Sleep Quality Among Patients with Rheumatoid Arthritis and it's Correlation with Disease Activity and Duration at Baghdad Teaching Hospital

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Abstract

Rheumatoid arthritis (RA) is a common chronic, progressive, autoimmune disease characterized by debilitating articular and extra articular manifestations. Sleep quality is defined as one's satisfaction with the sleep experience, integrating aspects of sleep initiation, sleep maintenance, sleep quantity, and refreshment upon awakening. To assess sleep quality in a sample of rheumatoid arthritis patients and compare it with healthy individuals, as well as it's a correlation to rheumatoid arthritis disease activity and duration. A case-control study was conducted at Baghdad Teaching Hospital, Rheumatology Unit during the period from September 2017 to August 2018. The study was included 100 Rheumatoid Arthritis patients who met the inclusion criteria, and 100 healthy individuals as a control, data were collected using a preconstructed data collection sheet. Questionnaires included demographic and clinical data of the patients and controls. Rheumatoid Arthritis was diagnosed with 2010 ACR/EULAR Classifications Criteria for RA (by Consultant Rheumatologist), sleep quality assessed by using The Pittsburgh Sleep Quality Index (PSQI). The mean age of the studied groups was 48.1±11.1 years and 46.3±10.0 years in rheumatoid arthritis and control groups, respectively. no statistically significant differences between both groups had been found in age, gender, BMI and other demographic variables (P value >0.05). Except for the Family history of RA was significantly higher in RA patients than controls. Poor sleep quality was found in 74% of patients with rheumatoid arthritis, while seen in 46% of controls. In the rheumatoid arthritis group, disease duration and Clinical Disease Activity Index (CDAI) was significantly and directly (positively) correlated with the global PSQI. Patients with poor sleep quality had significantly longer disease duration (mean duration=12.6 years) than those with good sleep quality (mean duration= 6.1 years). Similarly, RA patients with poor sleep quality had significantly higher CDAI (mean CDAI=20.7) than those with good sleep quality (mean CDAI=11.6). Poor sleep quality observed in 74% of Iraqi rheumatoid arthritis patients in comparison to 46% of control sleep quality positively correlated with clinical disease activity and duration of rheumatoid arthritis.

Keywords: RA; Sleep quality; Autoimmune inflammatory disease; Case-control study; Baghdad

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Introduction

Rheumatoid arthritis (RA) is a chronic, progressive autoimmune disease characterized by joint pain, joint swelling, fatigue, sleep disturbance, and functional disability [1]. Rheumatoid arthritis (RA) is the most common systemic autoimmune inflammatory disease [2]. The disease has a global distribution and involves all ethnic groups [3]. The prevalence of RA is about0.5-1% of the adult population, it can occur in patients at any age but The peak onset is between the fourth and sixth decade of the life, It effects woman about three times more frequent than men [4]. But sex differences diminish in older age groups [5]. Definite RA was observed in 1% of population samples in Iraq [6]. Rheumatoid arthritis is a complex immune disease involving interactions between immunological factors, genetic factors, hormonal factors, environmental triggers and chance [7]. Sleep is a periodically recurring condition characterized by reduced reactivity to external stimuli, suppressed mobility, and reduced cognitive ability [8]. Sleep quality is defined as one's satisfaction of the sleep experience, integrating aspects of sleep initiation, sleep maintenance, sleep quantity, and refreshment upon awakening. Insomnia symptoms impose daytime consequences and impairments associated with sleep disturbances (e.g., fatigue, change in mood, daytime sleepiness or cognitive difficulties).Insomnia affects 8-18% of the general population [9]. Most adults need to sleep 7-9 hours per night on a regular basis to promote optimal health [10]. Sleep problems and pain are common in patients with RA, which have significant relationship with inflammatory markers, and increased inflammatory markers can be affected by sleep problems and pain. As increase of markers without control would increase the intensity of disease. Sleep problems can also be a predicting factor of increasing CRP. So, in this way, by relieving pain and providing proper sleep we can decrease the intensity of disease and prevent of disease severity [11].

Methods

Study Design and Setting

This is a case-control study was conducted at Rheumatology Unit, Baghdad Teaching Hospital, during the periodfrom September 2017 to August 2018.

Patients Collection

A total of 100 Iraqi patients diagnosed with rheumatoid arthritis (by the Consultant Rheumatologists) after fulfilling 2010 ACR/EULAR Classifications Criteria for RA. Who attended Rheumatology Unit at Baghdad Teaching Hospital and met the inclusion criteria were enrolled in the study?

