The Assessment of Perceived Stress, Anxiety, Depression, Insomnia, Sleep Quality, and Drug Adherence in Patients with Systemic Lupus Erythematosus During the COVID-19 Pandemic

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Abstract

Background: Pandemics can increase psychosocial distresses. We evaluated both medication non-adherence and the incidence of perceived stress, anxiety, depression, sleep quality, and insomnia during the coronavirus disease 2019 (COVID-19) pandemic in systemic lupus erythematosus (SLE) patients.

Methods: A total of 211 participants, including 160 SLE patients and 51 healthy volunteers, were included. Questionnaire of Medication Adherence Reporting Scale (MARS-5), Perceived Stress Scale (PSS), Hospital Anxiety and Depression Scale (HADS-A, HADS-D), Pittsburgh Sleep Quality Index (PSQI), and Insomnia Severity Index (ISI) were assessed. Perceived stress related to the COVID-19 pandemic and its associations were investigated.

Results: The mean age of patients was 41.85 ± 12.97 years. Fifty-nine (36.9%) patients had high perceived stress, 16 (10.0%) had anxiety, 45 (28.1%) had depression, 77 (48.1%) had poor sleep quality, and 62 (38.8%) patients had insomnia. Perceived Stress Scale (23.64 ± 7.86 vs. 19.73 ± 4.80, P = .001), HADS-D (5.60 ± 3.40 vs. 4.08 ± 2.21, P = .003), PSQI (6.31 ± 3.62 vs. 4.43 ± 2.20, P = .001), and ISI (6.81 ± 4.98 vs. 4.53 ± 2.83, P = .002) were higher in the patient group. The presence of anxiety, depression, poor sleep quality, and insomnia was higher in patients with high PSS. High PSS was correlated with HADS-A, HADS-D, PSQI, and ISI. Medication non-adherence was detected in 79 (49.4%) of patients. Regression analysis revealed that high perceived stress is an independent predictor of depression [Exp(β) 95% CI: 1.488 (1.245-1.779), P < .001], and anxiety [Exp(β) 95% CI: 1.235 (1.026-1.487), P = .026].

Conclusion: Systemic lupus erythematosus patients demonstrated increased levels of perceived stress, depression, poor sleep quality and insomnia compared to the healthy population during the COVID-19 pandemic. Systemic lupus erythematosus patients with high perceived stress had more depression, anxiety, poor sleep quality, and insomnia than those without. Furthermore, high perceived stress was associated with depression and anxiety.

Keywords: Anxiety–depression, COVID-19 pandemic, drug adherence, insomnia–sleep quality, perceived stress, systemic lupus erythematosus

Introduction

In 2019, it was seen that there were cases of pneumonia of unknown origin in Wuhan, China.[1] It was determined that this epidemic was caused by a new coronavirus disease 2019 (COVID-19), called severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), and the virus continued to spread rapidly. The virus first became an epidemic, then spread rapidly from China to other countries and was declared a pandemic by World Health Organization on March 11, 2020.[2] Coronavirus disease 2019 can progress like a cold, but in more severe cases, it can cause acute respiratory distress syndrome, respiratory failure, and death.[3]

It has been observed that the COVID-19 epidemic, as well as its physical effects, can lead to serious negative effects on people's mental health and even psychological crises.[4] Epidemic situations such as the COVID-19 pandemic cause psychological problems such as anxiety, fear, sleep disorders, and depression. Frequency and fear of exposure to infected people, fear of infecting family members, lack of access to medical care,

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feelings of quarantine and loneliness, economic hardship, lack of available resources such as food and personal protective equipment, diminished personal freedoms and uncertainties about the pandemic may lead to psychiatric illnesses during the pandemic.[5] In addition, it has been shown that with the increase of the stress factor, symptoms of disease may increase, activity of disease and remission may be adversely affected, especially in people with autoimmune diseases.[6]

Systemic lupus erythematosus (SLE), an autoimmune, chronic disease, is mostly seen in reproductive age women and requires lifelong treatment and affects quality of life.[7] Depression, anxiety, and sleep disorders are common in SLE patients, and their prevalence varies between studies. Studies have shown that patients with SLE have more depression and poorer sleep quality than the general population.[8] The activity of disease is also associated with pain, poor sleep quality, sleep disorders, anxiety, and depression.[9] Medication non-adherence rates in SLE patients have been reported in a wide range from 3% to 76%.[10] Medication non-adherence, which is frequently observed in SLE patients, is also associated with disease exacerbations, hospitalizations, and worsening of organ involvement.[10] Data obtained from clinical studies show that medication adherence reduces disease involvement and activity and is associated with positive health outcomes.[11] Psychological disorders such as anxiety, depression and sleep disorders may increase medication non-adherence in lupus patients. Thus, it is important to

Main Points

- Psychological disorders such as anxiety, depression, and sleep disorders may increase medication non-adherence in lupus patients.

