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## ORIGINAL ARTICLE

# EFFECTS OF SLEEP QUALITY ON HEALTH -RELATED QUALITY OF LIFE IN RHEUMATOID ARTHRITIS PATIENTS AT ZAGAZIG UNIVERSITY HOSPITALS.

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### ABSTRACT

**Aim of the work:** to study sleep quality in RA patients and its effects on health related quality of life.

**Subjects and methods:** This study was carried out on 30 RA patients and 30 healthy controls. RA disease activity was measured by DAS-28. All patients were subjected to full history taking, clinical examination and laboratory investigations including: CBC, ESR, CRP, RF, anti-CCP antibodies, liver and kidney functions. Quality of life was evaluated by Health Assessment Questionnaire –Disability Index (HAQ-DI). Sleep quality was evaluated by Pittsburgh Sleep Quality Index (PSQI). Anxiety and depression was evaluated by Hospital Anxiety and Depression Scale (HADS). Pain was evaluated by visual analogue scale (VAS).

**Results:** Our study found that PSQI was higher in RA patients compared to controls without statistical significant difference. Depression and Anxiety were significantly higher compared to controls. We also found that RA patients with poor sleep had RF, Anti CCP, DAS28, ESR, CRP, depression, anxiety VAS and HAQ were significantly higher compared to good sleepers. Also, RA with a PSQI score  $\geq 5$  (poor sleepers) were significantly having DMARDs more frequently than those with good sleep. HRQoL also associated with sleep quality and its impaired was affected by physical pain or function.

**Conclusion:** We observed that 73% of RA patients had poor sleep quality compared with healthy controls affecting their HRQoL. We found essential need for systemic psychiatric screening and management to help RA patients get rid of their sleep problems and improve their HRQoL.

**Keywords:** Sleep quality; HRQoL; Rheumatoid arthritis.

### 1-INTRODUCTION

**R**heumatoid arthritis (RA) is a chronic multisystem disease of unknown etiology,

characterized by inflammatory synovitis. It is a symmetric polyarthritis with uneven probability for deformation, involving peripheral joints and

the spine. It affects 1% of the population, being three times more common in females than in males. It usually appears between 35 and 50 years of age, and its onset relates to genetic predisposition and to its interaction with environmental agents (1). The inflammatory process can spread to other systems and organs, causing extra-articular symptoms affecting about 40% of the patients, with equal men and women affection and can appear at any age. (2)

Some predictors of extra-articular symptoms are: male gender, severe joint affection, low functional capacity, high levels of inflammatory markers and high titers of autoantibodies, such as rheumatoid factor (RF) and anti-cyclic citrullinated peptide antibody (Anti-CCP). (3)

Many psychological symptoms are experienced at the onset of RA like fatigue, depression and emotional disturbance. (4)

Sleep disturbance is a common feature and may aggravate the symptoms of fatigue.

However, Sleep problems occur in 54-70% of RA patients, comprising difficulty falling asleep, poor sleep quality, non-restorative sleep, insomnia, awakening during the night and excessive daytime sleepiness. (5)

Poor sleep is one of the most common loading symptoms and has weakening outcome on physical, emotional, intellectual function and well-being. Therefore, detecting influences causative to poor sleep quality and revising the effects of sleep quality on HRQoL in RA patients is very important. (6)

It was noticed that poor sleep quality may contribute to more pain, disease activity and mood disorders, causing a flow of dysfunction for patients suffering from RA. Also, it is recognized that many contributors, such as socioeconomic status, disease activity and psychological disorders may impress sleep health, and that is common in RA patients. (7)

## **2-Subjects and Methods:**

### **2.1. Study design and subjects:**

This study was carried out in Rheumatology and Rehabilitation Department, Faculty of Medicine, Zagazig University Hospitals from August 2017 till January 2019. This study was

carried on two groups: The Patient group included 30 patients suffering from rheumatoid arthritis and fulfilled the 2010 American College of Rheumatology/European League against Rheumatism classification criteria for RA (The 2010 ACR/EULAR criteria) (8) and the control group included 30 apparently healthy volunteers, they were age and sex matched with the patient group. Both patients and control were subjected to assessment of their sleep quality and its affection on their HRQoL. Informed consents were signed by the RA patients and healthy controls.

