Factors Associated with Sleep Disturbances in SLE Patients: A Descriptive Cross-Sectional Study

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ABSTRACT
Background: Systemic lupus erythematosus (SLE), a diverse autoimmune inflammatory condition, affects various organs and systems. Determining the origin of sleep disturbances in systemic lupus erythematosus patients is essential to create specific and focused measures to enhance sleep quality.
Objective: This study aimed to evaluate the sleep quality of a group of patients with systemic lupus erythematosus and investigate the correlation between sleep quality and disease activity, severity, and different disease parameters.
Patients and methods: The present cross-sectional study included 73 systemic lupus erythematosus patients. Disease activity was assessed by means of the Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K). SLE severity was assessed by the SLICC/ACR damage index. Life quality was assessed by the short form quality of life (SF-36 QoL) scale. Assessment of sleep disturbances was conducted using the Pittsburgh Sleep Quality Index (PSQI).
Results: Patients with lower PSQI (21) scores showed significantly higher SLEDAI scores, indicating a more active disease compared to those with higher scores (p=0.001). Lower scores were associated with significantly greater SLICCs scores, indicating a more severe disease state (p=0.008). Patients with good PSQI 21 scores had slightly higher SF36 scores (mean=60.58) than those with poor scores (mean=54.11), nevertheless, the disparity did not exhibit statistical significance (p=0.071). **Conclusion:** Systemic lupus erythematosus patients often suffer from poor sleep quality. Disease features and sleep variables impact sleep quality. Poor sleep may negatively impact systemic lupus erythematosus patients' disease activity, damage, as well as well-being.
Keywords: Systemic lupus erythematosus, Sleep disturbances, PSQI 21.

INTRODUCTION

SLE is a health issue characterised by an abnormal immune response that targets multiple organ systems. The disease displays a diverse array of observable characteristics, with clinical manifestations ranging from mild symptoms affecting the skin and mucous membranes to severe impairment of multiple organs and the central nervous system. The course is marked by repetitive occurrences of relapse and remission [1].

Notwithstanding recent progress in knowledge of the clinical basis and risk factors linked to SLE, the precise cause of the disease remains unknown. SLE can be difficult to diagnose, and despite the fact that numerous classification criteria have been proposed, their clinical utility remains debatable. Involvement of organ systems dictates SLE management. Although, numerous medications have exhibited efficacy in the treatment of SLE, the condition remains a substantial contributor to morbidity and mortality among individuals with SLE [2].

The persistent and intense nature of SLE, along with its underlying physiological processes, are associated with a heightened susceptibility to psychiatric and neurological complications, including mood disorders, anxiety disorders, and sleep disruptions. Sleep is a dynamic and intricate state marked by significant physiological alterations in body temperature, muscle tone, the endocrine system, gastrointestinal physiology and cardiovascular functions [3]. A 2020 meta-analysis revealed that the sleep quality of patients with SLE is inferior to that of

the general populace [4]. Between 56.0% and 80.5% of individuals diagnosed with SLE experienced sleep disturbances together with decline in sleep quality. Prior research has indicated that sleep disruptions can exacerbate cardiovascular morbidity in individuals with SLE [5].

Sleeplessness worsens disease activity. Thus, detecting the causes of poor sleep in SLE patients is essential for targeted interventions towards improving sleep quality. Sleep disorders have unknown causes [6]. Psychological/social factors, especially depression, are the most common causes of SLE sleep disorders. It is worth to mention that depression affects 35.0% of SLE patients [7].

Some studies linked sleep disturbances to SLE disease activity, pain, and steroid use. Notably, sleep disruptions symptoms like pain and fatigue overlay with constitutional inflammatory symptoms of SLE and may resemble disease-related relapse [8].

The objective of this study was to assess the sleep quality of a cohort of patients with systemic lupus erythematosus and to examine the relationship between sleep quality and disease activity, severity, and various disease parameters in these patients.

PATIENTS AND METHODS

This descriptive cross-sectional study included 73 patients diagnosed with SLE. They were enrolled from Inpatient and Outpatient settings at the Rheumatology, Rehabilitation, and Physical Medicine Department of Benha University Hospitals, Egypt. The recruitment period spanned from June 2022 to June 2023.

