



Les troubles du sommeil au cours des rhumatismes chroniques : l'activité de la maladie est-elle le principal facteur déterminant ?

Sleep disturbances in chronic rheumatic diseases: Is disease activity the major determinant factor?

Wafa Hamdi, Mohamed Anis Souissi, Hanene Lassoued Ferjani, Kaouther Maatallah, Ines Cherif, Dhia Kaffel.

*Rheumatology department- Mohammed Kassab National Institute of Orthopaedics, La Mannouba- University of Tunis El Manar
Faculty of Medicine of Tunis,*

RÉSUMÉ

Les troubles du sommeil sont étroitement liés aux douleurs chroniques, en particulier chez les patients atteints de rhumatismes chroniques inflammatoires et dégénératifs.

Objectifs : Décrire le profil de sommeil au cours des rhumatismes chroniques inflammatoires et dégénératifs, et évaluer la part de l'activité de la maladie dans les troubles du sommeil au cours de ces rhumatismes

Méthodes : Nous avons mené une étude comparative entre 2 groupes de patients : le premier atteint de polyarthrite rhumatoïde (PR), le second présentant une gonarthrose primitive du genou. Les données anamnestiques ainsi que les données de l'examen physique et biologiques ont été rapportées. Tous nos patients ont répondu à des auto-questionnaires évaluant le sommeil (Medical Outcome Study Sleep Scale), la dépression (Beck Depression Inventory) et l'anxiété (Beck Anxiety Inventory).

Résultats : Le groupe PR était réparti en 54 femmes et 16 hommes avec un âge moyen de 51,9 ans. La PR évoluait en moyenne depuis 6,9 ans. Une altération de tous les domaines de sommeil a été mise en évidence au cours de la PR. Le groupe gonarthrose était réparti en 12 hommes et 28 femmes avec un âge moyen de 57,5 ans. L'ancienneté moyenne de la gonarthrose était de 4 ans. Les domaines les plus perturbés dans ce groupe étaient la somnolence et les troubles du sommeil. L'analyse multivariée a montré que les facteurs de risque indépendamment liés à la PR étaient : l'activité de la maladie, la gêne fonctionnelle, la dépression, l'anxiété et l'IMC. Le score d'activité de la PR était le seul paramètre influençant de tous les domaines du sommeil.

Conclusion : L'activité de la maladie est un facteur de risque indépendamment liée aux troubles du sommeil dans la polyarthrite rhumatoïde. Les troubles de l'humeur et l'obésité perturbent également plusieurs domaines du sommeil. Ces facteurs doivent être pris en compte dans la prise en charge des rhumatismes chroniques.

Mots clés : Sommeil ; polyarthrite rhumatoïde ; arthrose ; inflammation ; dépression ; anxiété.

SUMMARY

Sleep disturbances are closely related to chronic pain processes, especially in patients with inflammatory and mechanical joint diseases.

Objectives: This study aims to report sleep characteristics in patients with rheumatoid arthritis (RA) and knee osteoarthritis also to determine the responsibility of disease activity in the occurrence of sleep disturbances during chronic rheumatic diseases.

Methods: We conducted a comparative study between two groups of patients: the first with RA, the second with primary knee osteoarthritis. We reported sociodemographic and medical data (clinical and biological inflammatory syndrome data). Then, we assessed depression, anxiety, and sleep disturbances with respectively Beck Depression Inventory, Beck Anxiety Inventory and Medical Outcome Study Sleep Scale (MOS-SS).

Results: Seventy RA patients aged 51.9 years, with an average of 77.1% female were studied. The mean disease duration was 6.9 years. All sleep domains were altered in these patients. Forty patients with knee osteoarthritis aged 57.5 years with an average of 70% female were included. The mean disease duration was 4 years. The most impaired domains in this group were somnolence and sleep disturbance. Multivariate analysis concluded that risk factors independently related to RA were: disease activity score, functional disability, depression, anxiety, and body mass index. Disease activity score were the only parameter to influence all domains of sleep.

Conclusion: So we result that disease activity is a risk factor independently related to sleep disturbances in rheumatoid arthritis. Furthermore, mood disorders and obesity also deteriorate several sleep domains. These factors must be considered in the management of chronic rheumatic disorders.

Keywords: Sleep; rheumatoid arthritis; osteoarthritis; inflammation; depression; anxiety.