Control

There were 100 healthy control matched for age and sex enrolled in the study. Those were collected in the hospital as relatives of patients (but not those with rheumatoid arthritis), visitors and health workers.

Inclusion criteria

Patients who diagnosed with rheumatoid arthritis with disease onset after the age of 16 years regardless the disease duration, for both gender, were evaluated for 2010 ACR/EULAR Classifications Criteria for RA, all patients were on regular treatment of conventional and biological diseases modifying antirheumatic drugs for 3 months prior to study entry.

Exclusion criteria

- Chronic medical disease including neoplastic disease.

- History of mental disorders and substance abuse (diagnozed).

Exclusion done by full history, examination and investigations. All patients were investigated for complete blood count, full biochemistry, while other investigations were sent accordingly such as TSH (when thyroid disease suspected).

Data Collection

- Data were collected using a data collection sheet containing questionnaires for the patients and controls. The questionnaires included general demographic data: name, age, gender, height, weight, body mass index (measured for both groups according the equation $BMI = weight/height^2$), marital status (single, married, widow, divorced), education (illiterate, read and write, primary school, secondary school, college, postgraduate), occupation (unemployed, employee, retired, housewife), household crowding index (HCI).

- Data for RA evaluation included RF and ACPA were recorded from the patients' medical files, disease duration, family history of RA, Disease activity was evaluated by using clinical disease activity index CDAI with higher total score suggests increase in disease activity.

- Data for sleep quality evaluated by Pittsburgh sleep quality index (PSQI) which include 9 self-assessing questions each assigned the value of 0 to 3, where 0 meant "no problems in the area evaluated by this item" and 3 meant "major problems in the area evaluated by this item", The answers were evaluated in terms of seven factors: sleep quality, latency of falling asleep, sleep duration, sleep effectiveness, sleep interruptions, intake of sleep medications, and fatigue during the day. A completed questionnaire, with all items counted, yielded between 0 and 21 points with the lower number signifying a better quality of sleep.

Ethical considerations

Free verbal consent was taken from patients and controls for admission to the study.

Statistical Analysis

Data of both studied groups were entered and analyzed using the statistical package for social sciences (SPSS) version 25. Descriptive statistics presented as mean, standard deviation, standard error, range, median, interquartile range (IQR), mode, frequencies and proportions. All continuous original and new generated (PSQI score) variables were tested for statistical normal distribution using histogram and normal distribution curve, and all followed the normal distribution with slight skewness and kurtosis in some with no significant effect. Statistical tests applied according to the type of variables; Student's t test for two independent samples was used to compare two means of a continuous variable. Non-parametric median test used to compare medians. Chi-square and Fisher's exact (when chi-square inapplicable) tests used alternatively to compare frequencies. Bivariate Pearson's correlation test logistic regression curve estimation and linear logistic regression analysis were used to assess the correlations. Correlation coefficient (R) is an indicator of the strength and direction of correlation; its value ranged zero (complete no correlation) to one (perfect correlation) the higher R value close to one indicated stronger correlation, the positive (no sign) R value indicated a direct (positive) correlation and the negative signed R indicated an inverse correlation. Level of significance of ≤0.05 was considered as significant difference or correlation.

Results

There were 100 RA patients and 100 apparently healthy subjects (as controls) enrolled in this control study, they were almost matched for demographic characteristics, in all comparisons, of these variables, P>0.05, Except the Family history of RA was significantly higher in RA patients than controls, (Pvalue<0.05) (Table 1).

The disease related variables ofRA patients, are shown in the below table, the mean disease durationwas 10.4±8.7 years (range: 3 months to 35 year) and the mean CDAI was 17.6±9.1 (range: 4-57), other clinical parameters are shown in the same table (Table 2).

The comparison ofPSQI components are summarized in the table,RA patients had statistically higher scores in subjective sleep quality, sleep latency, sleep duration, sleep efficiency, sleep disturbance, and daytime dysfunction compared to the healthy controls (Pvalue<0.05). In component 6 (use of sleep medication) the difference was statistically insignificant, (Pvalue>0.05) (Table 3).

Further comparison of the mean scores of the PSQI components revealed that in all PSQI components the mean score was significantly higher in RA patients than controls, (P<0.001), except in component 6 (P>0.05) (Figure1).

