Association Between Systemic Lupus Disease Activity and Sleep Quality among Sample of Females with or without Depression at Baghdad Teaching Hospital

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Abstract

Systemic Lupus Erythematosus (SLE) is an autoimmune connective tissue disease with heterogeneous clinical manifestations that may involve many different organ systems. Sleep quality is a complex phenomenon associated with subjective estimates of the ease of sleep onset, sleep maintenance, total sleep time, and early awakening. Depression is a state of low mood and aversion to activity that affects persons' emotions, thoughts, behaviors, and sense of well-being. To evaluate sleep quality in SLE female patients with or without depression. To determine the effect of lupus disease activity and lupus duration on sleep quality. A cross-sectional study was conducted at Baghdad Teaching Hospital, Rheumatology Unit during the period from January to October 2018. The study Included 61 females with SLE who met the inclusion criteria. Data were collected using a pre-constructed data collection sheet. Questionnaires included demographic and clinical data of the patients. SLE was diagnosed after fulfilling the ACR revised criteria and SLICC criteria. Sleep quality was evaluated by the Pittsburgh Sleep Quality Index (PSQI) score. Depression was evaluated by DSM-5 criteria.The mean age of SLE female patients was 33.6±10.2. Poor sleep quality was reported in 59% of patients. Depression was reported in 42.6% of patients. There was a direct significant correlation between SLEDAI and each of the PSQI scores and DSM-5 criteria. Higher body mass index was significantly associated with higher SLEDAI. Longer duration of SLE was significantly associated with higher PSQI. While other variables showed no significant association with SLEDAI, PSQI, and DSM-5. Higher scores of the SLE disease activity index was associated with poor sleep quality and depressive symptoms.

Keywords: SLE; Autoimmune diseases; Sleep disorder; Depression; Baghdad

Introduction

The Systemic lupus erythematosus (SLE) is a multisystem autoimmune connective tissue disease that is associated with the production of a variety of autoantibodies directed against native DNA and other cellular constituents [1]. It is a prototypic disease with heterogeneous clinical manifestations that may involve many different organ systems [2]. The systems commonly involved include skin, joints and muscle, brain and peripheral nervous system, lungs, heart, kidneys, gastrointestinal tract, serous membranes, and components of the blood [3]. Prevalence rates of SLE vary widely in the literature. Reported prevalence frequencies worldwide range from 20-240 per 100,000 persons, Caucasian and African American patients, reported prevalence of 72.1-74.4 per 100,000 persons, African American women had the highest rates [4]. Iraqi patients reported prevalence of 53.6 per 100,000 persons and higher rates for women with 88.7 per 100,000 persons [5,6]. Ninety percent of patients are women of reproductive age [7]. The female: male ratio is approximately 6–10:1, while in both children and elderly patients, the female: male ratio is approximately 2-3:1 [8]. Interactions between susceptible genes and environmental factors result in abnormal immune responses which vary between individuals. Those responses may include: Abnormal activation of innate immunity (dendritic cells, monocyte and macrophages) and adaptive immunity cells (T and B lymphocytes) [9], and ineffective regulatory CD4+ and CD8+T cells and B cells can be attributed to inappropriate clearance of immune complexes and apoptotic cells [10]. Sleep is first and foremost a behavior, which is characterized by changes in body posture and eye state, which is dimensionally evaluated by self-report, behavioral, physiological, cellular, and genetic analysis, whereas such analysis is used to differentiate arousal states along a continuum from fully awake to deep sleep [11]. Sleep divided into wakefulness, non-rapid eye movement (NREM) sleep and rapid eye movement (REM) sleep [12]. Depression is a state of low mood and aversion to activity that affect persons' emotions, thoughts, behaviors and sense of well-being [13]. A person who is depressed usually experiences several feelings of sadness or emptiness, hopeless, anhedonia (a decrease or loss of ability to take

pleasure in ordinary activities), guilt, irritability, angry, lowered self-esteem and worthlessness, reduced energy and vitality, social isolation, slowness of thought or action, recurrent thoughts of death or suicide, loss of appetite or overeating, constipation or diarrhea, disturbed sleep or insomnia and decreased libido [14-16]. Depression is the most common mood disorder [17]. Overlap of depression and specific autoimmune diseases in the same individuals at a higher frequency than chance, investigating the relationship between depression and autoimmune diseases will inform theories that the etiology of depression involves immune processes [18]. The link between lupus and depression is controversial but it is known that negative life events, low socioeconomic status, lupus disease activity and lupus treatment may be contributing to depression. The psychiatric symptoms of lupus may vary from mild personality disorders to severe psychosis. Depression is the most frequent mental change in lupus (studies cited about half of lupus patients develop depression) [19,20].