Correspondance

Dhia Kaffel

Rheumatology department- Mohammed Kassab National Institute of Orthopaedics, La Mannouba
eldhia@gmail.com

INTRODUCTION

Sleep disturbances are closely related to chronic pain processes, especially chronic rheumatic diseases. However, they are often underestimated and poorly managed (1,2). During rheumatoid arthritis (RA) associated to an atlantoaxial luxation, obstructive sleep apnea prevalence varies from 53% up to 79% against 9 to 28% in the general population (3,4). Furthermore, the impact of sleep disturbances on well-being and physical abilities of patients with chronic inflammatory rheumatism is confirmed. The disease increases fatigue and reduce the pain perception threshold (5). In degenerative joint diseases such as knee osteoarthritis, sleep disturbances are also common, aggravate pain and rush the deterioration of the quality of life (6). Otherwise, there is a lack of data in the medical literature on the association of disease activity with Sleep disturbances. Thus, screening and management of sleep disturbances during chronic joint diseases seem necessary since they allow an improvement of patient's quality of life.

This study aimed to report sleep characteristics in patients with RA and knee osteoarthritis and to determine the responsibility of disease activity in the occurrence of sleep disturbances during chronic rheumatic diseases.

METHODS

Study design:

We performed a comparative study over a 12-month period. It consisted on a comparison between two groups of patients: the first with rheumatoid arthritis according to 1987 ACR criteria (7), the second with symptomatic primary knee osteoarthritis. Patients were recruited during a hospitalization or during outpatient clinic visits in the Department of Rheumatology of the Kassab Institute of Orthopedics in Ksar Said, Tunisia. Non-inclusion criteria were age under 18, patients with troubles of understanding questions, history of cancer, associated fibromyalgia or use of medications affecting sleep.

Sociodemographic and medical data:

For all patients, gender, age, body mass index (BMI), marital status, education level and household income level were gathered during screening assessments.

For Rheumatoid Arthritis subjects, we collected clinical parameters (disease duration, morning stiffness duration, pain assessment according to 100-mm visual analogic scale (PA 100-mm VAS), patient global assessment (PGA

100-mm VAS), tender joints count (TJC), swollen joints count (SJC)), disease evaluation tools (disease activity score in 28 joints: DAS28 by calculating a composite score derived from TJC, SJC, erythrocyte sedimentation rate (ESR) and PGA (8); health assessment questionnaire disability index: HAQ-DI (9), assessing functional capacity and limitations), extra-articular manifestations, radiographic evaluation (structural damages, screening for atlantoaxial luxation, hip arthritis, Van Der Heijde-modified Total Sharp Score (10) (TSS)), biologic parameters (ESR and C-reactive protein (CRP)) and previous and current therapeutics.

For knee osteoarthritis subjects, we collected clinical parameters (disease duration, pain assessment (PA 100-mm VAS), measurement of knee flexion/extension angles, Lequesne knee score (11)) and radiographic evaluation according to Kellgren and Lawrence classification (12).

The structural damages were evaluated by 2 rheumatologists.

Psychometric evaluation scales:

- Beck Depression Inventory (BDI): Depression was assessed by BDI (13). It is a patient self-report questionnaire. It is a reproducible psychometric test, used in everyday practice to measure the severity of depression. This self-report questionnaire includes 21 items each rated from 0 to 3. Depression is considered minimal when score varies between 0 and 3, mild between 4 and 7, moderate between 8 and 15 and severe beyond 16 (14).
- Beck Anxiety Inventory (BAI): Anxiety was assessed by BAI (15). This is also a reproducible psychometric test measuring the severity of anxiety. This questionnaire includes 21 items each rated from 0 to 3. Anxiety is considered minimal when score varies between 0 and 17, moderate between 18 and 24 and severe beyond 25 (16).
- Sleep evaluation: Medical Outcome Study Sleep Scale (MOS-SS) questionnaire is used to assess sleep disturbances (17). The MOS-SS is a 12-item questionnaire exploring key constructs of sleep during the last four weeks, with derived subscales for the following domains: sleep adequacy (2 items), sleep disturbance (4 items), somnolence (3 items), snoring (1 item), awakening due to short of breath or headache (1 item) and quantity of sleep (1 item). Additionally, two indexes can be generated: 6-item Sleep Problem Index I (SP I) and 9-item Sleep Problem Index II (SP II) which assess overall sleep problems. They include the 4-sleep disturbance items

and the 2-sleep adequacy items, 2 of the somnolence items, and the awakening due to short of breath/headache item. The difference between the two indexes is that the overlapping items have been eliminated in the SP I.