- In this study, we showed that patients with SLE had increased levels of depression, perceived stress, and insomnia compared to controls during the COVID-19 pandemic.

- Furthermore, SLE patients with higher levels of perceived stress were found to have more depression, anxiety, insomnia, and poor sleep quality, and a higher perceived stress level was associated with anxiety and depression.

- It is important to recognize a psychological disorder in the early stages, as it will make intervention strategies more effective and increase medication adherence.

diagnose psychological disorder in the early stages, as it will make intervention strategies more effective and increase medication adherence.[12]

The present study aims to evaluate both medication non-adherence and the incidence of perceived stress, anxiety, depression, sleep quality, and insomnia during the COVID pandemic in SLE patients.

Material and Methods

Study Design
A total of 211 participants aged 18 years and older, including 160 patients with a diagnosis of SLE and 51 healthy volunteers, who were followed at nephrology and rheumatology outpatient clinics between February and June 2021, were evaluated in this cross-sectional study. The exclusion criteria for the study were being under 18 years of age, pregnancy, and refusal to participate. Demographic information, date of diagnosis, comorbidities, medications, physical examination findings, medication adherence, and psychological status of the patients were recorded. The COVID-19 status of the participants was examined. History of COVID-19 infection, the severity of symptoms, hospitalization, and any problem in reaching the hospital during the pandemic were questioned and noted. A questionnaire of socio-demographics and COVID-19 status, Medication Adherence Reporting Scale (MARS-5), Perceived Stress Scale (PSS), Hospital Anxiety and Depression Scale (HADS-A and HADS-D), Pittsburgh Sleep Quality Index (PSQI), and Insomnia Severity Index (ISI) scales were assessed. Questions were asked face to face by the researcher and the answers were recorded. Perceived stress, sleep quality, insomnia, anxiety, and depression in SLE patients during the COVID-19 pandemic were analyzed, and medication adherence in patients was evaluated. The study was approved by the Ethis Committee of Marmara University Medical School on 05.02.2021 with the protocol number 09.2021.212. Written informed consent was obtained from the patients who agreed to take part in the study.

Study Surveys

Medication Adherence Reporting Scale
The MARS-5 includes 5 items related to medication adherence ("I forget to take," "I change the dose," "I stop taking it for a while," "I decide to skip a dose," and "I take less dose than I was told."). Each item is rated on a 5-point Likert scale, ranging from 1 to 5 points, from "5: never"

to "1: always." The MARS-5 total score ranges from 5 to 25, with a higher score indicating better adherence to medication.[13] A score of 23 or less was classified as "non-compliance," and a score of 24 and above was classified as "optimal adherence group."[14] Its validity and reliability has been carried out by adapting it to the Turkish population.[15]

Perceived Stress Scale
The PSS assesses how an individual views the stressfulness of certain situations in their life.[16] The scale includes 14 items, with participants rating each 1 on a 5-point Likert scale (ranging from "never: 0" to "very often: 4"). Total scores can range from 0 to 56, with a score of 25 or higher indicating a high level of stress. The validity and reliability of the scale have been assessed through its adaptation for the Turkish population.[17]

Hospital Anxiety and Depression Scale
Hospital anxiety and depression scale screens for anxiety and depression symptoms and is widely used. It contains a total of 14 questions, with 7 related to anxiety (HADS-A) and 7 related to depression (HADS-D). The questions consist of 4 items: "0: not at all" and "3: definitely."[18] Hospital anxiety and depression scale-Anxiety covers anxiety-related symptoms, while HADS-D covers depressive symptoms. It has been adapted to the Turkish population and its validity and reliability have been confirmed. The cut-off points are 10 for the anxiety scale and 7 for the depression scale.[19]