Sleep quality of RA patients and Controls

According to the global PSQI score, RA patients and controls categorized into two subgroups, those with good sleep quality (global PSQI<5) and those with poor sleep quality (PSQI≥5), the results of this new categorization are shown in the table where higher proportion (74%) of RA patients had poor sleep quality, compared to (46%) in controls, the difference was statistically significant (Pvalue<0.001) (Table 4).

Table 1: Demographic characteristics of the studied groups.

		Group				P value
		RA patients (n=100)		Controls (n=100)		
		No.	%	No.	%	
Age (year)*	<40	26	26.0	24	24.0	0.27
	40-49	32	32.0	44	44.0	
	50-59	21	21.0	12	12.0	
	≥60	21	21.0	20	20.0	
	Mean ±SD	48.1±11.1		46.3±10.0		
Gender	Male	17	17.0	24	24.0	0.22
	Female	83	83.0	76	76.0	
Marital status	Married	77	77.0	64	64.0	0.11
	Single	11	11.0	20	20.0	
	Divorced/Widow	12	12.0	16	16.0	
Education	Illiterate	14	14.0	12	12.0	0.93
	Read & Write	7	7.0	5	5.0	
	Primary	36	36.0	38	38.0	
	Secondary	28	28.0	27	27.0	
	College	15	15.0	18	18.0	
Occupation	Housewife	65	65.0	68	68.0	0.85
	Employee	19	19.0	15	15.0	
	Unemployed	10	10.0	12	12.0	
	Retired	6	6.0	5	5.0	
	Normal	30	30.0	32	32.0	0.46
	Overweight	34	34.0	40	40.0	
	Obese	36	36.0	28	28.0	
	Mean±SD	28.1±5.5		27.6±4.6		
Crowding index n (%)	Low	63	63.0	55	55.0	0.50
	Intermediate	17	17.0	22	22.0	
	Overcrowded	20	20.0	23	23.0	
Family history of RA		25	25.0	8	8.0	0.001

Table 2: Disease related variables of the RA patients.

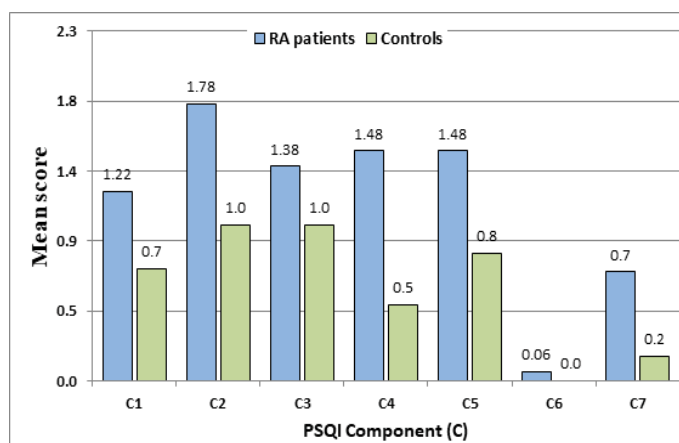| Parameter	Value
Mean disease duration(SD*) (year)	10.4(8.7)
Mean CDAI	17.6(9.1)
Mean ESR level (SD)	38(24)
RF Positive RA patientsn (%)	67(67.0)
ACPA Positive RA patients n (%)	39(39)

Figure 1: Graphical comparison of mean scores of PSQI Components of RA patients and controls.

Correlation between PSQI scores and RA duration and activity

Among RA patients, a correlation analysis using bivariate Pearson's correlation test revealed that disease duration and CDAI were significantly and directly (positively) correlated with the global PSQI, i.e. patients with longer duration had significantly higher PSQI (worse sleep quality), (R=0.504, P. value<0.05), and patients with higher CDAI had the higher PSQI score, (R=0.653, P value<0.001), however, the correlation between PSQI with CDAI was stronger (larger R value) than that with disease duration as shown in the below table (Table 5).

Comparison was made for the mean disease duration and CDAI across the global PSQI categories (poor and good), this comparison revealed that patients with poor sleep quality had significantly longer disease duration (mean duration=12.6) years than those with good sleep quality, (mean duration=6.1) years. Similarly, RA patients with poor sleep quality hadsignificantly higher CDAI (mean CDAI=20.7) than those with good sleep quality, (mean CDAI=11.6), in both comparisons, (Pvalue<0.001) as shown in the table (Table6) (Figure 2 and 3).

