it had statistical significance when $P < 0.05$ (two-sided), and we used SPSS (version 20.0) to analyze the data.

Results

Patient characteristics

Table 1 showed baseline participant characteristics in this analysis. SLE patients' mean (SD) age was 36.16 (11.80) years and 96.6% were female. Of them, 37.8% SLE patients used hormones more than 7.5 mg/d. The mean (SD) of disease duration and SLEDAI were 6.58 (5.51) years and 4.32 (3.36), respectively. There was no significant difference in gender, age, BMI, marital status, education, employment status, yearly income, personal health insurance, smoking use, alcohol use and exercise between the SLE patients and the controls ($P > 0.05$).

Comparison of fatigue and quality of life

From Figure 1, SLE patients scored higher than healthy controls on FSS, HADS-A and HADS-D and scored lower on

Table 1 Baseline characteristics of SLE patients and healthy controls

Variables	Cases (n=119)	Controls (n=105)	P-value
Gender, female, n (%)	115 (96.6)	100 (95.2)	0.848
Age (years), mean \pm SD	36.16 \pm 11.80	36.63 \pm 10.00	0.750
BMI (kg/m ²), mean \pm SD	22.47 \pm 3.82	22.24 \pm 2.98	0.632
Marital status, n (%)			0.605
Married	93 (78.2)	85 (81.0)	
Unmarried	26 (21.8)	20 (19.0)	
Education, n (%)			0.095
≤ 9 years	62 (52.1)	43 (41.0)	
> 9 years	57 (47.9)	62 (59.0)	
Occupation, n (%)			0.167
Employed	57 (47.9)	60 (57.1)	
Unemployed	62 (52.1)	45 (42.9)	
Yearly income (yuan), n (%)			0.138
$< 15,000$	31 (26.1)	28 (26.7)	
15,000–33,000	58 (48.7)	39 (37.1)	
$> 33,000$	30 (25.2)	38 (36.2)	
Personal health insurance, n (%)			0.889
Yes	76 (63.9)	68 (64.8)	
No	43 (36.1)	37 (35.2)	
Smoking use, yes, n (%)	1 (0.8)	1 (1.0)	1.000
Alcohol use, yes, n (%)	3 (2.5)	8 (7.6)	0.078
Exercise, n (%)			0.082
Yes	43 (36.1)	50 (47.6)	
No	76 (63.9)	55 (52.4)	
Disease duration (years), mean \pm SD	6.58 \pm 5.51		
SLEDAI, mean \pm SD	4.32 \pm 3.36		
Use of hormones (mg/d), n (%)			
≤ 7.5	74 (62.2)		
> 7.5	45 (37.8)		

Abbreviations: BMI, body mass index; SLEDAI, Systemic Lupus Erythematosus Disease Activity Index; SLE, systemic lupus erythematosus.

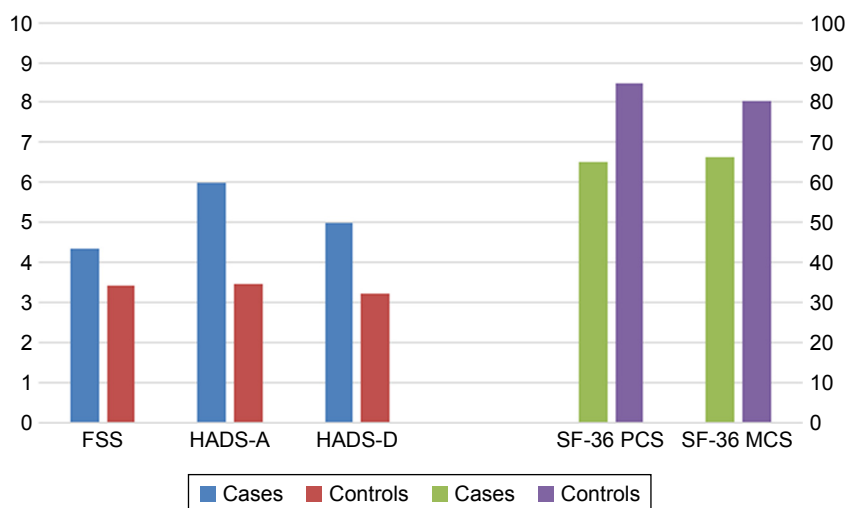


Figure 1 Comparison of fatigue and quality of life in cases and controls.