Pittsburgh Sleep Quality Index
The PSQI is a 24-question tool used to assess sleep disturbances and overall sleep quality.[20] Nineteen questions are self-reported and 5 questions should be answered by the roommate or bed partner. Eighteen questions are scored and 7 components are formed at the end (subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication, and daytime dysfunction). Each component contains scores between 0 and 3, and the scores of these components are summed to obtain a score between 0 and 21. Results of 5 and above are associated with poor sleep quality. It has been adapted to the Turkish population and its validity and reliability has been carried out.[21]

Insomnia Severity Index
The ISI was created by Morin to evaluate the severity of insomnia.[22] It includes 7 questions, each rated on a 5-point Likert scale, with responses ranging from "0: no problem" to "4: very serious problem." The total score can

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range from 0 to 28, with higher scores indicating poorer sleep quality. Scores between 0 and 7 suggest no insomnia, 8-14 indicate subthreshold insomnia, 15-21 reflect moderate insomnia, and scores of 22-28 are considered indicative of severe insomnia.[22] The reliability and validity of the scale were tested in a 2010 study by Boysan and colleagues in the Turkish population.[23]

Statistical Analysis

Statistical Package for the Social Sciences Statistics Package version 22.0 (IBM SPSS Corp.; Armonk, NY, USA) was used for statistical analysis. Variables were defined as numbers (n) and percent (%) and compared with the chi-square test. Continuous variables were presented as mean ± standard deviation. Continuous variables with parametric distribution were compared with independent samples t-test, and those without normal distribution were compared with Mann–Whitney U-test. Kolmogorov–Smirnov analysis was performed to determine whether continuous variables were normally distributed. According to the normality tests, those with $P \geq .05$ were considered to be normally distributed. The Pearson or Spearman correlation test was used where appropriate. Paired samples t-test was used to compare laboratory data before and during the pandemic. A P value <.05 was considered significant for all statistical analyses.

Results

A total of 211 individuals participated in the study, including 160 patients with SLE and 51 healthy controls. The mean age of the SLE patients was 41.85 ± 12.97 years. Among the patients, 142 (88.7%) were female. The patient and control groups were comparable in terms of both age and gender. Body mass index (25.62 ± 4.80 vs. 23.44 ± 2.78; P: .002), low socioeconomic status (33.8% vs. 9.8%; P: .001), and being married (84.4% vs. 66.7%; P: .009) were higher in the patient group. Smoking rate (12.5% vs. 29.4%; P: .008) was higher in healthy volunteers.

The number of previous COVID-19 infections was 31 (19.4%) in the patient group and 12 (23.5%) in the controls. In the patient group, mild symptoms were observed in 27 (87.1%) and severe symptoms in 4 (12.9%) patients. Seven (4.4%) patients were hospitalized and treated for COVID-19 infection. All of the control group had mild symptoms, and none of the healthy volunteers were hospitalized. There was no difference between the patient and control groups regarding their history of COVID-19 infection, symptoms, or hospitalization. The demographic details of both groups are presented in Table 1

Perceived Stress Scale score (23.64 ± 7.86 vs. 19.73 ± 4.80; P: .001), HADS-D score (5.60 ± 3.40 vs. 4.08 ± 2.21; P: .003), total PSQI score (6.31 ± 3.62 vs. 4.43 ± 2.20; P: .001), and ISI score (6.81 ± 4.98 vs. 4.53 ± 2.83; P: .002) were significantly higher in patients with SLE. However, the HADS-A score (6.40 ± 2.87 vs. 5.67 ± 2.22; P: .096) was similar between the groups. While high perceived stress (36.9% vs. 11.8%; P: .001), presence of depression (28.1% vs. 3.9%; $P<$ .001) and insomnia (38.8% vs. 19.6%; P: .017) were higher in the patient group, the presence of anxiety (10.0% vs. 3.9%; P: .252) and poor sleep quality (48.1% vs. 31.4%; P: .051) were similar (Table 2).