Statistical analysis:

The data was entered using the Excel software (Microsoft Office 2007) and analyzed using the Statistical Package for the Social Sciences software (SPSS, French version 18.0). In comparing averages, we used analysis of variance (ANOVA). The comparison of percentages was performed by Pearson's Chi-2 test and by Fisher's exact test if the Chi-2 was not applicable. For correlations, we used Pearson's r coefficient. Significance for all statistical tests was set at $p < 0.05$. Univariate analysis was performed, and the knee osteoarthritis group was used as a control group. Since MOS-SS variables were continuous, we considered the medians of the control group for sleep variables as cut off to obtain dichotomous variables. T

hat allows us to change them from quantitative variables to qualitative variables with two classes: '≤ median of controls' versus '> median of controls'. Similarly, disease parameters were changed from quantitative variables to qualitative variables. This method allowed us to calculate crude odds ratios.

Multivariate logistic regression analysis was also performed to identify risk factors independently related to RA. This method allowed us to calculate adjusted odds ratios, measuring the specific role of each factor.

Our study was approved by the "KASSAB Ethics Committee" under number: 102/12.

All participants provided informed consent before participating in the study.

RESULTS

Rheumatoid arthritis group:

Seventy RA patients participated in the study with a male-to-female gender ratio of 0.29. The mean age was 51.9 ± 12.2 years and the mean BMI was 26 ± 3.4 Kg/m². No patient presented atlantoaxial luxation. RA was deforming in 27.1% of cases. A biological inflammatory syndrome was noted in 91% of cases. RA was seropositive in 75% of cases. ACPAs were positive in 27% of cases. Antinuclear antibodies were positive in 13% of cases with an average rate of 1/200. Table 1 summarizes clinical, radiological, biological, and psychometric parameters.

Depressive symptoms in the severe score range was

noted in 23.3% of patients with RA and severe anxiety in 16.2% of them. The study revealed an alteration of all sleep domains in RA patients. Most altered domains were sleep inadequacy, sleep disturbance and somnolence. DAS28 and HAQ were positively correlated with all areas of the MOS-SS and negatively with the quantity of sleep. The PA 100-mm VAS was positively correlated with the areas of sleep disturbance, awakening due to short of breath/headache, somnolence and overall SP I and SP II scores, and negatively correlated with the quantity of sleep. A significant positive correlation was found between ESR and the overall score SP II. We did not find any significant correlation between CRP and sleep disturbance.

Table 2 highlights the correlations between sleep domains and RA patients' characteristics.

Table 1. Clinical, radiological, biological, and psychometric characteristics of patients with RA

| RA (n=70) parameters | Mean ± Standard Deviation |
|-----------------------------------|---------------------------|
| Disease duration (years) | 6.9 ± 8.4 |
| PA 100-mm VAS | 49 ± 21 |
| Tender joints count (TJC) | 7.8 ± 7.5 |
| Swollen joints count (SJC) | 3.9 ± 5.2 |
| DAS28 | 4.8 ± 1.5 |
| HAQ | 1.4 ± 0.7 |
| Modified Total Sharp Score (mTSS) | 107.1 ± 99.5 |
| ESR (mm/hour) | 41.6 ± 28.5 |
| CRP (mg/Liter) | 20.1 ± 22 |
| Psychometric evaluation | |
| Beck Depression Inventory (BDI) | 16.5 ± 10.2 |
| Beck Anxiety Inventory (BAI) | 16.2 ± 9.5 |

PA : pain assessment ; DAS28 : disease activity score 28 joints ; HAQ : health assessment questionnaire ; ESR : erythrocyte sedimentation rate ; CRP : c-reactive protein

Knee osteoarthritis group:

A total of 40 subjects with knee osteoarthritis were a subject for this study with a male-to-female gender ratio of 0.42. The mean age was 57.5 ± 12.9 years and the mean BMI was 29.6 ± 5.8 Kg/m². Radiographic assessment found grade 3 or 4 knee osteoarthritis according to Kellgren and Lawrence classification in 17.5% of patients. Table 3 illustrates clinical and psychometric characteristics. Depressive symptoms in the severe score range was noted in 63% of patients and severe anxiety in 20% of them. The most impaired MOSSS domains in these patients were