Inclusion criteria: Patients with SLE who met EULAR/ACR diagnostic criteria 2019 [9]. Age over 16 years of both genders.

Exclusion criteria: Other disorders of connective tissue. Patients with documented cognitive impairments. Morbid obesity. Systemic conditions such as respiratory and cardiovascular diseases. Thyroid dysfunction. Patients administered medications that may disrupt sleep, such as analgesics, hypnotics, antidepressants, and muscle relaxants.

Patients' clinical profile:

Each patient underwent a thorough clinical evaluation and meticulous documentation of their medical history. The evaluation of disease activity in SLE was conducted by means of the Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI- 2K). The activity was categorized into five levels: no activity (SLEDAI = 0), mild (score: 0-10), moderate (score: 11-20), severe (score: 21-45), and very severe (score > 45) [10]. The severity of SLE disease was assessed by means of the SLICC/ACR damage index (SDI), which quantifies the cumulative damage to the organs caused by SLE [11]. Life quality was evaluated utilizing the SF-36 QoL (short form quality of life) scale [12]. The evaluation of sleep disturbances was conducted by the Pittsburgh Sleep Quality Index (PSQI). The questionnaire comprises 19 self-reported issues, each of which falls into one out of seven sections: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication, and daytime dysfunction [13].

Ethical consideration:

Written informed consent was gained from each subject. The research study received approval from The Ethical Board of the Faculty of Medicine, Benha University (No. MS6-5-2022). The Helsinki Declaration was followed throughout the study's conduct.

Statistical analysis

IBM Corp. Released 2017's Statistical package for Social Science was employed for revision, coding, and tabulation [IBM SPSS Statistics for Windows 25.0 (Armonk, NY: IBM Corp.)]. For descriptive statistics, Mean ± SD, median, and range were used in case of numerical data. Non-numerical data were analyzed using frequency and percentage. Student T-Test determined study group mean differences' significance. The Mann-Whitney Test (U-test) determined the statistical significance of a non-parametric data. Kruskall Wallis tested nonparametric variable differences between study groups for statistical significance. Two qualitative variables were compared by a Chi-Square test. Qualitative variables with an expected count of less than 5 in over 20% of cells were analyzed using the Fisher Exact or Monte Carlo test. A p-value ≤ 0.05 with 95% confidence interval was considered significant.

RESULTS

Table (1) showed demographic and anthropometric data for the 73 SLE patients in the study. Patients were mostly females (87.7%). The mean patient age was 29.70 ± 11.0 years. The median age was 27.0, ranging from 17.0 to 58.0. The mean BMI was 23.78 kg/m^2, ranging from 19 to 33. Disease duration was 4.51 ± 6.11 years. The median disease duration was 2.0 years, ranging from 0.17 to 35. The majority of the 73 patients (50.7%) had severe disease activity, with mild (13.7%), moderate (34.2%), and very severe (1.4%). The median SLEDAI score was 21.0 (range: 3.0–47.0), with a mean of 21.32 ± 5.20. The mean SLICCs score was 1.68 ± 0.41, with a median of 1.0 (range: 0.0 to 14.0). The average score on the SF36 100 was 57.48 ± 14.10, with a median of 59.0 (range: 10.0 - 79.0). The PSQI 21 score ranged from 1.0 to 12.0, with a median of 4.0 and a mean of 5.08 ± 1.12.

Table (1): Demographic, anthropometric and disease characteristics of the studied SLE patients

	SLE patients N = 73	
	No.	**%**
Sex		
Male	9	12.3
Female	64	87.7
Age (years)		
Mean ± SD.	29.70 ± 11.0	
Median (Min. – Max.)	27.0 (17.0 – 58.0)	
BMI		
Mean ± SD.	23.78 ± 3.06	
Median (Min. – Max.)	23 (19-33)	
Disease duration (years)		
Mean ± SD.	4.51 ± 6.11	
Median (Min. – Max.)	2.0 (0.17 – 35.0)	
SLEDAI		
Mild	10	13.7
Moderate	25	34.2
Severe	37	50.7
Very severe	1	1.4
Mean ± SD.	21.32 ± 5.20	
SLICCs		
Mean ± SD.	1.68 ± 0.41	
SF36 100		
Mean ± SD.	57.48 ± 14.10	
PSQI 21		
Mean ± SD.	5.08 ± 1.12	

SD.: Standard deviation, Min.: Minimum, Max.: Maximum

As shown in figure (1), 52.1% of SLE patients reported good sleep quality (PSQI 21), whereas 47.9% reported poor sleep quality.