To control any confounding effect of the demographic and clinical variables of the RA patients on the correlation between disease duration and CDAI with PSQI score, linear logistic regression analysis was performed using the PSQI score as dependent variable and the demographic and clinical variables as independent variables, this analysis revealed that the correlation between disease duration and CDAI with the PSQI scores still significant, (P value<0.05), after adjustment for other variables, while none of the clinical or demographic variables appeared to have an effect on the PSQI score (Table7).

Table 3: Comparison of the PSQI components between the rheumatoid arthritis patients and healthy controls.

PSQI Component	Evaluation	RA patients (n=100)		Controls (n=100)		P. value
		No.	%	No.	%	
Subjective sleep quality	No difficulty	13	13.0	40	40.0	<0.001
	Mild difficulty	57	57.0	48	48.0	
	Moderate difficulty	25	25.0	12	12.0	
	Severe difficulty	5	5.0	0	0.0	
Sleep latency	No difficulty	30	30.0	50	50.0	<0.001
	Mild difficulty	5	5.0	16	16.0	
	Moderate difficulty	22	22.0	18	18.0	
	Severe difficulty	43	43.0	16	16.0	
Sleep duration	No difficulty	21	21.0	32	32.0	<0.001
	Mild difficulty	38	38.0	48	48.0	
	Moderate difficulty	23	23.0	8	8.0	
	Severe difficulty	18	18.0	12	12.0	
Sleep efficiency	No difficulty	36	36.0	71	71.0	<0.001
	Mild difficulty	14	14.0	14	14.0	
	Moderate difficulty	16	16.0	10	10.0	
	Severe difficulty	34	34.0	5	5.0	
Sleep disturbance	No difficulty	10	10.0	28	28.0	<0.001
	Mild difficulty	39	39.0	62	62.0	
	Moderate difficulty	44	44.0	10	10.0	
	Severe difficulty	7	7.0	0	0.0	
Use of sleep medication	No difficulty	97	97.0	100	100.0	0.250
	Mild difficulty	1	1.0	0	0.0	
	Moderate difficulty	1	1.0	0	0.0	
	Severe difficulty	1	1.0	0	0.0	
Daytime dysfunction	No difficulty	55	55.0	90	90.0	<0.001
	Mild difficulty	26	26.0	4	4.0	
	Moderate difficulty	13	13.0	6	6.0	
	Severe difficulty	6	6.0	0	0.0	

Table 4: Comparison of sleep quality according to global PSQI of the studied groups.

Sleep quality	RA patients (n =100), %		Controls (n=100), %	
Poor sleep quality	74	74.0	46	46.0
Good sleep quality	26	26.0	54	54.0
Chi-square=16.33, Pvalue<0.001				

Table 5: Correlations analysis of global PSQI score with disease duration and clinical disease activity of RA patients.

Disease duration	R	0.504
CDAI	P value	<0.001
	R	0.653
	P value	<0.001
R: Correlation coefficient Correlation is significant at the 0.01 level		

Figure 2: Graphical comparison of mean disease duration of RA patients according to sleep quality.

Table 6: Comparison of mean disease duration and CDAI according to sleep quality of RA patients.

		Global PSQI score		Student's t test	P value
		Poor sleep quality	Good sleep quality		
Disease duration	Mean (SD)	12.6 (9.7)	6.1 (5.3)	3.67	<0.001
CDAI	Range	0.7-35	0.3-25		
	Mean	20.7 (9.4)	11.6 (4.3)	5.4	<0.001
	Range	7.0-57	4.0-22		

Discussion

Sleep problems are common in patients with chronic diseases and the prevalence of poor sleep is high in rheumatoid arthritis patients compared to healthy individuals [12]. To the best of our knowledge there was no local study discussed sleep problems in rheumatoid arthritis patients. In this study, we have evaluated the sleep quality in patients with rheumatoid arthritis and assessed their relationship with disease activity and duration.

In the current study, (74%) of rheumatoid arthritis patients suffered from poor sleep compared to (46%) in healthy individuals. The sleep quality was evaluated by using PSQI which is commonly used for sleep quality evaluation in various diseases or health status worldwide
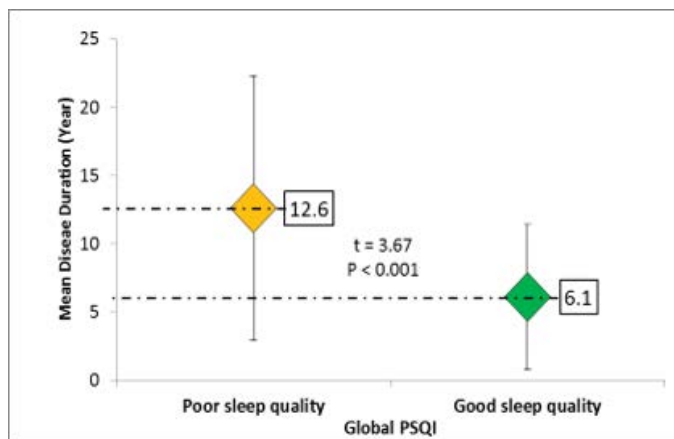
Table 7: Results of linear logistic regression analysis for the correlation of PSQI score with other variables.