Table 2. Correlations between MOS-SS Domains and RA patients' characteristics

| Medical Outcome Study Sleep Scale (MOS-SS) domains | Mean \pm SD | DAS28 | PA | TJC | SJC | CRP | HAQ | mTSS | BDI | BAI | BMI |
|--|-----------------|---------------------|---------------------|---------------------|---------------------|---------------------|---------------------|---------------------|---------------------|---------------------|---------|
| Sleep adequacy | 58 \pm 22.5 | r=0.488 p<0.001 | r=0.197 p=0.102 | r=0.233 p=0.052 | r=0.213 p=0.076 | r=0.104 p=0.392 | r=0.494 p<0.001 | r=0.223 p=0.179 | r=0.484 p<0.001 | r=0.351 p=0.003 | p=0.248 |
| Sleep disturbance | 55 \pm 21.1 | r=0.631 p<0.001 | r=0.280 p=0.019 | r=0.278 p=0.020 | r=0.165 p=0.172 | r=0.185 p=0.126 | r=0.568 p<0.001 | r=0.350 p=0.031 | r=0.493 p=0.001 | r=0.493 p=0.001 | p=0.828 |
| Somnolence | 53.3 \pm 20.5 | r=0.613 p<0.001 | r=0.372 p=0.002 | r=0.382 p=0.001 | r=0.276 p=0.021 | r=0.079 p=0.515 | r=0.523 p<0.001 | r=0.331 p=0.043 | r=0.485 p<0.001 | r=0.443 p<0.001 | p=0.174 |
| Snoring | 41.1 \pm 36.5 | r=0.380 p=0.001 | r=0.192 p=0.111 | r=0.299 p=0.012 | r=0.167 p=0.168 | r=-0.137 p=0.257 | r=0.402 p=0.001 | r=0.084 p=0.617 | r=0.209 p=0.082 | r=0.237 p=0.049 | p=0.031 |
| Awakening due to short of breath/headache | 39.7 \pm 33.6 | r=0.510 p<0.001 | r=0.291 p=0.015 | r=0.345 p=0.003 | r=0.596 p=0.065 | r=0.056 p=0.643 | r=0.547 p<0.001 | r=0.284 p=0.084 | r=0.467 p<0.001 | r=0.439 p<0.001 | p=0.215 |
| Quantity of sleep (hours) | 4.9 \pm 1.3 | r=-0.459 p<0.001 | r=-0.318 p=0.007 | r=-0.359 p=0.002 | r=-0.119 p=0.326 | r=0.012 p=0.921 | r=-0.437 p<0.001 | r=-0.149 p=0.372 | r=-0.461 p<0.001 | r=-0.337 p=0.004 | p=0.056 |
| SP I | 55.1 \pm 20.2 | r=0.647 p<0.001 | r=0.318 p=0.007 | r=0.342 p=0.004 | r=0.180 p=0.135 | r=0.165 p=0.172 | r=0.630 p<0.001 | r=0.422 p=0.008 | r=0.593 p<0.001 | r=0.458 p<0.001 | p=0.469 |
| SP II | 53.2 \pm 20.9 | r=0.713 p<0.001 | r=0.336 p=0.004 | r=0.272 p<0.001 | r=0.254 p=0.034 | r=0.132 p=0.275 | r=0.672 p<0.001 | r=0.352 p=0.047 | r=0.569 p<0.001 | r=0.454 p<0.001 | p=0.417 |

PA : pain assessment; DAS28 : disease activity score 28 joints ; HAQ : health assessment questionnaire ; TJC : tender joints count ; SJC : swollen joints count ; CRP : c-reactive protein ; mTSS : modified total Sharp score ; BAI : Beck Anxiety Inventory ; BDI : Beck Depression Inventory ; BMI : body mass index ; SP I : sleep problem index I ; SP II : sleep problem index II ; SD : standard deviation

somnolence and sleep disturbance. The duration of Knee osteoarthritis was positively correlated with all areas of the MOS-SS except Quantity of sleep. The intensity of knee pain was positively correlated with the domains of sleep disturbance, somnolence, sleep adequacy, awakening due to short of breath/headache, as well as the overall SP I and SP II scores and negatively correlated with quantity of sleep. A significant positive correlation was found between the Lequesne index and the domains of somnolence, awakening due to short of breath/headache as well as the overall SP I and SP II scores. Correlation between osteoarthritis disease parameters and MOS-SS domains is presented in Table 3.