Percentage of PSQI 21

47.9

52.1

■ Good ■ Poor
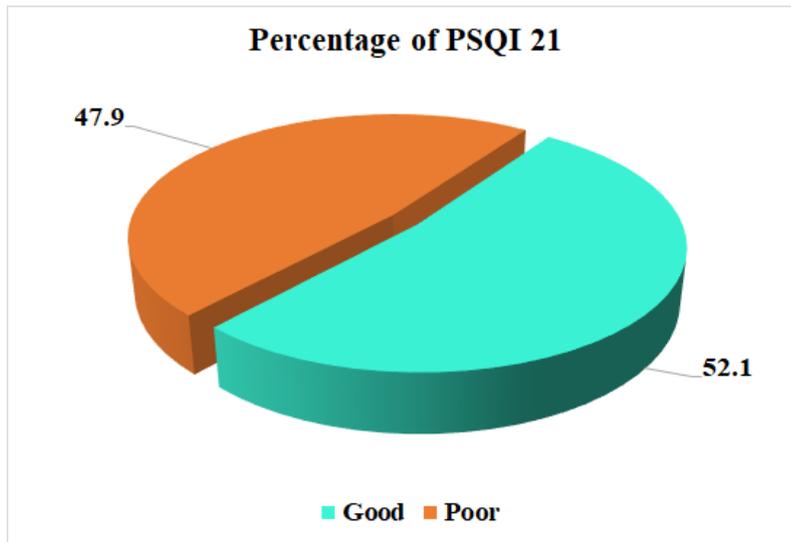
Figure (1): Pie chart for PSQI 21 among SLE patients.

There were statistically insignificant differences in average PSQI 21 scores based on the presence or absence of fever, rash, oral ulcer, alopecia, arthralgia, arthritis, nephritis, cardiac symptoms, respiratory symptoms, gastrointestinal symptoms and psychosis or seizures (p>0.05). Nonetheless, when seizures or headaches were present, the average PSQI 21 scores increased significantly (p=0.021 or p=0.001, respectively) (Table 2).

Table (2): Relation between PSQI 21 and clinical data

		PSQI 21			Test	P-value
		Mean ± SD.	Median	Min. – Max.		
Fever	No, n=31	4.71 ± 1.90	4.0	2.0 – 9.0	U= 729.5	0.375
	Yes, n=42	5.36 ± 2.57	5.0	1.0 – 12.0		
Rash	No, n=8	4.25 ± 1.16	4.0	3.0 – 6.0	U= 313.0	0.343
	Yes, n=65	5.18 ± 2.41	5.0	1.0 – 12.0		
Oral ulcer	No, n=11	5.18 ± 2.23	6.0	1.0 – 9.0	U= 317.0	0.708
	Yes, n=62	5.06 ± 2.35	4.0	2.0 – 12.0		
Alopecia	No, n=10	4.60 ± 1.78	4.50	1.0 – 7.0	U= 340.0	0.684
	Yes, n=63	5.16 ± 2.40	4.0	2.0 – 12.0		
Arthralgia	No, n=5	5.20 ± 2.49	5.0	3.0 – 9.0	U= 168.0	0.975
	Yes, n=68	5.07 ± 2.33	4.0	1.0 – 12.0		
Arthritis	No, n=40	4.83 ± 2.12	4.0	1.0 – 9.0	U= 734.5	0.403
	Yes, n=33	5.39 ± 2.54	6.0	2.0 – 12.0		
Nephritis	No, n=30	4.57 ± 2.01	4.0	2.0 – 9.0	U= 785.0	0.112
	Yes, n=43	5.44 ± 2.47	5.0	1.0 – 12.0		
Cardiac	No, n=58	4.78 ± 1.99	4.0	2.0 – 9.0	U= 564.0	0.074
	Yes, n=15	6.27 ± 3.10	7.0	1.0 – 12.0		
Respiratory	No, n=36	4.56 ± 1.80	4.0	2.0 – 9.0	U= 811.5	0.104
	Yes, n=37	5.59 ± 2.66	6.0	1.0 – 12.0		
GIT	No, n=72	5.10 ± 2.33	4.0	1.0 – 12.0	–	–
	Yes, n=1		4.0			
Psychosis	No, n=72	5.07 ± 2.33	4.0	1.0 – 12.0	–	–
	Yes, n=1		6.0			
Seizures	No, n=66	4.86 ± 2.23	4.0	1.0 – 12.0	U= 353.0*	0.021*
	Yes, n=7	7.14 ± 2.27	8.0	3.0 – 9.0		
Headache	No, n=45	4.36 ± 1.94	4.0	1.0 – 9.0	U= 912.0*	0.001*
	Yes, n=28	6.25 ± 2.43	6.0	2.0 – 12.0		