Methods

Study Design and Setting

A cross-sectional study was conductedat Rheumatology Unit, Baghdad Teaching Hospital, during the period from the 1st of January to the 31st of October 2018.

Patients Collection

A total of 61 Iraqi female patients attending the Rheumatology Unit at Baghdad Teaching Hospital, were evaluated. A brief interview (20-30 min) was conducted in a private quiet room in order to take the illness history of each patient prior to enrollment. All patients enrolled diagnosed with SLE (by the Consultant Rheumatologists) after fulfilling at least 4 criteria of the ACR revised criteriafor SLE and after fulfilling at least 4 criteria or biopsy-proven lupus nephritis with positive ANA or Anti-DNA of the SLICC criteriafor SLE. The patients were diagnosed with depression (by the Consultant Psychiatrists) after having at least 5 of the DSM-5 criteria for depression.

Inclusion Criteria

Female patients were diagnosed with SLE with disease onset after the age of 18 years regardless the disease duration was evaluated for sleep quality according to the PSQI scoring and depression according to the DSM-5 criteria. Because mostof the persons with SLE are females, for clarity and feasibility, we studied females only.

Exclusion Criteria

• Chronic medical diseases including end-stage renal disease, ischemic heart disease, hypertension, diabetes mellitus and active neoplastic disease.

• Overlap, mixed connective tissue diseases and antiphospholipid syndrome.

• Pregnancy and lactation.

• Substance abuse including smoking and alcohol.

Data Collection

• Data were collected using a data collection sheet containing questionnaires for the patients. The questionnaires included general demographic data: name, age, height, weight, body mass index, marital status (single, married, widow, divorced), education (illiterate, read & write, primary school, secondary school, college, postgraduate), employment (unemployed, employed, retired, housewife) and household crowding index.

• Data for SLE evaluation included disease duration and disease activity.Disease activity was evaluated by using SLEDAI which based on clinical and laboratory variables, scores may range from no flare ≤3, mild or moderate flare >3-12, and severe flare >12.

• Sleep quality was evaluated by using data collection questionnaire, derived from Pittsburgh Sleep Quality Index (PSQI) a widely used and standardized questionnaire, 19 questions are combined into seven clinically derived component scores, each exploring a different sleep feature, The seven component scores are then added in order to obtain a global score rating from 0-21, with a global score ≥5 points was defined as poor sleep quality. The following PSQI-derived data were also analyzed: increased sleep latency (>30 min) (component 2), difficulty in maintaining sleep and early morning awakening (component 5).

• Depression was evaluated by using data collection questionnaire, derived from DSM-5 criteria which is anine-question questionnaire to assess depressive symptoms during the previous two weeks, with a global score≥5 points.

Ethical Issue, Approval and Official Permission

Prior to data collection, a verbal consent was taken from all patients to participate in the study. The study protocol was reviewed; approval and official permission were obtained from the Ministry of Higher Education and Scientific Research, Baghdad University, College of Medicine to conduct the present study.

Statistical Analysis

All statistical procedures, analysis and tests were applied using the statistical package for social sciences (SPSS) version 25. Descriptive statistics presented as mean, standard deviation, median, inter-quartile range (IQR), frequencies and percentages. Continuous variables were tested for normal distribution using the histogram, normal distribution curve and for dataset smaller than 2000 elements, the Shapiro-Wilk test was used. The total PSQI and DSM-5 appeared to be normally distributed with minimal skewness but both passed the Shapiro-Wilk testing, while SLEDAI appeared to have large skewness and did not pass the Shapiro-Wilk test (i.e. it was not normally distributed). Independent student's t test was used to compare two means of normally distributed variable. The Mann-Whitney U test used to compare SLEDAI across two subgroups. The Kruskal-Wallis test (one-way ANOVA on ranks) used to compare SLEDAI of the patients in the 4 subgroups according to combination of sleep quality and depression. The bivariate Pearson's correlation test used to assess the correlation among DSM-5, PSQI and SLEDAI as continuous variables, and because the SLEDAI was not normally distributed, Pearson's Bivariate correlation test used with Bootstrapping. Level of significance was set at 0.05 below which the difference or correlation considered to be significant.