Comparison between RA and OA:

A comparison for both groups (RA, OA) (table 4) and a multivariate logistic regression analysis was performed for all variables, factors significantly (crude OR) and independently (adjusted OR) related to sleep disturbances in RA patients were mentioned in Table 5. The disease activity assessed by the DAS28 was a risk factor for sleep

disorders in most areas of the MOS-SS except sleep quantity. The functional impairment assessed by HAQ was a risk factor for sleep disorders in the areas of Sleep adequacy, headache/ awakening due to short of breath, snoring and overall SPI and SPII scores. Depression assessed by the BDI was a risk factor for sleep disorders in somnolence. Anxiety assessed by BAI was a risk factor for sleep disorders in headache/ awakening due to short of breath. BMI was an independent risk factor for sleep disorders in snoring. The difference between PA 100-mm VAS in RA and OA was not significant ($p = 0.070$) (table 4), so pain was not a confounding factor.

DISCUSSION

Our study concludes that disease activity is a risk factor independently related to sleep disturbances in rheumatoid arthritis. Our results identified various risk factors involved in the occurrence and worsening of sleep disturbances in rheumatoid arthritis and knee osteoarthritis. Mood disorders, obesity and mainly disease severity are the most influencing factors.

Table 3: Correlations between MOS-SS Domains and Knee osteoarthritis patients' characteristics

| | | Disease duration (years) | PA 100mm VAS | LAI | BDI | BAI |
|--|-----------------|---------------------------|---------------------------|---------------------------|---------------------------|---------------------------|
| | Mean ±SD | 4± 0 | 55 ±17 | 11.2 ±4.8 | 18.6 ±10.7 | 15.6 ±11.1 |
| Parameters Sleep adequacy | 35.4 ±16.8 | r=0.333 p=0.036 | r=0.430 p=0.006 | r=0.287 p=0.072 | r=0.173 p=0.285 | r=0.692 p<0.001 |
| Sleep disturbance | 37.7 ±16.5 | r=0.484 p=0.002 | r=0.418 p=0.045 | r=0.288 p=0.071 | r=0.269 p=0.093 | r=0.571 p=0.004 |
| Somnolence | 36.1 ±17.7 | r=0.568 p<0.001 | r=0.321 p=0.044 | r=0.321 p=0.004 | r=0.215 p=0.184 | r=0.664 p=0.002 |
| Snoring | 47 ±25.8 | r=0.410 p=0.009 | r=0.219 p=0.174 | r=0.219 p=0.174 | r=0.302 p=0.059 | r=0.250 p=0.303 |
| Awakening due to short of breath/headache | 33.2 ±18.3 | r=0.372 p=0.018 | r=0.526 p<0.001 | r=0.590 p<0.001 | r=0.609 p<0.001 | r=0.634 p=0.001 |
| Quantity of sleep (hours) | 6.9 ±1.7 | r=-0.245 p=0.128 | r=-0.063 p=0.007 | r=-0.187 p=0.248 | r=0.158 p=0.329 | r=-0.316 p=0.480 |
| SP I | 38.9 ±16 | r=0.579 p<0.001 | r=0.416 p=0.008 | r=0.410 p=0.009 | r=0.270 p=0.092 | r=0.642 p=0.001 |
| SP II | 38.5 ±14.1 | r=0.51 p=0.001 | r=0.428 p=0.006 | r=0.413 p=0.008 | r=0.301 p=0.059 | r=0.605 p=0.003 |

BAI : Beck Anxiety Inventory ; BDI : Beck Depression Inventory ; LAI : Lequesne algofunctional index ; PA : pain assessment ; VAS : visual analogic scale ; SP I : sleep problem index I ; SP II : sleep problem index II ; SD : standard deviation

Table 4: Comparison of variables between rheumatoid arthritis and osteoarthritis groups BMI : body mass index ; SP I : sleep problem index I ; SP II : sleep problem index II

| | RA | OA | P |
|---|-------------|-------------|-------------------|
| BMI | 25.9 ± 3.4 | 27.2 ±2.4 | <10 ⁻³ |
| Anxiety | 16.2 ± 9.5 | 15.6 ± 11.1 | 0.82 |
| Depression | 16.5 ± 10.2 | 10.4 ± 9.1 | 0.31 |
| PA 100-mm VAS | 49 ± 21 | 55.8 ± 13.8 | 0.07 |
| Sleep disturbance | 55 ± 21.1 | 37.7 ± 16.5 | <10 ⁻³ |
| Snoring | 41.4 ± 36.5 | 47 ± 25.8 | 0.4 |
| Headache/ Awakening due to short of breath | 39.7 ± 33.6 | 33.2 ± 18.3 | 0.26 |
| Sleep adequacy | 58 ± 22.5 | 35.4 ± 16.8 | <10 ⁻³ |
| Somnolence | 53.3 ± 20.6 | 36.1 ± 17.7 | <10 ⁻³ |
| Quantity of sleep | 4.9 ± 1.3 | 6.9 ± 1.7 | <10 ⁻³ |
| SP I | 55.1 ± 20.2 | 38.9 ± 16 | <10 ⁻³ |
| SP II | 53.2 ± 20.9 | 38.5 ± 14 | <10 ⁻³ |