Note: Y-axes represent the number corresponding to the mean of the x-coordinate variable, both are numeric values.

Abbreviations: FSS, Fatigue Severity Scale; HADS, Hospital Anxiety and Depression Scale; MCS, Mental Components Summary; PCS, Physical Components Summary; SF-36, the Short Form 36 health survey.

SF-36 PCS and SF-36 MCS, which demonstrated that SLE patients obviously had more serious fatigue, higher levels of anxiety, depression and worse quality of life compared with the healthy controls.

Differences between non-fatigued patients and fatigued patients in SLE

As indicated in Table 2, a great number of demographic, clinical and psychological factors were checked for possible differences between non-fatigued patients and fatigued patients in SLE. Fatigued patients tended to have longer disease duration ($P=0.041$), higher degree of anxiety ($P=0.006$), higher degree of depression ($P=0.001$), worse subjective sleep quality ($P=0.038$) and severer sleep disorders ($P=0.003$) compared with non-fatigued patients. However, there was no significant difference in the degree of disease activity ($P=0.882$).

Determinants of fatigue in SLE patients

Logistic regression analysis was used to explore predictors of fatigue, as presented in Table 3. We examined that HADS-D ($\beta=0.158$, $P<0.05$) and sleep disorders ($\beta=0.889$, $P<0.05$) were the predictors of fatigue.

Effects of fatigue on quality of life in SLE patients

Comparison of non-fatigued patients and fatigued patients in terms of quality of life was exhibited in Table 4. Fatigued patients in SLE had significantly lower quality of life in all domains of the SF-36 scale ($P<0.05$).

Discussion

Fatigue problems are common. Overman et al²³ reported that one out of every two patients with a rheumatic disease was severely fatigued. In SLE patients, fatigue has been found to have an impact on multiple aspects of SLE patients' life, such as work and activities of daily living, emotions, cognition, social and family activities.²⁴ In the present study, depression and sleep disorders were independent predictors of fatigue in SLE patients. What's more, fatigued patients had impaired quality of life than non-fatigued patients.

Previous studies found that the degree of disease activity was associated with fatigue.^{12,13} However, Wang et al²⁵ concluded that fatigue in SLE patients did not correlate with disease activity using scales of SLEDAI and FSS. A recent study in Turkey showed that disease activity was not related to fatigue.¹⁵ Our study has indicated that fatigue was not associated with disease activity, but it was related to the disease duration. The possible explanation may be that the proportion of SLE patients with damage increased significantly with disease duration,²⁶ which may affect SLE patients' fatigue and the quality of life.

An increasing number of studies have indicated that depression was consistently associated with fatigue in SLE patients.^{27,28} It has been reported that the prevalence of depression in SLE patients was two times higher than that in the general population.²⁹ In our previous study, the incidence of depression in SLE patients was up to 32.9%.³⁰ Depression had a huge impact on SLE patients, including suicide ideation,³¹ increased incidence of cardiovascular disease,³²