Results

A total of 61 SLE patients were enrolled in this cross-sectional study, with a mean age of 33.6 (±10.2), moreover, 26 patients (42.6%) aged 20-29 years. Married patients were 39 (63.9%). Level of education of the patients ranged from illiterate to postgraduate with higher proportion of the patients had secondary level of education and below. Housewives patients were 48 (78.7%). Obese patients were 21 (34.4%). Crowding index ranged between 1 to more than 3, and majority, (82%),

of the patients with crowding index of less than 3, as shown in the table (Table 1).

The below table shows the clinical disease related variables of SLE patients, the disease duration ranged betweenless than 3 years in some patients to more than 8 years in others; where the median duration of SLE was 3 (IQR: 2-7) years (Table 2).

According to the SLEDAI, it was ranged from 1-42 with a mean of 12.87±9.83 and median of 8.0 (IQR: 5.0-19.0), the disease was inactive in 7 patients (11.5 %), mild or moderate flare in28 patients (45.9%) and severe flare in 26 patients (42.6%).

Assessment of the patients according to the DSM-5 criteria for diagnosis of depressionrevealed that 26 patients (42.6%) were depressed compared to 35patients (57.4%) were not, as shown in the figure (Figure 1).

The assessment of sleep quality of the studied group according to the 7 components of the PSQI score, are shown in the table (Table 3).

The total PSQI ranged between 0 to 18 with a mean of 6.31±2.29 and median (IQR) of 5.0 (3.0-9.0). Moreover, according to the cutoff point (5.0 point) of the total PSQI, Poor sleep quality (PSQI≥5) was reported in 36 patients (59.0%) while the remaining 25 patients (41.0%) had a total PSQI of <5 (Good sleep quality), as shown in the figure (Figure 2).
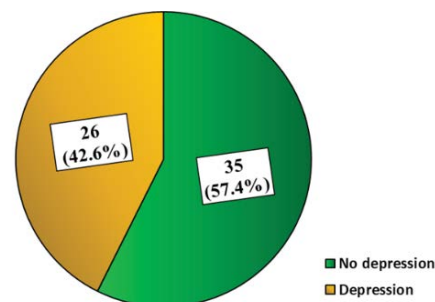

Figure 1: The prevalence of depression among SLE patients according to the DSM-5 criteria for depression (DSM-5: diagnostic and statistical manual of mental disorders).
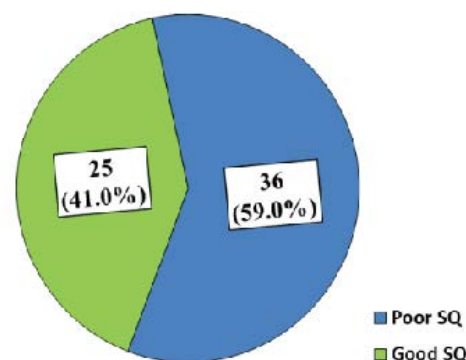

Figure 2: Distribution of sleep quality among SLE patients according to the PSQI score. Where: PSQI is Pittsburgh sleep quality index and SQ is sleep quality.

The mean disease activity index (SLEDAI) of patients with poor sleep quality (SQ) was 15.8±1.8, while that of patients with good SQ was 8.6±1.3. The comparison of SQ subgroups, using the Mann-Whitney U test revealed that patients with poor SQ had significantly higher levels of SLEDAI than those with good SQ, indicated that poor sleep quality associated with more active disease, (P value=0.005). Secondly, the SLEDAI was compared with depression, where patients with depression had significantly higher disease activity index, and the mean SLEDAI of patients with poor and good SQ was 18.8±2.1 *vs.* 8.5=1.1, respectively, (P value<0.001), as shown in the below table (Table 4).