This study was approved by the institutional review board (IRB) of the faculty. Patients with Serious infection and any comorbid chronic disease such as DM, HPN, Cardiac, respiratory, gastrointestinal, endocrinal disease, neurological and psychiatric disease were excluded from the study.

The work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

### **2.2. Clinical assessment:**

- All patients were subjected to full history taking, thorough clinical examination, radiological and laboratory investigations including complete blood count (9), erythrocyte sedimentation rate (ESR) using westergren method recorded mm/hr. The reading of first hour is taken (10), CRP was detected by latex agglutination test (11), rheumatoid factor (RF) by QUANTA ELISA Lite TM RF IgM (12), anti-cyclic citrullinated peptide (anti-CCP) antibodies using ImmunoscanCCPlus test kit which is an enzyme-linked immunosorbent assay (ELISA), (13), liver and kidney functions.(14)

Rheumatoid arthritis disease activity was evaluated by DAS-28 (15)

Quality of life was evaluated by Health Assessment Questionnaire –Disability Index (HAQ-DI): An index measuring the quality of life related to health, derived from the longer HAQ. This index considers how arthritis has an impact on everyday life. The questionnaire is

designed to be completed by the patient himself, without the help of a doctor. (16)

Sleep quality was evaluated by Pittsburgh Sleep Quality Index (PSQI): It is used to measure the quality and patterns of sleep in the older adult. It differentiates “poor” from “good” sleep by measuring seven domains: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, and sleep disturbances, use of sleep medication, and daytime dysfunction over the last month (17)

Anxiety and depression was evaluated by Hospital Anxiety and Depression Scale (HADS). This questionnaire is designed to help doctors know how patients feel. Each item is read and a circle is put around the answer which comes closest to how patients have been feeling in the past week. Immediate reaction to each item will probably be more accurate than a long thought out response. Scores of 0-7 in respective subscales are considered normal, with 8-10 borderline and 11 or over indicating clinical 'cases' (18)

Pain was evaluated by visual analogue scale (VAS): Assessment of pain in the past week measured on an anchored horizontal 10 cm VAS, with “no pain” at one end (scored 0) and “very severe pain” at the other end (scored 10).(19)

### 2.3. Statistical methods.

The data were coded, entered and analyzed by SPSS program version 14 (statistical package for social sciences) data were summarized as mean  $\pm$  Standard deviation and percentage. T test was used for comparison of mean of the two groups, chi square for comparison of qualitative data Pearson's correlation test was used to test relation between two numeric variables. Multiple regression test to find out the most important variables affecting QOL.

Cut off level:  $P \leq 0.05$  = Significant (\*),  $P \leq 0.001$  = highly significant (\*\*)

### 3-Results:

#### **RA patients are classified according to sleep quality into 2 groups: good sleepers (PSQI<5 score) and poor sleepers (PSQI $\geq$ 5)**

In table (1): anxiety and depression were significantly higher in RA patients with poor sleep more than those with good sleep (59.1% and 54.5% respectively).

Table (2) showed that mean values of ESR and CRP were statistically significantly higher among poor than good sleepers. (Mean $\pm$ SD 33.43  $\pm$  19.26 and 16.91  $\pm$  6.83)

Table (3) showed that there was a significant association between poor sleep in RA patients and severe pain as severe VAS was 54.5%.

Also, there was a significant association between poor sleep in RA patients and severe HAQ as moderate to severe HAQ was 45.5%.

In table (4): disease activity mean values were statistically significantly higher among poor sleepers than good sleepers regarding DAS-28. (Mean $\pm$ SD=4.91 $\pm$ 1.22).