Table 2 Differences between non-fatigued patients and fatigued patients in SLE

Variables	FSS<4 (n=51)	FSS≥4 (n=68)	P-value
Female	51 (100)	64 (94.1)	0.212
Age (years)	37.14±13.80	35.43±10.09	0.457
BMI (kg/m ²)	22.69±4.09	22.30±3.63	0.588
Marital status			0.701
Married	39 (76.5)	54 (79.4)	
Unmarried	12 (23.5)	14 (20.6)	
Education			0.832
≤9 years	26 (51.0)	36 (52.9)	
>9 years	25 (49.0)	32 (47.1)	
Occupation			0.368
Employed	22 (43.1)	35 (51.5)	
Unemployed	29 (56.9)	33 (48.5)	
Yearly income (yuan)			0.406
<15,000	12 (23.5)	19 (27.9)	
15,000–33,000	23 (45.1)	35 (51.5)	
>33,000	16 (31.4)	14 (20.6)	
Personal health insurance			0.582
Yes	34 (66.7)	42 (61.8)	
No	17 (33.3)	26 (38.2)	
Smoking use, yes	0 (0.0)	1 (1.5)	1.000
Alcohol use, yes	0 (0.0)	3 (4.4)	0.353
Exercise			0.869
Yes	18 (35.3)	25 (36.8)	
No	33 (64.7)	43 (63.2)	
Disease duration (years)	5.40±5.12	7.47±5.66	0.041*
SLEDAI	4.37±3.44	4.28±3.33	0.882
Use of hormones (mg/d)			0.623
≤7.5	33 (64.7)	41 (60.3)	
>7.5	18 (35.3)	27 (39.7)	
HADS-A	4.86±4.10	6.87±3.71	0.006**
HADS-D	3.76±3.23	5.93±3.52	0.001**
Subjective sleep quality	0.98±0.58	1.22±0.64	0.038*
Sleep latency	0.96±1.00	1.21±0.97	0.181
Sleep duration	0.80±0.96	0.72±0.91	0.630
Habitual sleep efficiency	0.53±0.78	0.79±1.02	0.111
Sleep disorders	1.04±0.49	1.32±0.53	0.003**
Use of sleep medications	0.12±0.59	0.18±0.67	0.618
Daytime dysfunction	0.47±0.54	0.65±0.59	0.098
PSQI total	4.90±3.31	6.09±3.43	0.060

Note: *P<0.05, **P<0.01.

Abbreviations: BMI, body mass index; FSS, Fatigue Severity Scale; HADS, Hospital Anxiety and Depression Scale; PSQI, the Pittsburgh Sleep Quality Index; SLEDAI, Systemic Lupus Erythematosus Disease Activity Index; SLE, systemic lupus erythematosus.

and a decline in quality of life.³³ In the present study, we also found that fatigued patients had significantly higher levels of HADS-A and HADS-D scores compared with non-fatigued patients. Interestingly, logistic regression analysis indicated that depression played an important role in fatigue, which was consistent with previous studies.^{15,34} The data suggested the need for systemic psychiatric screening and management and the importance of helping SLE patients to develop cognitive,

behavioral and emotional strategies, which can relieve fatigue and improve quality of life.^{4,35}

Previous research found that sleep disorders were also related to fatigue in SLE patients.³⁶ Our study has also shown fatigued patients tended to have severer sleep disorders compared to non-fatigued patients. Importantly, logistic regression analysis indicated that sleep disorders had significant impacts on fatigue. In chronic inflammatory diseases including SLE, sleep disorders were thought to worsen the disease symptoms including fatigue and lower the patients' quality of life.³⁷ This suggests that it is necessary to take measures to improve sleep quality, such as sleep management including sleep education and cognitive-behavioral interventions, so as to alleviate fatigue.³⁸

SLE, as a chronic disease, led to patients' physical and mental impacts and decreased their quality of life.³⁹ Our study also showed SLE patients had worse quality of life than healthy controls. Studies indicated that fatigue can affect the quality of life of patients in SLE.⁴⁰ In the present study, we found that fatigued patients in SLE had significantly lower quality of life compared with non-fatigued patients. Therefore, it is very important to intervene in fatigue and improve their quality of life in SLE patients.