From other point of view, for more precise assessment of the correlation between SQ and depression from one side and disease activity from the other side, bivariate Pearson's correlation test was used for the testing of the correlation between total PSQI, DSM-5 and SLEDAI, and because SLEDAI was not-normally distributed the bivariate Pearson's correlation test used with bootstrapping, then the correlation results were evaluated and revealed a direct significant correlation between SLEDAI and each of PSQI (R=0.417, P value=0.001) and DSM-5 (R=0.440, P value<0.001), moreover, a significant direct correlation was found between DSM-5 and PSQI (R=0.512, P value<0.001), as shown in (Table 5) (Figures 4 and 5).

SLE patients were categorized according to their SQ and presence or absence of depression, as shown in the below table, where 4 subgroups had been generated; 21 patients had Poor SQ with Depression, 15 patients had Poor SQ without Depression, 5 patients had Good SQ with Depression and 20 patients had Good SQ without Depression (Table 6).

Further comparison was made according to the 4 combined subgroups, this comparison revealed that patients who had Poor SQ

Table 1: Demographic characteristics of SLE patients (Number=61).

Variable		No.	%
Age (year) *	20-29	26	42.6
	30-39	17	27.9
	≥40	18	29.5
Marital status	Married	39	63.9
	Single	15	24.6
	Divorced/Widowed	7	11.5
Education	Illiterate	3	4.9
	Read & write	19	31.1
	Primary	19	31.1
	Secondary	9	14.8
	College	5	8.2
	Postgraduate	6	9.8
Occupation	Housewife	48	78.7
	Employed	7	11.5
	Other**	6	9.8
BMI category*	Normal	17	27.9
	Overweight	23	37.7
	Obese	21	34.4
Crowding index	1	9	14.8
	2	22	36.1
	3	19	31.1
	>3	11	18

Table 2: Disease related variables of SLE patients (No.=61).

Variable		No.	%
SLE duration (year)*	<3	22	36.1
	3-5	21	34.4
	6-8	10	16.4
	>8	8	13.1
SLEDAI	Inactive	7	11.5
	Mild or moderate flare	28	45.9
	Severe flare	26	42.6
	Mean±SD: 12.87±9.83	-	-
	Median (IQR): 8.0 (5-19)	-	-

Table 3: Distribution of the sleep quality related difficulties of different PSQI components.

PSQI component	No difficulty		Mild difficulty		Moderate difficulty		Severe difficulty		Total
	No.	%	No.	%	No.	%	No.	%	
Subjective sleep quality	10	16.4	22	36.1	16	26.2	13	21.3	61
Sleep latency	14	23	13	21.3	13	21.3	21	34.4	61
Sleep duration	35	57.4	9	14.8	9	14.8	8	13	61
Sleep efficiency	46	75.4	6	9.8	4	6.6	5	8.2	61
Sleep disturbance	9	14.8	41	67.2	11	18	0	0	61
Use of sleep medication	57	93.4	4	6.6	0	0	0	0	61
Daytime dysfunction	41	67.2	3	5	11	18	6	9.8	61

Table 4: Comparison of mean SLEDAI across the sleep quality and depressioncategories of SLE patients (No.=61).

Variable	SLEDAI (Mean ± SD)	P value
Sleep Quality		
Poor SQ	15.8±1.8	0.005
Good SQ	8.6±1.3	
Depression		
Depression	18.8±2.1	<0.001
No depression	8.5±1.1	

Table 5: Results of bivariate Pearson's correlation test of the intercorrelation of SLEDAI, DSM-5 and PSQI of SLE patients (No.=61).

Variable	Statistics	PSQI	DSM-5
SLEDI	R	0.417	0.44
	P value	0.001	<0.001
DSM-5	R	0.512	-
	P value	<0.001	-

Table 6: Comparison of mean SLEDAI across the SQ-Depression combined subgroups.