In table (5) mean values of HAQ components scores were statistically significantly higher among poor than good sleepers regarding dressing, reach and grooming (mean $\pm$ SD 1.65 $\pm$ .671, 1.75  $\pm$  .639 and 1.8  $\pm$  .768 respectively).

Chart (1) showed that 76.9% of RA patients with poor sleep were taking Methotrexate as a DMARD, Salazopyrine 11.5%, leflunamide 7.7% hydroxychloroquine was only used by 3.8% of RA patients with poor sleep.

While in RA patients with good sleep: Methotrexate was 50%, Salazopyrine and leflunamide was 25%, while hydroxychloroquine was 0%.

Chart (2) showed that rheumatoid factor (RF) (u/ml) positivity was higher than Anti-CCP as their mean values were 70% and 56.6% respectively.

**Table (1): Comparison between good (<5 score) and poor (≥5 score) sleepers in RA patients as regard anxiety and depression.**

characters	Good sleepers (<5 score) (N=8)		Poor sleepers (≥5 score) (N=22)		$\chi^2$ test	p-value
	No	%	No	%		
<b>Anxiety</b>						
Normal	5	62.5	3	13.6		
Borderline	1	12.5	6	27.3	7.165	<b>0.028*</b>
Cases	2	25	13	59.1		
<b>Depression</b>						
Normal	5	62.5	4	18.2		
Borderline	2	25	6	27.3	6.246	<b>0.044*</b>
Cases	1	12.5	12	54.5		

**Table (2): Sleep quality and mean values of laboratory profile.**

Laboratory profile	Good sleepers (<5 score) (N=8)	Poor sleepers (≥5 score) (N=22)	t-test	P-value
	mean±SD	mean±SD		
RBCs	3.98 ± .671	3.94 ± .734	.092	.928
WBCs	9.38 ± 2.29	8.18 ± 2.79	1.085	.287
PLT	281.6 ± 98.28	287.59 ± 88.05	.159	.875
ESR	16.5 ± 4.54	33.43 ± 19.26	2.436	<b>.021*</b>
CRP	10.72 ± 2.02	16.91 ± 6.83	2.502	<b>.018*</b>
ALT	16.99 ± 7.99	14.89 ± 4.58	.882	.386
AST	19.15 ± 2.99	19.31 ± 7.25	.060	.953
Albumin	3.98 ± .333	3.98 ± .452	.004	.997
Urea	12.88 ± 9.18	14.92 ± 12.68	.365	.718
Creatinine	.62 ± .189	.696 ± .217	.869	.392

WBCs: white blood cells

RBCs: red blood corpuscles

PLT: platelets

ESR: erythrocyte sedimentation rate

CRP: C- reactive protein

**Table (3) Comparison between good (<5 score) and poor (≥5 score) sleepers in RA patients as regard sleep and quality of life.**

Health and sleep scores	Good sleepers (N=8)	sleepers' (<5 score)	Poor sleepers (N=22)	(≥5 score)	$\chi^2$ test	p-value
	No	%	No	%		
<b>VAS score</b>						
Mild	5	62.5	3	13.6		
Moderate	2	25	5	22.7	<b>8.386</b>	<b>.039*</b>
Severe	1	12.5	12	54.5		
Very severe	0	0	2	9.1		
<b>HAQ score</b>						
Mild to moderate	0	0.0	7	31.8		
Moderate to severe	8	100.0	10	45.5	7.273	<b>.026*</b>
Severe to very severe	0	0.0	5	22.7		

VAS: visual analogue scale

HAQ: health assessment scale

**Table (4): RA disease activity and sleep quality.**

RA disease activity score	Good sleepers (<5 score) (N=8)	Poor sleepers (≥5 score) (N=22)	t-test	P-value
	mean±SD	mean±SD		
DAS-28	3.85±1.14	4.91±1.22	2.119	<b>0.043*</b>