To our knowledge, this study is the first to examine the related factors of fatigue and the impact of fatigue on the quality of life in Chinese SLE patients. However, we still had several shortcomings. First, because all SLE patients participated in our survey were from a single clinic of rheumatology and sample sizes were relatively small, it should be cautious to generalize findings to other population. Second, we cannot check causal relationships between variables due to cross-sectional design. Further research with expanded sample sizes, targeted fatigue measures and prospective researches on SLE patients' fatigue should be implemented, which is more conducive to alleviating fatigue and improving the quality of life.

Conclusion

In short, this study is the first known assessment of the contributors of fatigue and the effects of fatigue on quality of life in Chinese patients with SLE. Our study has found that severity of fatigue in SLE patients was higher than in healthy individuals, and fatigue may significantly damage patients' quality of life. Depression and sleep disorders play important roles in fatigue of SLE patients. The results suggest that overall assessment and targeted management (eg, systemic psychiatric screening and sleep intervention) of

Table 3 Stepwise logistic regression analysis of demographic, medical and psychological variables in relation to FSS in SLE patients

	Fatigue	Beta	SE	P-value	Exp (B)	(95% CI)
Step 1	Disease duration	0.060	0.039	0.126	1.061	0.983, 1.146
	HADS-A	-0.017	0.082	0.836	0.983	0.837, 1.154
	HADS-D	0.163	0.092	0.078	1.177	0.982, 1.411
	Subjective sleep quality	0.148	0.354	0.676	1.160	0.579, 2.322
	Sleep disorders	0.810	0.449	0.072	2.247	0.931, 5.421
Step 2	Disease duration	0.060	0.039	0.127	1.061	0.983, 1.146
	HADS-D	0.149	0.066	0.023	1.161	1.020, 1.321
	Subjective sleep quality	0.138	0.351	0.695	1.148	0.577, 2.283
	Sleep disorders	0.796	0.444	0.073	2.216	0.928, 5.289
Step 3	Disease duration	0.061	0.039	0.115	1.063	0.985, 1.148
	HADS-D	0.158	0.062	0.011	1.171	1.036, 1.324
	Sleep disorders	0.818	0.441	0.064	2.265	0.955, 5.372
Step 4	HADS-D	0.158	0.062	0.010*	1.171	1.038, 1.321
	Sleep disorders	0.889	0.434	0.041*	2.433	1.039, 5.694

Note: * $P < 0.05$.

Abbreviations: FSS, Fatigue Severity Scale; HADS, Hospital Anxiety and Depression Scale; SLE, systemic lupus erythematosus.

Table 4 Effects of fatigue on quality of life in SLE patients

Variables	FSS < 4 (n=51)	FSS ≥ 4 (n=68)	P-value
PF	86.86±15.59	69.85±21.67	<0.01**
RP	68.14±41.86	38.60±40.39	<0.01**
BP	87.24±17.70	78.85±22.07	0.028*
GH	59.96±19.45	40.94±20.30	<0.01**
VT	68.73±16.97	52.13±17.18	<0.01**
SF	81.62±16.84	72.24±20.92	0.010*
RE	82.35±32.22	51.47±42.88	<0.01**
MH	71.45±16.86	60.94±15.35	0.001**
SF-36 PCS	75.55±19.69	57.06±19.34	<0.01**
SF-36 MCS	76.04±16.92	59.20±19.71	<0.01**

Note: * $P < 0.05$, ** $P < 0.01$.

Abbreviations: BP, body pain; FSS, Fatigue Severity Scale; GH, general health perception; MCS, Mental Components Summary; MH, mental health; PCS, Physical Components Summary; PF, physical function; RE, role limitations due to emotional problems; RP, role limitations due to physical problems; SF, social function; SF-36, the Short Form 36 health survey; VT, energy/vitality; SLE, systemic lupus erythematosus.

SLE patients are needed to relieve symptoms of fatigue and finally improve their quality of life.

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Author contributions

All authors contributed toward study design, data analysis, drafting and critically revising the paper, and agreed to be accountable for all aspects of the work.

Disclosure

The authors report no conflicts of interest in this work.

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