This comparative study confirmed the high frequency of sleep disturbances in both inflammatory and degenerative rheumatism. Sleep disturbances were multifactorial, related mainly to specific parameters of each disease and elevated symptoms of mood disorders. These data were confirmed by most of studies in chronic rheumatic diseases such as Sjögren syndrome (18) and systemic lupus erythematosus (19). Indeed, a vicious circle is created between these factors. The severity of the articular disease will increase the risk of depression and anxiety disorders. On the other hand, the depression will aggravate the impact of the chronic disease on the quality of life and adherence to treatment. All these factors will be responsible for sleep disturbances due to both disease activity and mood disturbances, finally, sleep disturbances will alter the general perception of the patient's health status. In our study, multivariate logistic regression analysis identified independent risk factors of sleep disturbances in RA: disease activity, functional disability, depression, anxiety, and BMI. A strong correlation between DAS28 and sleep disturbances was found. Many authors have shown a close association between these parameters (20,21). During a rheumatoid arthritis flare, sleep disturbances are more important compared to the

Table 5: Uni and multivariate analysis: risk factors of sleep disturbances independently related to RA

| Parameters | DAS 28 | | HAQ | | Depression | | Anxiety | | BMI | |
|--|--------------------|-----------------|--------------------|----------------|--------------------|----------------|--------------------|----------------|--------------------|----------------|
| | Crude OR 95% CI | Adjusted OR | Crude OR 95% CI | Adjusted OR | Crude OR 95% CI | Adjusted OR | Crude OR 95% CI | Adjusted OR | Crude OR 95% CI | Adjusted OR |
| Sleep disturbance | 15.4 [3.4-68.6] | 12 [2.4 - 60.3] | - | - | 3.6 [0.9-14.1] | - | 3.3 [0.6-16.6] | - | - | - |
| Snoring | 10 [1.2-82.6] | 3 [0.2 - 32.6] | 3.7 [1.3-10.3] | 4.2 [1.4-12.3] | 6[1.2-29.1] | - | 2.4 [0.9-6.7] | - | 5.3 [0.7-38.3] | 6 [1-37.7] |
| M O S Headache/ - S S Awakenings due to short of breath | 15.3 [1.8-126.1] | 4.1 [0.4-40.5] | 8.2 [2.8-24.2] | 6.5 [2.1-20.5] | 9.4 [1.9-45.6] | - | 6.5 [2.2-19.3] | 4.9 [1.5-16.2] | - | - |
| D O M A I N S Sleep adequacy | 23.4 [5.2-104.1] | 15.7[2.9-85.2] | 7.4 [1.5-36.3] | 2.2 [0.3-14.4] | 5.2[1.4-18.5] | - | 2.7 [0.6-10.9] | - | - | - |
| Somnolence | 8.9 [2.1-37] | 4.4 [1 -22] | 4.9 [1-25] | 0.7 [0.07-7.8] | 9.7[2.3-40.1] | 5.6 [1.1-26.8] | 0.5 [0.4-0.6] | - | - | - |
| Quantity of sleep | 0.2 [0.01-3.6] | - | 1.1 [0.06-18.7] | - | 0.2[0.01-4.7] | - | 1.6 [0.1-27] | - | - | - |
| SP I | 13.6 [3.3-55.2] | 4.7 [1-21.9] | 17.3 [2.1-141.7] | 6.7 [0.7-64.5] | 5.2[1.4-18.5] | - | 11.2 [1.3-92] | - | - | - |
| SP II | 10.5 [2.7-41.2] | 4.5 [1-22.2] | 69 [2.2-2148.5] | 31.5[1.9-501] | 3.9[1.1-12.7] | - | 8.1 [1.7-39] | - | - | - |

DAS28 : disease activity score 28 joints ; HAQ : health assessment questionnaire ; BMI : body mass index ; SP I : sleep problem index I ; SP II : sleep problem index II

remission period including a reduction in the quantity of sleep and a high number of awakenings (22). In addition, our study confirmed that DAS28 was an independent risk factor for the occurrence of sleep disturbances with OR = 3. This result corroborates a Turkish study noting an OR = 2 (23). Functional disability measured by HAQ was strongly correlated with sleep problems in our series, as reported in literature (23,24). It was identified as an independent risk factor for sleep disturbances. Thus, the inability to perform daily activities can lead to depression and affects sleep (25). A strong correlation between mood disorders and sleep problems are reported in the literature.