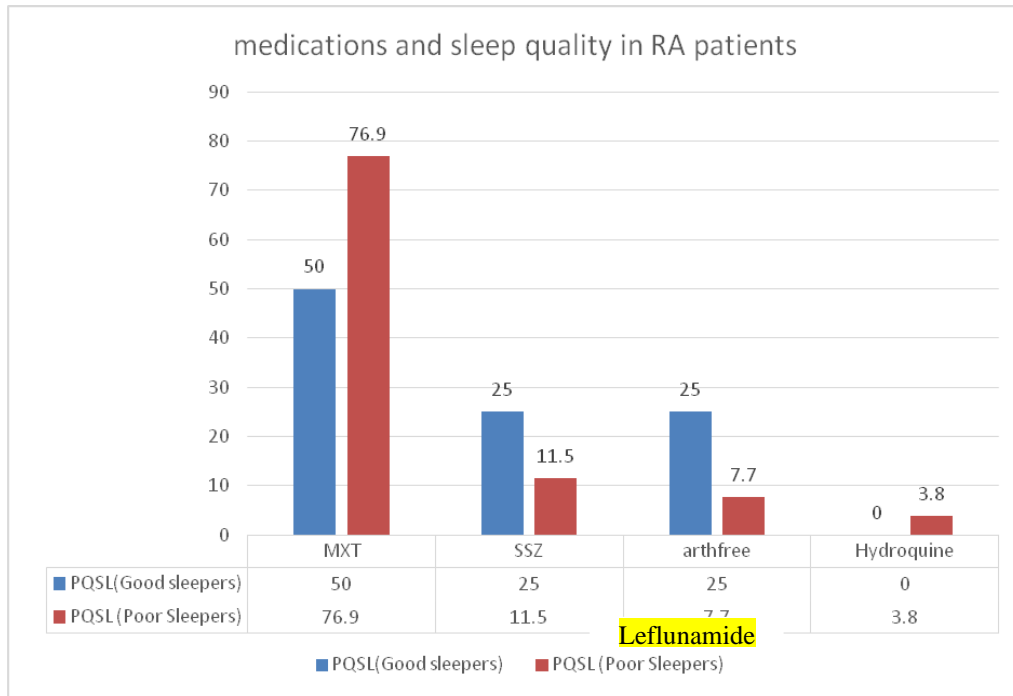
DAS: disease activity score

**Table (5) Comparison between good (<5 score) and poor (≥5 score) sleepers in RA patients as regard Health assessment components'.**

HAQ components scores	Good sleepers (<5 score) (N=8)	Poor sleepers (≥5 score) (N=22)	t-test	P-value
	mean±SD	mean±SD		
Dressing	0.75 ± .886	1.65±.671	2.927	<b>.007*</b>
Arising	1.38 ± .744	1.25 ± .639	.447	.659
Eating	1.38 ± .916	1.25 ± .786	.363	.720
Walking	1.75 ± 1.04	1.65 ± .745	.287	.776
Hygiene	1.38 ± .744	1.3 ± .657	.263	.795
Reach	1.25 ± .463	1.75 ± .639	2.114	<b>.047*</b>
Grip	1.13 ± .835	1.55 ± .605	2.206	<b>.044*</b>
Grooming	1.75 ± .463	1.8 ± .768	.171	.866