SD.: Standard deviation, Min.: Minimum, Max.: Maximum. U: Mann Whitney test.   P: Comparing between different categories. *: Significant when p value <0.05

Table (3) displayed the correlation between the PSQI score and different parameters among patients with SLE. Out of the parameters examined, only the protein level in the 24-hour urine (r = 0.241, p = 0.040), SLEDAI score (r = 0.416, p < 0.001), and SLICC score (r = 0.359, p = 0.002) exhibited significant positive associations with the PSQI score. The PSQI score exhibited significant negative correlations with albumin (r = -0.250, p = 0.033) and SF-36 score (r = -0.345, p = 0.003).

Table (3): Correlation between PSQI 21 and different parameters among SLE patients

	PSQI 21	
	Correlation coefficient	P-value
Age (years)	0.020	0.864
BMI (kg/m²)	0.233	0.058
Duration	0.198	0.093
WBC (mcL)	-0.054	0.648
Hb (g/dL)	0.084	0.481
Platelets (mcL)	0.006	0.962
ESR (mm/hr)	0.201	0.088
CRP (mg/L)	-0.034	0.775
Creatinine (mg/dl)	0.049	0.680
Urea (mg/dL)	0.033	0.785
Albumin (g/L)	-0.250*	0.033*
AST (U/L)	0.148	0.211
ALT (U/L)	0.212	0.071
C3	-0.230	0.051
C4	-0.086	0.471
Protein in 24h urine	0.241*	0.040*
SLEDAI	0.416*	<0.001*
SLICCs	0.359*	0.002*
SF36 100	-0.345*	0.003*

r: Spearman's rho. *: Significant when p value <0.05.

Table (4) examines the correlation between PSQI 21 scores and the activity, severity, and quality of life of SLE patients. Patients who obtained low PSQI 21 scores exhibited elevated SLEDAI scores, suggesting a greater activity of disease in contrast to those with high scores (p=0.001).

Patients with lower scores exhibited higher SLICCs scores indicating a more severe disease state, in comparison with patients with higher scores (p=0.008). Patients who obtained good PSQI 21 scores exhibited marginally higher SF36 scores (mean=60.58) in comparison with those with poor scores (mean=54.11), however the difference was not statistically significant (p=0.071).

Table (4): Comparison of good and poor sleep quality patients based on SLE disease activity, severity and quality of life.

	PSQI 21				Test	P-value
	Good (PSQI>5) N = 38		Poor (PSQI<5) N = 35			
	No.	%	No.	%		
SLEDAI						
Mild	6	15.8	4	11.4	X²= 5.735	MC 0.084
Moderate	17	44.7	8	22.9		
Severe	15	39.5	22	62.9		
Very severe	0	0.0	1	2.9		
Median	17.0		29.0		U= 960.5*	0.001*
Min. – Max.	8.0 – 33.0		3.0 – 47.0			
SLICCs						
Median	0.0		1.0		U= 894.5*	0.008*
Min. – Max.	0.0 – 14.0		0.0 – 10.0			
SF36 100						
Mean ± SD.	60.58 ± 13.64		54.11 ± 16.46		t= 1.833	0.071
Median	62.0		54.0			
Min. – Max.	10.0 – 79.0		12.0 – 78.0			

Median and Min. – Max: Non-parametric test. SD.: Standard deviation, Min.: Minimum, Max.: Maximum, U: Mann Whiteny test. X²: Chi–Square, MC: Monte Carlo, p: Comparing good and poor PSQI 21. *: Significant when p value <0.05.