Based on their perceived stress levels, the patients were categorized into 2 groups: high PSS score and low PSS score. No significant differences were found between the 2 groups in terms of socio-demographic factors or COVID-19 data. Hospital anxiety depression scale-Depression score (8.32 ± 3.05 vs. 4.01 ± 2.45; $P < .001$), HADS-A score (8.27 ± 2.52 vs. 5.31 ± 2.48; $P < .001$), PSQI score (8.27 ± 3.82 vs. 5.17 ± 2.96; $P < .001$), and ISI score (9.88 ± 4.93 vs. 5.01 ± 4.06; $P < .001$) were higher in the high PSS group. Similarly, the presence of depression (62.7% vs. 7.9%; $P < .001$), anxiety (20.3% vs. 4.0%; P: .001), poor sleep quality (76.3% vs. 31.7%; $P < .001$), and insomnia (69.5% vs. 20.8%; $P < .001$) were also higher in the high PSS group (Table 3).

In the Pearson correlation analysis, a positive relationship was observed between the perceived stress level and HADS-D scores (r: 0.689; $P < .001$), HADS-A (r: 0.671; $P < .001$), PSQI (r: 0.468; $P < .001$), and ISI (r: 0.541; $P < .001$). In multivariate logistic regression analysis, HADS-A and HADS-D scores were found to be independent predictors of high perceived stress level (Table 4).

We further evaluated medication adherence in SLE patients, and medication non-adherence was detected in 79 (49.4%) patients. However, when medication non-adherence was evaluated according to the perceived stress status, there was no significant difference between MARS-5 scores (22.80 ± 2.42 vs. 22.90 ± 2.11; P: .772) and non-adherence rates (49.2% vs. 49.5%; P: 1.000). Sixty-eight (42.5%) patients reported difficulty in reaching the hospital during the pandemic period.

When laboratory results of the patients before and during the first year of the pandemic were compared, sedimentation rate values (28.19 ± 16.16 vs. 24.17 ± 16.24 mm/hr; $P < .001$) were higher, while albumin (4.02 ± 0.55 vs. 4.12 ± 0.53 g/dL; $P = .002$) were lower in the pre-pandemic period. As for proteinuria, 57 (35.6%) patients had proteinuria and 4 (2.5%) of them were in the nephrotic range before the COVID-19 pandemic. During the pandemic, 60 (37.5%) patients had proteinuria and 2 (1.25%) of them were in the nephrotic range. Comparison of proteinuria data of the patients before and during the first year of the pandemic (0.52 ± 1.06 vs. 0.44 ± 0.79 g/day; $P = 0.137$) was similar. The laboratory data of patients were further evaluated according to the PSS groups. In the high

Table 1. Demographic Characteristics and COVID-19 Data of the Patient and Control Groups

Variable	Patients (n:160)	Controls (n:51)	P
Age, years	41.85 ± 12.97	41.08 ± 12.00	.696
Body mass index, kg/m^2	25.62 ± 4.80	23.44 ± 2.78	.002
Female gender, n (%)	142 (88.7)	43 (84.3)	.463
Smoking, n (%)	20 (12.5)	15(29.4)	.008
Alcohol, n (%)	2 (1.2)	3 (5.9)	.092
Marital status (maried), n (%)	135 (84.4)	34 (66.7)	.009
Education status, n (%)	158 (98.8)	51 (100)	1.000
Socioeconomic status (low), n (%)	54 (33.8)	5 (9.8)	.001
Presence of psychological illness, n (%)	5 (3.1)	0 (0)	.339
History of COVID-19, n (%)	31 (19.4)	12 (23.5)	.551
COVID-19 symptoms, mild/severe, n (%)	27 (87.1)/4 (12.9)	12 (100.0)/0 (0.0)	.314
Hospitalization, n (%)	7 (4.4)	0 (0)	.200

Data presented as mean ± SD or number (percent).

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Table 2. Perceived Stress Level, Anxiety, Depression, Sleep Quality, and Insomnia Data of the Patient and Control Groups

Variable	Patients (n:160)	Controls (n:51)	P
PSS score	23.64 ± 7.86	19.73 ± 4.80	.001
HADS-D score	5.60 ± 3.40	4.08 ± 2.21	.003
HADS-A score	6.40 ± 2.87	5.67 ± 2.22	.096
PSQI score	6.31 ± 3.62	4.43 ± 2.20	.001
ISI score	6.81 ± 4.98	4.53 ± 2.83	.002
High perceived stress level, n (%)	59 (36.9)	6 (11.8)	.001
Presence of depression, n (%)	45 (28.1)	2 (3.9)	<.001
Presence of anxiety, n (%)	16 (10.0)	2 (3.9)	.252
Poor sleep quality, n (%)	77 (48.1)	16 (31.4)	.051
Insomnia, n (%)	62 (38.8)	10 (19.6)	.017

Data presented as mean ± SD or number (percent).HADS-A, Hospital Anxiety and Depression Scale-Anxiety; HADS-D, Hospital Anxiety and Depression Scale-Depression; ISI, Insomnia Severity Index; PSS, Perceived Stress Scale; PSQI, Pittsburg Sleep Quality Index.