Subgroup	No. of patients	SLEDAI (Mean±SD)
Poor SQ with Depression	21	21.0±2.3
Poor SQ without Depression	15	8.5±1.5
Good SQ with Depression	5	9.6±2.3
Good SQ without Depression	20	8.4±1.6
Pairwise comparison of subgroups		**P value**
Poor SQ with Depression vs. Poor SQ without Depression		0.001
Poor SQ with Depression vs. Good SQ without Depression		< 0.001
Poor SQ with Depression vs. Good SQ with Depression		0.028
Poor SQ without Depression vs. Good SQ without Depression		0.726
Poor SQ without Depression vs. Good SQ with Depression		0.716
Good SQ without Depression vs. Good SQ with Depression		0.538

with Depression had the highest mean SLEDAI (21.0±2.3) and was significantly higher than the SLEDAI levels of patients who had Poor SQ without Depression, Good SQ without Depression, and Good SQ with Depression, (P value< 0.05), while no significant differences had been found among other subgroups in SLEDAI, (P value>0.05).

As it shown in the table, higher body mass index was significantly associated with higher SLEDAI (P value=0.009) (Table 7). Longer duration of SLE was significantly associated with higher PSQI (P value=0.001).Other variables showed no significant association with DSM-5, PSQI and SLEDAI, (P value>0.05).

Discussion

There are several reports available concerning prevalence of poor sleep quality in SLE [21]. To the best of our knowledge therewere no previous reports about poor sleep quality among Iraqi patients with SLE. The purpose of this study was to evaluate sleep quality in lupus women with or without depression.Inthe current study sleep quality
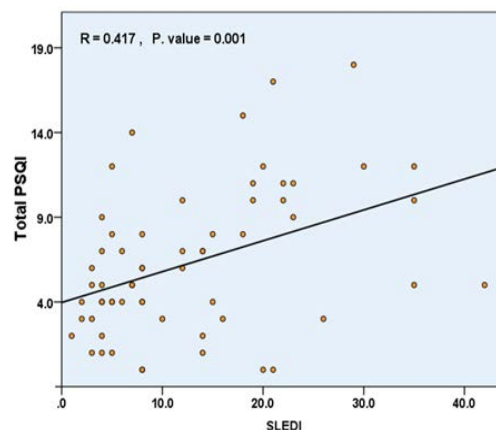

Figure 3: Regression curve estimation for the correlation between SLEDAI and Total PSQI; correlation is direct (positive).
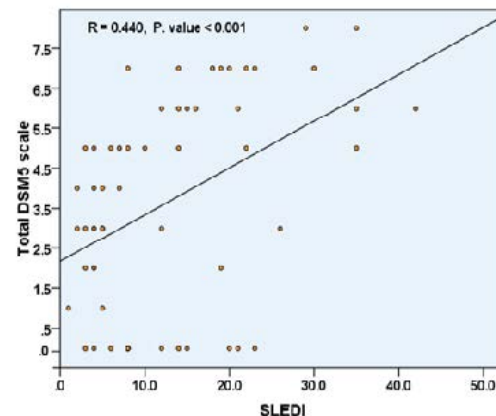

Figure 4: Regression curve estimation for the correlation between SLEDAI and Total DSM-5; correlation is direct (positive).

was evaluated by using PSQI score, SLE patients had statistically high scores insubjective sleep quality, sleep latency, sleep duration, sleep efficiency, sleep disturbance, anddaytime dysfunction. These results are in line with Mirbagher L, et al. (2016), Abad VC, et al. (2008) and Chandrasekhara PK, et al. (2009) [22-24]. In the present study, poor sleep quality was reported in **(59%)** of SLE patients. These results were like Tench CM, et al. (2009) (British study) which reported poor sleep quality in 60% of SLE female patients [25]. As well as Palagini L, et al. (2014) (Italian study) which demonstrated the presence of poor sleep quality in almost two-thirds of the SLE cohort [26]. The similarities between these studies were all enrolled a small sample size and used PSQI score in their samples.Poor sleep quality was high in SLE studies and lupus disease activity may be the contributing factor.The second

Table 7: Results of Bivariate correlation tests of the demographic variables and each of SLEDAI, DSM-5 and PSQI of SLE patients (No.=61).