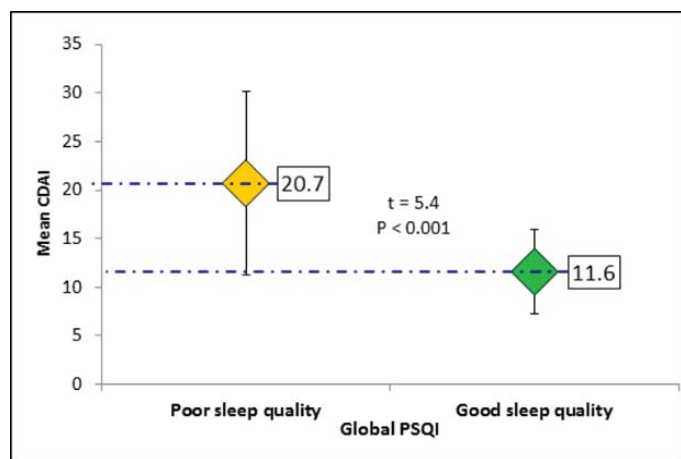|	Standardized Coefficients (Beta)	t	P
Age	0.002	0.027	0.978
Gender	0.011	0.090	0.928
BMI	-0.062	-0.783	0.436
Marital status	-0.073	-0.877	0.383
Education	0.139	1.563	0.122
Occupation	-0.057	-0.471	0.639
Crowding index	-0.031	-0.367	0.715
Family history of RA	0.015	0.184	0.855
Disease duration	0.255	2.533	0.013
CDAI	0.539	5.832	0.000
ESR	0.002	0.023	0.982
RF	-0.089	-0.981	0.330
ACPA	0.067	0.784	0.435

Figure 3: Graphical comparison of mean CDAI of RA patients according to sleep quality.

[13,14]. Patients with rheumatoid arthritis had statistically significant higher scores in subjective sleep quality, sleep latency, sleep duration, sleep efficiency, sleep disturbance, and daytime dysfunction compared to the healthy controls.

We were trying to compare the results of this study with studies of a similar environmental, religious and cultural background. Unfortunately there were no such studies except one Turkish study by Sariyildiz MA et al. (2014), in which 94 patients diagnosed with rheumatoid arthritis and 52 healthy controls were enrolled, similar to the current study sleep disturbances were higher in rheumatoid arthritis patients than healthy control, poor sleep was observed in 64.1% of the patients with rheumatoid arthritis, they had significantly higher scores in the subjective sleep quality, sleep latency, habitual sleep efficiency, sleep disturbance domains and the total PSQI score compared to the healthy control [15].

Other studies that supported the results of this study include a Chinese study by Genkai Guo et al. (2016), A self- report survey was administered to 131 rheumatoid arthritis patients and 104 healthy individuals using the Pittsburgh Sleep Quality Index (PSQI) for sleep quality, which found that 78.6% of rheumatoid arthritis patients suffered from poor sleep [16]. In addition, a Brazilian study by Goes AC et al. (2016) revealed that 81.5% of patients had poor sleep quality [17].

Other studies have lower prevalence of poor sleep among patients with rheumatoid arthritis comparing to the current study but still significantly higher than the healthy control enrolled in those studies, such as the Korean study by Son CNet al. (2015) on 130 patients with rheumatoid arthritis and 67 age- and sex-matched healthy controls, reported that poor sleep was observed in 38.5% of rheumatoid arthritis patientswhich is much more common than in healthy controls 13.4% [18].

Recently a cross-sectional study by Grabovac I, et al. (2018) 95 rheumatoid arthritis patients visiting the rheumatology outpatient clinic of the Kaiser Franz Josef Hospital in Vienna were analyzed, reported that 57% of rheumatoid arthritis patients had non-optimal sleep duration [19].