PSS group, laboratory data were similar before and during the pandemic. However, in the low PSS group, pre-pandemic sedimentation rates (26.68 ± 14.86 vs. 22.20 ± 14.03 mm/hr; P < .001) were significantly higher, while albumin

Table 3. Comparison of Baseline Characteristics and Clinical Data of SLE Patients According to Perceived Stress Scale (PSS)

Variable	High PSS (n:59)	Low PSS (n:101)	P
Age, years	41.14 ± 12.45	43.07 ± 13.83	.379
Body mass index, kg/m^2	25.79 ± 5.05	25.32 ± 4.37	.536
Female gender, n (%)	52 (88.1%)	90 (89.1%)	1.000
Smoking, n (%)	6 (10.2%)	14 (13.9%)	.623
Alcohol, n (%)	0 (0%)	2 (2%)	.532
Marital status, maried, n (%)	54 (91.5%)	81 (80.2%)	.071
Socioeconomic status (low), n (%)	23 (39.0%)	31 (30.7%)	.303
History of COVID19, n (%)	16 (27.1%)	15 (14.9%)	.065
Hospitalization due to COVID-19, n (%)	5 (8.5%)	2 (2%)	.102
Disease duration, years	10.02 ± 6.08	10.51 ± 7.66	.676
HADS-D score	8.32 ± 3.05	4.01 ± 2.45	<.001
HADS-A score	8.27 ± 2.52	5.31 ± 2.48	<.001
PSQI score	8.27 ± 3.82	5.17 ± 2.96	<.001
ISI score	9.88 ± 4.93	5.01 ± 4.06	<.001
MARS-5 score	22.80 ± 2.42	22.90 ± 2.11	.772
Presence of depression, n (%)	37 (62.7%)	8 (7.9%)	<.001
Presence of anxiety, n (%)	12 (20.3%)	4 (4.0%)	.001
Poor sleep quality, n (%)	45 (76.3%)	32 (31.7%)	<.001
Insomnia, n (%)	41 (69.5%)	21 (20.8%)	<.001
Drug non-adherence, n (%)	29 (49.2%)	50 (49.5%)	1.000

Data presented as mean ± SD or number (percent)HADS-A: Hospital Anxiety and Depression Scale-Anxiety; HADS-D,: Hospital Anxiety and Depression Scale-Depression; ISI, Insomnia Severity Index; MARS-5, Medication Adherence Reporting Scale-5; PSS, Perceived Stress Scale; PSQI, Pittsburg Sleep Quality Index.

values (4.05 ± 0.51 vs. 4.18 ± 0.45 g/dL; P = .001) were lower (Table 5).

Discussion
This study demonstrated that SLE patients experienced higher levels of perceived stress, depression, and insomnia compared to the healthy population during the COVID-19 pandemic. Furthermore, SLE patients with higher levels of perceived stress were found to have more depression, anxiety, insomnia, and poor sleep quality, and a higher perceived stress level was associated with anxiety and depression.

In the current study, an increased perceived stress level was present in 36.9% of SLE patients. Several studies have investigated the prevalence of psychological problems in patients with rheumatological diseases during the pandemic. Patients with rheumatoid arthritis and ankylosing spondylitis were shown to exhibit a worse psychological state during the pandemic compared to the healthy population.[24] Santos-Ruiz et al[25] showed in a study comprising 428 SLE patients that depression and stress levels were higher during quarantine compared to the pre-pandemic era. In another study conducted during the pandemic with 405 SLE and 107 rheumatoid arthritis patients, the authors found that 12.3% of the patients had moderate-to-severe stress symptoms, 38.7% had moderate-to-severe anxiety, and 27.7% had moderate to severe depression.[26] Our findings are in accordance with the literature mentioned above, and the different rates reported in various studies are probably due to the use of different scales in the evaluation of symptoms.

