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Original Article

# Can rheumatoid arthritis affect sleep in Egyptian patients?

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ABSTRACT

*Aim of the work:* To investigate sleep problems in rheumatoid arthritis (RA) patients and to correlate sleep scores with disease characteristics and activity.
*Patients and methods:* 100 RA patients and 40 matched controls were included. Disease activity score (DAS28), visual analogue scale (VAS) for pain, modified health assessment questionnaire (MHAQ) and medical outcomes study short form-36 (SF-36) were assessed and the van der Heijde-modified Sharp score (vdHSS) calculated. The Pittsburgh Sleep Quality Index (PSQI) was used to investigate the sleeping habits, sleep difficulty was assessed using the Athens Insomnia Scale (AIS) and daytime sleepiness was measured using the Epworth Sleepiness Scale (ESS).
*Results:* The patients were 84 females and 16 males (F:M 5.25:1) with mean age of 48.1 ± 12.4 years, disease duration of 6.9 ± 5.9 years, DAS28 was 4.3 ± 1.4, MHAQ was 0.95 ± 0.6 and VAS was 45.2 ± 21.1. The sleep scores PSQI, AIS and ESS were significantly increased in patients (6.98 ± 2.8, 9.6 ± 4.4 and 7.4 ± 2.6) compared to control (2.6 ± 1.9, 2.7 ± 1.8 and 3.3 ± 2.03 respectively; p = 0.01 each). Sleep scores tended to be lower in females and were significantly higher in those with positive C-reactive protein. Rheumatoid factor positive patients and those not receiving methotrexate had significantly higher PSQI and AIS scores. Sleep scores significantly correlated with age, erythrocyte sedimentation rate, DAS28, VAS, MHAQ and vdHSS and negatively with SF-36 physical component score (PCS) (p = 0.01 for all). Disease duration, DAS28, VAS and SF36 (PCS) were significant risk factors for sleep problems.
*Conclusion:* A high frequency of sleep disturbances in RA patients was observed. Interplay of pain, fatigue, activity and disability may lead to poor sleep quality.


## 1. Introduction

Rheumatoid Arthritis (RA) is a chronic inflammatory autoimmune disease characterized by joint pain and swelling, morning stiffness, fatigue, depression, sleep problems and disability [1]. It has been reported that 54–70% of RA patients report sleep disturbances, including difficulty falling asleep, poor sleep quality, non-restorative sleep, awakenings during the night and excessive daytime sleepiness [2]. Sleep problems may share to the pain, disease activity, stiffness, fatigue and mood troubles in RA patients [3].

Sleep problems may lead to fatigue, which in turn may decrease work productivity, the ability to accomplish daily activities, and social functioning in patients with RA [4]. Sleep quality and daytime sleepiness are important and meaningful patient-reported outcomes [5] that can be measured using specific, validated methods [6]. Particularly, quality of sleep is a complex multidimensional outcome that can be related to one or more of the following components: prolonged sleep latency, decrease sleep efficiency and/or an increase in the number of awakenings during the night, arousals, or wake time after sleep onset [7]. The RA disease activity may be a common factor for sleep problems by producing pain and release of cytokines that affect many neuro-biologic factors [8]. Sleep disturbances in RA patients may be associated with other factors not related to disease activity, such as fatigue and depression [4].

Questionnaires are often the tools of choice to assess sleep [6]. The patient-reported measures include the Pittsburgh Sleep Quality Index (PSQI), which assesses perceived sleep quality, the Epworth Sleepiness Scale (ESS) which measures daytime sleepiness [9] and the Athens Insomnia Scale (AIS) that assesses sleep difficulty [10].

The aim of the present work, to investigate sleep problems in RA patients and to study the relation of the sleep scores with the disease activity and characteristics.

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## 2. Patients and methods

This study was carried out on 100 adult RA patients and 40 age and sex matched healthy volunteers as a control group were recruited from Rheumatology and Internal Medicine departments at Beni-Suef University Hospital from December 2013 to January 2015. All subjects fulfilled 2010 American College of Rheumatology/European League Against Rheumatism classification criteria for RA [11]. Informed consent was obtained from the patients and controls. The study was performed with the approval of local ethics committee. Exclusion criteria included, past history of major depressive disorder, psychiatric illness, substance abuse, concurrent diagnosis of fibromyalgia, a lifestyle that placed the patient at serious risk of sleep disturbances (i.e., shift work or night work), traveling through more than 3 time zones during the week before screening or during the study, a body mass index >35, sleep-related breathing disorders and past or present history of sleep medications or anti-histamine therapy.

All patients were subjected to full history taking, clinical examination, laboratory investigations including complete blood count (CBC), erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), rheumatoid factor (RF) and anti-cyclic citrullinated peptide (ACCP) antibodies [12] and radiological scoring of plain X-ray of both hands and feet using van der Heijde-modified Sharp Score (vdHSS) [13]. Disease Activity Score 28 (DAS 28) [14], modified health assessment questionnaire (MHAQ) [15] and pain intensity according to the visual analogue scale (VAS) [16] were assessed. Health status was assessed using the medical outcomes study Short Form-36 (SF-36) [17] comprising the physical (PCS) and mental (MCS) component scores.