The link between depression and sleep disturbances was confirmed by several authors (5,26). In a two-year longitudinal study of 242 RA patients, self-reported sleep disturbances were independently associated with depression regardless of pain and functional disability (5). It seems to be a bidirectional relationship: on the one hand, depression and pain impair sleep, on the other hand, altered sleep exacerbates pain and worsens depression. A Moroccan study noted a correlation between anxiety and sleep disturbances during RA with a crude OR = 10.8 (26). Otherwise, body mass index was an independent risk factor for snoring in our study. This result confirms relation

between obesity and snoring, in general population and in chronic rheumatic diseases, as shown in literature (27,28). A novel perspective in the pathophysiological background of sleep disturbances in RA is the circadian rhythms with a release of pro-inflammatory cytokines and chemokines (29,30). Nevertheless, the limitation of being using a control group of disease in a comparative study does not allow formal causal relation between disease clinical parameters and sleep disturbances. A longitudinal follow up of these patients could confirm this relationship and evaluate their weight as independent risk factors. Otherwise, polysomnographic analysis could provide a more objective assessment and evaluate other aspects of sleep disturbances (31,32). Screening and specialized management of mood disorders may be helpful, hence the importance of close collaboration between rheumatologists and psychiatrists.

Therapeutic management of sleep disorders requires control of these various factors, primarily the disease activity. These factors must be considered in the management of chronic rheumatic disorders. Further prospective studies with a greater sample are needed in the future.

PRACTICAL CLINICAL MESSAGES

The important clinical teaching of our study is that disease activity seems to be a risk factor independently related to sleep disturbances in rheumatoid arthritis. Mood disorders and obesity also deteriorate several sleep domains. These factors should be considered in the management of patients with rheumatic disorders.

REFERENCES

- 1- Beunaver LF, Smith MT. Sleep in rheumatic diseases and other painful conditions. *Curr treat options Neurol.* 2007;9:325-36.
- 2- Moldofsky H. Sleep and pain. *Sleep Med Rev.* 2001;5:387-98.
- 3- Abad VC, Sarinas P, Guilleminault C. Sleep and rheumatologic disorders. *Sleep Med Rev.* 2008;12:211-28.
- 4- O'Brien EM, Waxenberg LB, Atchison JW, Gremillion HA, Staud RM, McCrae CS et al. Negative mood mediates the effect of poor sleep on pain among chronic pain patients. *Clin J Pain.* 2010;26:310-9.
- 5- Chalder T, Berelowitz G, Pawlikowska T, Watts L, Wessely S, Wright D et al. Development of a fatigue scale. *J psychosom res.* 1993;37:147-53.
- 6- Williams DA, Arnold LM. Measures Applied to the Assessment of

Fibromyalgia. *Arthritis Care Res.* 2011;63:86-97.