The linear regression analysis was conducted to identify predictive factors for sleep quality in the SLE patients under study. In the univariate analysis, many factors were examined separately to determine their relationship with sleep quality. Cardiac affection, seizures, headache, higher SLEDAI, SLICCs, and a lower SF36 100 were associated with higher sleep quality scores and were more probable to possess poor sleep quality.

Other factors, such as gender, age, BMI, duration of SLE, ESR, CRP, C3, C4, pyuria, casts, protein in 24-hour urine, fever, rash, oral ulcer, alopecia, arthralgia, arthritis, nephritis, and respiratory symptoms, did not reach statistical significance.

In the multivariate analysis, significant factors were considered concurrently to determine their independent association with sleep quality while controlling for other variables. Among these factors, higher SLEDAI, SLICCs, and lower SF36 100 were found to be significant predictors of poor sleep quality.

Table (5): Linear regression analysis for predictive factors of sleep quality in the studied SLE patients

	Univariate		Multivariate	
	β	P	β	P
Gender	0.347	0.677		
Age	0.007	0.770		
BMI	0.172	0.053		
Duration	0.039	0.384		
ESR	0.103	0.119		
CRP	-0.014	0.214		
C3	-0.017	0.076		
C4	-0.017	0.575		
Pyuria	-0.232	0.674		
Hematuria	1.210	0.088		
Casts	0.160	0.848		
Protein in 24h urine	0.181	0.119		
Fever	0.647	0.241		
Rash	0.935	0.285		
Oral ulcer	-0.117	0.878		
Alopecia	0.559	0.483		
Arthralgia	-0.126	0.907		
Arthritis	0.569	0.300		
Nephritis	0.875	0.113		
Cardiac	1.491	0.025*	0.020	0.977
Respiratory	1.039	0.055		
Seizures	2.279	0.012*	0.813	0.374
Headache	1.894	<0.001*	0.816	0.236
SLEDAI	0.115	<0.001*	0.042	0.032*
SLICCs	0.343	0.002*	0.082	0.045*
SF36 100	-0.061	<0.001*	-0.026	0.029*

B, regression coefficient. *: Significant when p value <0.05

DISCUSSION

SLE, a diverse autoimmune inflammatory condition, affects various organs and systems. Low immune tolerance to autoantigens along with aberrant activation of pathogenic autoantibodies cause immune complexes to form in the blood or tissues. The worldwide prevalence of SLE varies. Globally, 20–240/100,000 people have SLE [14].

Sleep disruptions are prevalent in SLE patients, with 56–80% prevalence. In China, **Makimoto et al.** [4] found more sleep disorders in SLE patients than in other chronic disease patients. Chronic diseases are more common in people who suffer from sleep disorders, like SLE and cardiovascular disease in people of all ages.

This study revealed that 47.9% of the patients with SLE exhibited substandard quality of sleep, based on the Pittsburgh Sleep Quality Index (PSQI 21), whereas 52.1% demonstrated satisfactory sleep quality. The average PSQI 21 score was 5.08 ± 2.32, with a middle value of 4.0 (range: 1.0 - 12.0).

The research performed by **Mesquita et al.** [15] documented the presence of sleep disruptions in critically ill patients with SLE. The average global PSQI score was 7.8 ± 3.9, and 20 patients (66.7%) were diagnosed with poor-quality sleep (PSQI > 6). In

their study, **Mirbagher et al.** [16] discovered that the PSQI total score for patients with SLE was 7.0 ± 4.6 (ranging from 1 to 19). Out of the total number of patients, 44 individuals (57.1%) were categorised as 'poor sleepers' based on the global PSQI score of 6 or higher. Patients with SLE exhibit markedly elevated scores in global sleep quality (P < 0.001), as well as in the domains of sleep efficiency (P = 0.006), sleep period (P = 0.006) and sleep disturbance (P < 0.001), as well as reliance on sleep medications (P < 0.001).