Sleep scales including the Pittsburgh Sleep Quality Index (PSQI) [18], Athens Insomnia Scale (AIS) [19] and Epworth Sleepiness Scale (ESS) [20] were measured for all patients. The PSQI [18] measures sleep quality over the past 4 weeks via 7 sleep subscales: quality, latency, duration, habitual sleep efficiency, sleep disturbances (number of awakenings during the night and number of arousals), use of sleep medication and daytime dysfunction. Each subscale is rated (0–3) where 3 reflects a more severe sleep complaint. Score range: 0–21 points, with higher scores indicating worse sleep quality. A total PSQI score $\geq$5 is indicative of a poor sleeper. The AIS [19] measures sleep difficulty and its items assess sleep induction, night time and early morning awakenings, total sleep duration, overall sleep quality and the effect of nocturnal sleep disturbance on daytime performance. Each item is scored from 0 (no problem) to 3 (very serious problem), corresponding with the experience of sleep difficulty in each item for at least 3 times a week, during the last month. Total scores range from 0 (absence of any sleep-related problem) to 24 (the most severe degree of insomnia), with a cut off score of $\geq$6 for a diagnosis of insomnia. The ESS [20] measures excessive day time sleepiness over the past 2 weeks. Respondents are asked how likely they are to doze in the following situations: sitting and reading, watching television, sitting inactive in a public place (e.g., a meeting), as a passenger in a car for an hour without a break, lying down to rest in the afternoon when circumstances permit, sitting and talking to someone, sitting quietly after a lunch without alcohol and in a car while stopped for a few minutes in traffic. Each situation is scored from 0 (would never doze) to 3 (high chance of dozing). Score range: 0–24, with higher scores indicating greater daytime sleepiness. A score of $\geq$9 indicates excessive daytime sleepiness.

*Statistical analysis:* Data were analyzed using SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA) version 20. Data were described in terms of range, mean ± standard deviation, frequencies and percentages when appropriate. Cross tabulation test: was used for comparison between percentage values. Student *t*-test: was used for comparison between means of two groups with a normal distribution. Mann-Whitney or Kruskall-Wallis tests: were used to compare nonparametric variables. Correlation was carried out using the Spearman's correlation test. Multiple linear regression analysis was performed to detect independent predictors for the occurrence of sleep disturbances. We used sleep scores as dependent variables. Significance was considered at p-value < 0.05.

## 3. Results

The 100 RA patients included 84 females and 16 males (F:M 5.25:1) with a mean age of 48.1 ± 12.4 years (21–75 years), disease duration of 6.9 ± 5.9 years (0.25–30 years) and morning stiffness of 26.4 ± 33.5 min (0–120 min). The 40 control were matched for gender: 34 females (85%) and 6 males (15%) (F:M 5.7:1) (p = 0.62) and age 42.4 ± 12.4 years (24–65 years) (p = 0.08). The mean DAS28 was 4.3 ± 1.4 (1.7–7.3) MHAQ was 0.95 ± 0.6 (0–2.3) and VAS was 45.2 ± 21.1 (10–85). The mean PCS was 31.4 ± 11.7 (6–53.8) and MCS was 44.3 ± 9.9 (5–59.6).

In RA patients, the mean PSQI score was 6.98 ± 2.8 (1–13), AIS score was 9.6 ± 4.4 (0–19) and ESS score was 7.4 ± 2.6 (2–15). These scores were significantly higher than in the control; mean PSQI was 2.6 ± 1.9 (0–5), AIS was 2.7 ± 1.8 (0–5) and ESS was 3.3 ± 2.03 (0–6) (p = 0.01 for all scores) (Fig. 1). Comparing the sleep scores (PSQI, AIS and ESS) among RA patients according to the gender, positivity of RF, ACCP and CRP as well as medications received are shown in Table 1. The sleep scores tended to be lower in females than in males. RF positive patients had significantly higher PSQI and AIS scores and a tendency to a higher ESS score compared to RF negative patients. The scores were comparable between patients with positive and negative ACCP. Scores were significantly higher in CRP positive patients. Patients receiving methotrexate (MTX) had significantly lower PSQI and AIS scores and a tendency to a lower ESS score than those not. Scores tended to be higher in those receiving steroids.

Correlations between the sleep scores values in the RA patients with some of demographic, clinical, laboratory and radiographic characteristics of the disease are shown in Table 2 and graphically presented in Fig. 2. Multiple linear regression analysis revealed a

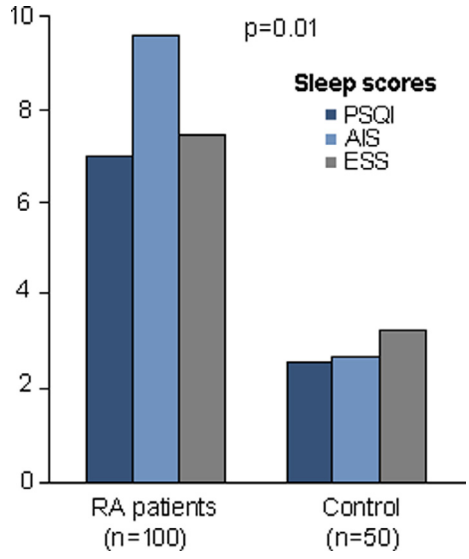


**Fig. 1.** The mean sleep scores PSQI, AIS and ESS in rheumatoid arthritis (RA) patients and control.

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