Another Malaysian study by Rajalingam S, et al. (2015) revealed that the percentage of poor sleepers was significantly higher among rheumatoid arthritis patients, 47.83%, compared to 9.57% in healthy individuals [20].

The difference in prevalence of poor sleep quality in these studies may be attributed to the different environmental factors that study participants were exposed to. Iraqi people suffered from a long history of wars, explosions and displacement like the internal or external displacement of due to the war against Islamic State of Iraq and Levant (ISIL) which might put rheumatoid arthritis patients as well as healthy individuals under more stressful conditions that can affect their sleep in a negative manner. Another factor is the difference in the quality of infrastructure services which might affect the general life quality of patients including their sleep. Studies with differing results come from developed countries in which the health care facilities and drug availability may contribute to better disease control and subsequently less sleep disorders. Moreover, differences in the anti-rheumatoid arthritis drugs used in the management of patients in the different studies can also be another contributing factor to the difference of prevalence of poor sleep quality this factor may need further studies to evaluate the drugs as a risk factor for poor sleep quality among patients with RA.

Other factors may include religious practices, there are numerous Muslim sleep traditions that Muslims try to follow in order to be in accordance with the practice of the Prophet peace be upon him (pbuh) one of these is early bedtime and early wake up time. The prophet Muhammad (Pbuh) encouraged his companions not to be involved in any activity after Ishaprayer (darkness prayer, which is around 1.5-2 hours after sunset), and wake up for Fair prayer, which is about one hour before sunrise [21]. So if people sleep according to the Islamic traditions they will get healthy sleep duration and quality, but unfortunately the complexity of the modern life such as delay work time of family members, social media and other recent life requirements make some of our people delay in their sleep time which subsequently makes any cause of early morning awakening such as for prayer is difficult ,for that some of our patients may have a difficulty in falling in the sleep after awakening in the early morning which make them more prone to sleep disturbances compared to other RA patients from different religious backgrounds.

Searching for the Correlation between PSQI scores and rheumatoid arthritis duration and activity, the results revealed that rheumatoid arthritis duration and activity have a significant positive correlation with the global PSQI. The relationship between sleep quality and rheumatoid arthritis disease activity and duration is still poorly understood as it is unclear to what extent they affect each other. Patients with rheumatoid arthritis suffer from a variety of symptoms such as joint pain and

swelling, stiffness, fatigue and functional disability, that impair their quality of life and subsequently disturb their sleep. Conversely, sleep problems can cause a decrease in pain threshold which worsen sleep problems and tend to increase inflammatory markers that augment pain sensitivity.

These results are in line with previous studies conducted by Sariyildiz MA et al. (2014), and Westhovens R, et al. (2014) which revealed a positive correlation between poor sleep quality and rheumatoid arthritis disease activity and duration [15,21].

Other studies displayed different results. Son CN, et al. (2014), and Grabovac I, et al. (2018) have found no effects of disease duration and activity on sleep quality in rheumatoid arthritis patient [18,19]. While Genkai Guo, et al. (2016), found that disease activity is independent predictor of poor sleep quality in rheumatoid arthritis patients although there was no association between disease duration and poor sleep quality [16].

The difference in the results in these studies may be attributed to the difference in the number of the patients between the studies. Another factor could be that different indices were used to evaluate rheumatoid arthritis disease activity (DAS28 vs. CDAI in our study).

All demographic and disease related variables were analyzed for their relationship with sleep quality. It was found that none of these variables appeared to influence the PSQI score. In the current study age did not seem to affect the sleep quality. One explanation for this may be the fact that most of the enrolled patients were middle aged so we didn't have much different age group to evaluate this factor, another one is the wide range of normal sleep duration (7-9 hrs). Similarly, the Chinese, Korean, and Austrian studies revealed there was no association between sleep disturbances and age [16,18,19]. Alternatively, others such as the Turkish study found a significant correlation between age and poor sleep which is in accordance to the normal physiological effects of age on sleep [15].

Conclusion

Poor sleep quality observed in 74% of Iraqi RA patients in comparison to 46% of control. Sleep quality positively correlated with clinical disease activity and duration of rheumatoid arthritis. Early diagnosis and management of rheumatoid arthritis have a great effect on the sleep quality and subsequently the general wellbeing. Good evaluation and management of sleep disorders in rheumatoid arthritis patients is preferable as poor sleep can affect the functional activity of patients. Further studies with larger sample size and duration are highly suggested for further investigations and estimation of the prevalence of poor sleep disorders among rheumatoid arthritis patients.

Conflict of interest: None.

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