In our study, SLE patients had increased rates of depression and insomnia compared to the healthy population. However, there was no difference between the 2 groups in terms of increased anxiety and poor sleep quality. Poor sleep quality was 48.1% in SLE patients and 31.4% in healthy patients, with a difference that did not reach statistical significance between the 2 groups. This can be explained by a balanced increase in poor sleep quality in both groups after the pandemic or by the insignificance of the difference between the groups due to the insufficient number of patients. Compared to the healthy population, people with SLE have a 7-fold increase in depression, 2.5-fold increase in anxiety, 1.5-fold increase in poor sleep quality, 1.9-fold increase in insomnia, and 3-fold increase in perceived stress in our cohort. In the current study, 28.1% of SLE patients had depression, while 10%

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Table 4. Parameters Associated with High Perceived Stress Level in Multivariate Regression Analysis

	Exp(β)	95% CI	P
Age	1.009	0.973-1.045	.640
Gender	1.236	0.300-5.096	.769
HADS-D	1.484	1.242-1.775	<.001
HADS-A	1.241	1.029-1.497	.024
PSQI	0.900	0.674-1.202	.477
ISI	1.215	0.974-1.518	.085

HADS-A, Hospital Anxiety and Depression Scale-Anxiety, HADS-D: Hospital Anxiety and Depression Scale-Depression; ISI, Insomnia Severity Index; PSQI, Pittsburg Sleep Quality Index.

had anxiety. In a meta-analysis conducted by Moustafa et al[27] in the pre-pandemic period, 69 studies involving 23 386 SLE patients were evaluated, and the rate of depression was found to be in the range of 8.7%-78.6%, and in 38 studies involving 4439 SLE patients, the anxiety rate was in the range of 1.1%-71.4%, depending on the scales used. In the same meta-analysis, the prevalence of depression was 24.4% in 14 studies involving 1238 SLE patients using the HADS-D scale, while the prevalence of anxiety was reported as 38.3% in 12 studies involving 1099 patients using the HADS-A scale.[27] In these studies, the cut-off point for anxiety and depression was taken as 8. The cut-off point of the HADS-D and HADS-A scales used in our study was 10 for anxiety. The prevalence of depression found in our study is in accordance with previous literature. Since different studies use different scales to evaluate patients and furthermore, SLE comprises a heterogeneous patient population, it is completely plausible to see different results reported in various studies. In addition, the majority of studies were conducted before the pandemic, while our study was carried out strictly during the quarantine period during the pandemic. Therefore, it may not be accurate to compare our results with those from other studies. We also found that 48.1% of patients had poor sleep quality, while 38.8% had insomnia. In a meta-analysis conducted in 2021, the sleep quality of SLE patients was found to be worse than the general population, which is consistent with our results.[8]

Patients were further divided into 2 groups as those with high and low perceived stress levels and patients with high perceived stress levels had more depression, anxiety, poor sleep quality and insomnia. We also showed that high perceived stress was associated with HADS-A and HADS-D scores, indicating anxiety and depression. In light of these data, the perceived stress level in the SLE patient group may not be a simple disorder; on the contrary, it may cause or worsen more serious problems affecting patient endpoints such as anxiety and depression. There are other studies in the literature conducted during the pandemic period that support our findings. In a study conducted with 1045 healthcare professionals in China during the pandemic period, HADS-A, HADS-D, and PSS scales were used, and a positive correlation was found between anxiety, depression, insomnia, and stress levels.[28] In another study conducted with 106 kidney transplant patients during the pandemic period, HADS-A, HADS-D, PSS, PSQI, and ISI scales were used, and an increase in anxiety, depression, insomnia, and poor sleep quality was found in patients with high perceived stress.[29] On the other hand, according to our data, lupus patients had a lower socioeconomic status than controls. The low socioeconomic status might affect the questionnaire. The association between low socioeconomic status and anxiety, depression, perceived stress level, and sleep disorders is well known.[30,31] However, when we compared patients according to perceived stress levels, the socioeconomic status was similar between the high and low perceived stress level groups (39.0% vs. 30.7%, P = .303).

Medication non-adherence is a serious problem in patients with chronic conditions, especially in SLE patients. We observed that 49.4% of the patients were non-adherent to medications. However, there was no correlation between non-adherence and increased perceived stress levels. In the literature, non-compliance rates in SLE patients have been reported in a wide range from 3% to 76% in different series.[10] The majority of studies report non-adherence in about half of the patients, which is in parallel with our findings.