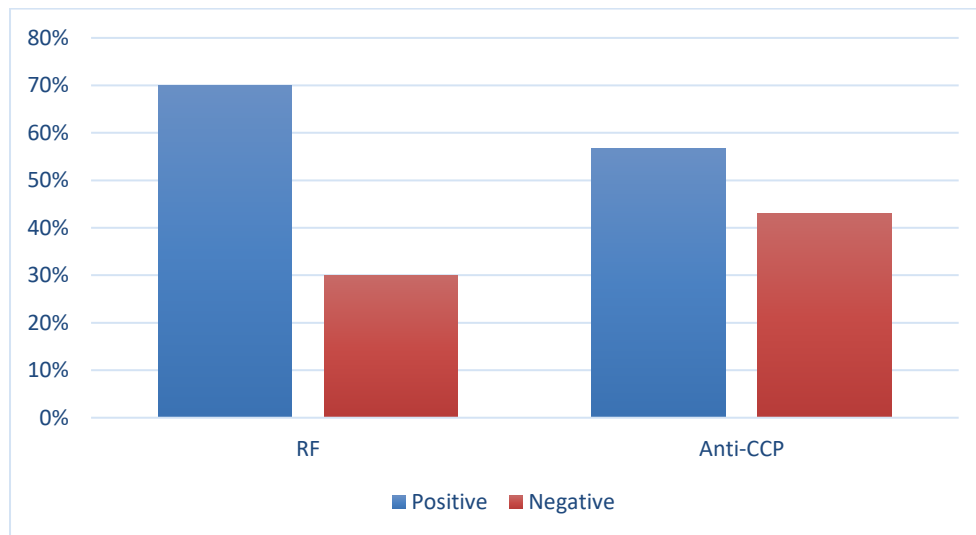
HAQ: health assessment questionnaire

**Figure (1): Medications and sleep quality among RA cases.**



Mtx: Methotrexate      SSZ: Salazopyrine  
 PSQI: Pittsburgh Sleep Quality Index      Leflunamide

**Figure (2): Percentage of RF and Anti-CCP among RA cases.**



RF: rheumatoid factor.      Anti-CCP: anti-cyclic citrulinated peptide

**DISCUSSION**

The aim of this study was to assess the characteristics of sleep quality in patients with RA and to investigate the association

between poor sleep quality and disease activity and to compare HRQL in RA patients according to their sleep quality.

We found that depression and Anxiety were significantly higher in RA compared to controls and this was agreed by *Kim et al.* who reported that disease activity and depression were dominant predictors of poor sleep quality in RA patients. (20)

We also observed that ESR and CRP levels were significantly higher in poor sleepers compared to good sleepers. In consistence with our finding, *Guo et al.* found that ESR, DAS28, VAS and HAQ were significantly higher in poor sleepers. However in disagreement with our findings, they found no significant difference in CRP, RF and Anti CCP. This may be due to treating active inflammation of patients in their study so inflammatory markers had no strict impact on sleep quality while other variables were not affected by this treatment. (21)

The prevalence of poor sleep quality presented in this study is similar with previous studies that show that 50%–70% of patients with RA have poor sleep quality as *Kim et al.* revealed that patients with RA have a higher risk for sleep disturbances compared with individuals without RA. (20)

It was found that mean values of HAQ components were statistically significantly higher among patients with poor sleep than with good sleep regarding dressing, reach and grooming (mean±SD 1.65±.671, 1.75 ± .639 and 1.8 ± .768 respectively) and this was in consistent with *Ji et al*, who stated that there was high significant negative correlation between quality of life in RA patients and the level of their functional disability. (22)

In this study we found that RA patients with a PSQI score  $\geq 5$  (poor sleepers) were significantly having synthetic DMARDs more frequently than RA patients with good sleep as 76.9% of RA patients were taking methotrexate, 11.5% of them were taking Salazopyrine, 7.7% were taking leflunamide and finally only 3.8% of RA patients were taking hydroxychloroquine.

These results were against *Huscher et al* who found no association between synthetic

DMARDs and sleep quality while examining sleep disturbance in RA patients. (23)

### 5-conclusion

We observed that 73% of RA patients have poor sleep quality compared with healthy controls which affect their HRQoL. We found essential need for systemic psychiatric screening and management to help RA patients get rid of their sleep problems resulting in improving their HRQoL.

**Conflict of Interest: no conflict of interest**

**Financial Disclosures: no financial disclosure**  
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