In their study, **Kasitanon et al.** [17] discovered that the average total PSQI score was 7.86 ± 5.42. Out of the 56 patients, 31 of them (55.36%) were categorized as inadequate sleepers, alongside a total score of 6. The majority of prior studies assessed the quality of sleep in patients with SLE utilizing the Pittsburgh Sleep Quality Index (PSQI). The PSQI ratings of 7.74 3.21 and 7.25 4.63, as stated by **Magro et al.** [18] and **Cheng et al.** [19], were consistent with the results seen in these investigations. A higher PSQI score of 10.71 ± 3.68 was reported by **Li et al.** [20]. Nevertheless, all of these studies consistently demonstrated that patients with SLE generally experienced subpar sleep quality. The disparity in mean PSQI score, as well as the percentage of good and poor sleepers, may be attributed to the comparatively limited sample size and differences in disease status and features of our SLE patients.

In our study, we found no significant relationship between disease duration and sleep quality. This is consistent with **Kasitanon et al.** [17], who observed that there was no difference in the occurrence of poor sleepers among patients with a disease duration of less than or equal to three years and more than three years in 15 (53.3%) vs. 23 in 41 (56.1%) patients, p >1.00). On the other hand, **Rady et al.** [21] found that sleep disruptions were significantly linked with disease duration. **Palma and Tufik** [22] carried out a comparable study on lupus-ridden mice. They found that sleep disturbance in the affected group increased with the progression of the disease.

In this study, we elucidated that patients with poor PSQI 21 scores had higher SLEDAI scores indicating more severe disease activity, than those with good scores (p=0.001). Patients with poor scores had higher SLICCs scores than those with good scores (p=0.008). This is parallel to many previous studies [15, 23, 24, 25].

Additionally, these findings align with the research conducted by **Chandrasekhara et al.** [26], which proposed that the primary factor participating in sleep disturbances in SLE patients is the activity of the disease itself. This may be partially due to the decreased levels of physical activity observed in these patients. Furthermore, it has been found that atypical periodic limb movements are highly widespread in SLE, with specific research demonstrating a threefold higher occurrence of "restless leg syndrome" [26].

Regarding the quality of life, our findings indicated that patients with favorable PSQI 21 scores exhibited slightly higher SF36 scores (mean=60.58) in comparison with those with unfavorable scores (mean=54.11). However, it is important to note that this difference did not achieve statistical significance (p=0.071). In a study carried out by **Baba** *et al.* [27], it was discovered that there was a strong negative correlation between the quality of life and PSQI scores (r: −0.66, p: 0.001) in patients diagnosed with SLE.

LIMITATION

This study had some limitations. The first was that SLE patients were gathered from a single rheumatology center as a result, it is not possible to draw broad conclusions from this study. Secondly, we did not specifically examine sleep disorders, instead we relied on a self-reported measure of sleep quality. Therefore, more studies with objective sleep measures are needed. Thirdly, we cannot determine whether variables are causally related because our study was cross-sectional. So, to find out what needs changing to make sleep better for SLE patients, prospective studies are needed. Finally, our sample size was small; given the numerous potential factors to sleep quality, larger patient samples are needed for more precise analyses.

CONCLUSION

Patients with SLE typically experienced subpar sleep quality. Both disease features and sleep variables can have an impact on the quality of sleep. In individuals with systemic lupus erythematosus, inadequate sleep can have a negative effects on disease activity, damage, and overall well-being.

ABBREVIATIONS

- **BMI:** Body mass index. **CRP:** C reactive protein **ESR:** Erythrocytes sedimentation rate.
- **PSQI 21:** Pittsburgh Sleep Quality Index.
- **SF-36:** Short form quality of life 36.
  SLE: Systemic lupus erythematosus.
- **SLEDAI:** Systemic lupus erythematosus disease activity index.
- **SLICCs:** Systemic lupus erythematosus international collaborating clinics damage index.

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