Variable	Statistics	DSM-5	PSQI	SLEDAI
Age (older)	Correlation coefficient*	0.004	0.307	-0.002
	P value	0.974	0.016	0.988
BMI (larger)	Correlation coefficient*	-0.064	0.133	0.331
	P value	0.622	0.306	0.009
SLE duration (longer)	Correlation coefficient*	0.207	0.405	-0.041
	P value	0.109	0.001	0.751
Marital status (single)	Correlation coefficient	-0.21	-0.24	0.19
	P value	0.11	0.06	0.13
Education (Higher)	Correlation coefficient	-0.23	-0.01	0.01
	P value	0.07	0.97	0.92
Occupation (Employee)	Correlation coefficient	-0.32	-0.02	0.03
	P value	0.01	0.87	0.81
Crowding index (1)	Correlation coefficient	-0.11	-0.12	-0.09
	P value	0.41	0.35	0.51
*Pearson's test used, while Spearman's test used in other variables				

part of this study was aimed at identifyingthe relationship between depression and sleep quality in the SLE cohort. The depressed mood might play an important role inthe pathogenesis of poor sleep quality in SLEand sleep disturbances are frequently associated with depression and in the absence of sleep complaints, a diagnosis of depression should be made with caution.In the present study, depression was reported in (42.6%) of SLE women. This finding was agreed to the results of Palagini L, et al. (2014) (Italian study) in which the prevalenceof depressive symptoms was about 35% of SLE patients [26]. Despite of we were used DSM-5, while Palagini L, et al. (2014) were used Beck depression inventory (BDI) [26]. This result was close to another study, Meszaros ZS, et al. (2012) (American study) in which depression was present in up to 39% of SLE patients [27]. In both studies the enrolled patients were adults of any age who fulfilled the ACR criteria for SLE. The current study was comparable to Adeli AM, et al. (2016) (Iranian study) which reported that depression prevalence in SLE was 33.3% [28]. This is a little bit difference probably because of Adeli AM, et al. (2016) were studiedthe prevalence of cognitive disorders in SLE patients rather than focusing on depression only, another difference that we were used DSM-5, while they used BDI and finally our patients were suffered from a more stressful environment that play a key role on the impact of sleep quality. Iraqi people are being exposed to a great deal of violence and threats range from vehicle-borne bombings to displacement crisis, kidnappings and murders by Islamic State in Iraq and Al Sham (ISIS) and organized criminal gangs [28].

In Iraq, depression has been reported in few previousstudies. Salman S, et al. (1995) observed that neuropsychiatric manifestation in SLE were present in 34.6% and depression is seen in 9.6% [29]. This is much less than the (42.6%) that found in our study, possible explanation of thisdifference maybe related to difference in sample size, data measurement, long periods of time between the two studies (23 years) and increasing stressful events, and probably due to the fact that we have concentrated more on depression than other neuropsychiatric manifestations.

The present study demonstrated that a high disease activity and longer disease duration were contributed significantly to poor sleep quality. This findings was agree with studies done byCosta DD, et al. (2005), Mirbagher L, et al. (2016), Chandrasekhara PK, et al. (2009), and Palagini L, et al. (2014) [22,24,26,30]. This result may show that living with a chronic disease has an impact on sleep quality.

The other predictors of poor sleep quality in the present studywas

a higherbody mass index was significantly associated with higher SLEDAI (P value=0.009) and this result was like Zonana NA, et al. (2008) (American study) which reported that obesity and metabolic syndrome were related with pain and functional status suggesting disease activity [31].

While other demographic variables including age, marital status, education, occupation, crowding indexshowed no significant association with sleep quality, depressive symptoms and disease activity (P value>0.05), the probable explanation that we studied only women and our sample was dominant for married and housewives and the majority of them their crowding index was less than 3. These results were agreeing to the studies done by Costa DD, et al. (2005), Chandrasekhara PK, et al. (2009) and Palagini L, et al. (2014) but disagree regarding age with Mirbagher L, et al. (2016) (Iranian study) which reported that old age was a determinant of poor sleep quality [22,24,26,30]. This difference may be because the majority (two thirds) of our sample were younger than 40 years and may be related to the difference in sample size.

Conclusion

Poor sleep quality among SLE women in the current study was (59%). Depression among SLE women in the current study was (42.6%). Higher scores of SLE disease activity index was associated with poor sleep quality and depressive symptoms. These results highlight the need to assess sleep quality in SLE population. The PSQI (a brief, self-administered instrument) could be used in a clinical setting to measure sleep complaints in SLE. Early depression screening for SLE patients for early management.

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