Table 5. Laboratory Data of High PSS and Low PSS Groups Before and During the Pandemic

Laboratory Variables	High PSS (n:59)			Low PSS (n:101)		
	Before Pandemic	During Pandemic	P	Before Pandemic	During Pandemic	P
BUN (mg/dL)	16.34 ± 10.23	16.17 ± 9.90	.822	15.77 ± 7.86	15.68 ± 8.89	.862
Creatinine (mg/dL)	0.91 ± 1.08	0.89 ± 0.85	.785	0.84 ± 0.65	0.82 ± 0.56	.268
GFR (mL/min/1.73 m^2)	113.41 ± 50.08	108.45 ± 45.23	.236	102.48 ± 36.75	103.09 ± 33.82	.695
CRP (mg/L)	7.70 ± 9.66	7.84 ± 11.69	.925	5.17 ± 7.61	4.46 ± 6.22	.272
Sedimentation rate (mm/hour)	30.78 ± 18.01	27.54 ± 19.11	.075	26.68 ± 14.86	22.20 ± 14.03	<.001
Hemoglobin (g/dL)	11.89 ± 1.69	11.73 ± 2.11	.199	12.28 ± 1.66	12.22 ± 1.73	.541
Leukocyte(10^3/μL)	6794.75 ± 2396.60	8408.47 ± 13817.04	.366	5893.66 ± 1985.21	6698.61 ± 10633.32	.432
Platelet (10^3/μL)	261 ± 116	276 ± 135	.136	241 ± 797	279 ± 282	.179
Albumin (g/dL)	3.97 ± 0.62	4.02 ± 0.62	.389	4.05 ± 0.51	4.18 ± 0.45	.001
24-h urine proteinuria (g/day)	0.55 ± 1.16	0.39 ± 0.55	.796	0.50 ± 1.01	0.47 ± 0.90	.493

Data presented as mean ± SDBUN, blood urea nitrogen; CRP, C-reactive protein; PSS, Perceived Stress Scale.

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During the quarantine period, 42.5% of the patients who participated in our study stated that they had difficulty reaching the hospital and getting their prescriptions. Similarly, in a study involving 1040 SLE patients in India during the pandemic period, it was reported that approximately 54% of patients missed their planned follow-up visits and 37% could not have their examinations done due to the closure of laboratories and hospitals.[32] We also investigated the effect of this period on laboratory values. However, interestingly, no difference was detected between the pre- and post-pandemic periods, except for sedimentation rates and albumin values. Although the change in sedimentation rates and albumin values showed statistical significance, the numerical differences were not clinically relevant. Laboratory values before and after the pandemic were also similar in patients with high levels of perceived stress.

There were certain limitations in our study. It was primarily a cross-sectional and single-center study. The study was also conducted only during the first phase of the pandemic when a quarantine order was in place. Therefore, it may not be possible to make an accurate comparison with data from other studies conducted before or during different time points throughout the pandemic. Overall, there is a clear difference between SLE patients and controls regarding perceived stress, depression, poor sleep quality and insomnia during the COVID-19 pandemic. However, whether these differences are solely due to pure social isolation or other factors such as fear of exposure to infection, lack of access to medical care, economic hardship, lack of available resources, or diminished personal freedom is uncertain. Moreover, disease activity based on Systemic Lupus Erythematosus Disease Activity Index (SLEDAI), disease damage based on Systemic Lupus International Collaborating Clinics-Damage Index (SLICC-DI), and medications (including polypharmacy) were not taken into account when interpreting stress and depression. In addition, the number of participants is relatively small, and a re-evaluation with more comprehensive and multi-center studies will better reflect the impact of the quarantine and the pandemic on the psychological well-being of SLE patients.

In conclusion, SLE patients demonstrated increased levels of perceived stress, depression, poor sleep quality and insomnia compared to the healthy population during the quarantine period of the COVID-19 pandemic. SLE patients with high perceived stress had more depression, anxiety, poor sleep quality and insomnia than those without. Furthermore, high perceived stress was associated with depression and anxiety. It needs to be determined whether these findings will have an impact on patient outcomes during long-term follow-up. In order to obtain more comprehensive results, multi-center studies with a larger number of participants are needed.

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