- 7- Arnett FC, Edworthy SM, Bloch DA, McShane DJ, Fries JF, Cooper NS, Healey LA, et al. The American Rheumatism Association 1987 revised criteria for the classification of rheumatoid arthritis. *Arthritis Rheum.* 1988;(3):315-24.
- 8- Prevoo ML, van't Hof MA, Kuper HH. Modified disease activity scores that include twenty- eight-joint counts. Development and validation in a prospective longitudinal study of patients with rheumatoid arthritis. *Arthritis Rheum.* 1995;38:44-8.
- 9- Bruce B, Fries JF. The Stanford Health Assessment Questionnaire: Dimensions and Practical Applications. *Health Qual Life Outcomes.* 2003;1:20.
- 10- Van der Heijde D. How to read radiographs according to the Sharp/van der Heijde method. *J Rheumatol.* 1999;26:743-5.
- 11- Lequesne MG. The algofunctional indices for hip and knee osteoarthritis. *J Rheumatol.* 1997;24:779-81.
- 12- Kellgren JH, Lawrence JS. Radiologic assessment of osteoarthritis. *Ann Rheum Dis.* 1987;16:494-501.
- 13- Beck AT, Beamesderfer A. Assessment of depression: the depression inventory. *Mod Probl Pharmacopsychiatr.* 1974;7:151-69
- 14- Young T, Palta M, Dempsey J, Skatrud J, Weber S, Badr S. The occurrence of sleep-disordered breathing among middle-aged adults. *N Engl J Med.* 1993;328:1230-5.
- 15- Beck AT, Epstein N, Brown G, Steer RA. An inventory for measuring clinical anxiety: Psychometric properties. *J Consult Clin Psychol.* 1988;56:893-7.
- 16- Solak O, Fidan F, Dundar U, Türel A, Ayçiçek A, Kavuncu V et al. The prevalence of obstructive sleep apnoea syndrome in ankylosing spondylitis patients. *Rheumatology.* 2009;48:433-5.
- 17- Hays R., and Stewart A.: Sleep measures. In Stewart A., and Ware J. (eds): *Measuring functioning and well-being approach: the medical outcomes study.* Durham, NC: Duke University Press, 1992.
- 18- Gudbjornsson B, Broman JE, Hetta J, Hallgren R. Sleep disturbances in patients with primary Sjogren's syndrome. *Br J Rheumatol.* 1993;32:1072-6.
- 19- Chandrasekhara PK, Jayachandran NV, Rajasekhar L, Thomas J, Narsimulu G. The prevalence and associations of sleep disturbances in patients with systemic lupus erythematosus. *Mod Rheumatol.* 2009;19:407-15.
- 20- Wolfe F, Michaud K, Li T. Sleep disturbance in patients with rheumatoid arthritis: Evaluation by medical outcomes study and visual analog sleep scale. *J Rheumatol.* 2006;33:1942-51.
- 21- Houssien DA, McKenna SP, Scott DL. The Nottingham Health Profile as a measure of disease activity and outcome in rheumatoid arthritis. *Br J Rheumatol.* 1997;36:69-73.
- 22- Bourguignon C, Labyak SE, Taibi D. Investigating sleep disturbances in adults with rheumatoid arthritis. *Holist Nurs Pract.* 2003;17:241-9.
- 23- Sariyildiz MA, Batmaz I, Bozkurt M, Bez Y, Cetincakmak MG, Yazmalar L et al. Sleep Quality in Rheumatoid Arthritis: Relationship Between the Disease Severity, Depression, Functional Status and the Quality of Life.

J Clin Med Res. 2014;6:44-52.

- 24- Hakkou J, Rostom S, Mengat M, Aissaoui N, Bahiri R, Hajjaj Hassouni N. Sleep disturbance in Moroccan patients with ankylosing spondylitis: Prevalence and relationships with disease specific variables, psychological status and quality of life. *Rheumatol int.* 2013;33:285-90.
- 25- Katz PP, Yelin EH. Activity loss and the onset of depressive symptoms: do some activities matter more than others?. *Arthritis Rheum.* 2001;44:1194-202.
- 26- El Bouchti I, Amine M , El Hassani S . Les troubles du sommeil au cours de la polyarthrite rhumatoïde. *Rev Mar Rhum.* 2012;20:52-5.
- 27- Murphy SL, Lyden AK, Phillips K, Clauw DJ, Williams DA. Subgroups of older adults with osteoarthritis based upon differing comorbid symptom presentations and potential underlying pain mechanisms. *Arthritis Research Ther.* 2011;13:135.
- 28- Shin MH, Kweon SS, Choi BY, Kim MK, Chun BY, Shin DH et al. Self-reported snoring and metabolic syndrome: the Korean Multi-Rural Communities Cohort Study. *Sleep Breath.* 2014;18:423-30.
- 29- Coskun-Benlidayi I. Sleep impairment: an obstacle to achieve optimal quality of life in rheumatoid arthritis. *Rheumatol Int.* 2018; 38(12):2183-92.
- 30- Cutolo M. Circadian rhythms and rheumatoid arthritis. *Joint Bone Spine.* 2019; 86(3):327-33.
- 31- Drewes AM, Nielsen KD, Hansen B, Taagholt SJ, Bjerregård K, Svendsen L. A longitudinal study of clinical symptoms and sleep parameters in rheumatoid arthritis. *Rheumatology.* 2000;39:1287-9.
- 32- Mahowald MW, Mahowald ML, Bundlie SR, Ytterberg SR. Sleep fragmentation in rheumatoid arthritis. *Arthritis Rheum.* 1989;32:974-83.