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Screening for depressive symptoms in patients with rheumatoid arthritis: relationship with pain severity, disease activity, and sleep quality

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Abstract

Background: Rheumatoid arthritis (RA) is an autoimmune systemic condition that primarily affects all synovial joints, eventually leading to deformity and clinical disability. Much progress has been made in the evaluation of inflammation and disease activity in recent years; however, other factors that can influence these patients' quality of life, including depression, stress, fatigue, sleep problems, fibromyalgia, sexual activity, and obesity, are often not evaluated by rheumatologists. Our purpose was to explore depressive symptoms in patients with RA and determine how they connected to other aspects of the disease, including pain severity, disease activity, and sleep quality.

Results: A cross-sectional study including 1200 patients with RA was performed. Patients with RA were classified into two groups based on the presence or absence of depressive symptoms using the Beck Depression Inventory-II (BDI-II). Group 1 included patients with both RA and depressive symptoms of varying severity; group 2 included patients with RA but without depressive symptoms. The patients underwent clinical evaluation and application of the Pittsburgh Sleep Quality Index (PSQI), Health Assessment Questionnaire for pain (HAQ-pain), and the Multidimensional Assessment of Fatigue scale (MAF). RA disease activity was evaluated using the DAS28 score. Depressive symptoms of varying severity were prevalent in 96% of our patients with RA, of whom 43.3% had minimal depression, while 13.7% had severe depression. The RA group with depression had a longer duration of disease, prolonged morning stiffness, and high disease activity measured by the DAS28 score than patients with only RA. In RA patients with concomitant depression, pain, sleep, and fatigue scores were also worse.

Conclusions: The presence of depression among patients with RA was associated with worse DAS28, HAQ, PASQI, and fatigue scores. Screening and recognition of such psychosocial disorders may help patients achieve optimal disease control and a good outcome.

Keywords: Depression, RA, DAS28, PASQI

Background

Rheumatoid arthritis (RA) is a chronic inflammatory condition that predominantly affects small and large joints. It can become deformable and debilitating if not properly diagnosed and treated [1]. With a prevalence of 0.4 to 1.3% and an incidence rate of 0.5 to 1%, RA is one of the 50 most common disorders causing global disability [2]. According to reports, 50–70% of patients with RA

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are seropositive [3]. Females outweigh males in terms of prevalence, with a ratio of 3:1 [4].

Depressive disorders affect approximately 38% of patients with RA [5]. Various mechanisms have been implicated in the pathophysiology of depression in RA. Socioeconomic factors such as low income, a lack of educational attainment, and unemployment are likely to act as possible factors in the development of depression in RA [6]. Patient factors such as age, race/ethnicity, and residence are all documented potential risk factors for depression, and they all have a direct impact on the alteration in depression scores in patients with RA [7].

It has been proposed that systemic chronic inflammatory conditions such as RA can cause, induce, or influence depressive symptoms [8]. As a result, depression in RA has been linked to activated inflammatory pathways and elevated proinflammatory cytokines like interleukin (IL-6) [9] and tumor necrosis factor (TNF- α) [10, 11]. Moreover, rather than being influenced by the acute clinical features of RA disease activity, depression in patients with RA may be a result of long-term functional limitations caused by arthritic joint damage [6].

Chronic inflammation that accompanies RA can inhibit the physiological coping mechanisms and stress reactions, which results in depression and a poor long-term prognosis for RA [12]. Furthermore, depression may also have an impact on RA patients, leading to lower medication adherence, difficulty sleeping, a higher risk of suicidal behavior, and a lower chance of reaching complete symptom remission [13].

The link between depression and sleep problems in patients with RA has been established [14]. Most sleep problems in patients with RA have been linked to a lower pain threshold, pain severity, depression, and activated inflammatory pathways [13]. This implies that sleep deprivation can lead to depression and that depression increases the likelihood of having sleep issues [15].

The necessity of proper recognition of these psychosocial disorders has received less research work in rheumatology, and they are frequently underdiagnosed, resulting in a delay in achieving good disease control [1]. The goal of this study was to screen for depression in patients with RA and explore its relationship to pain severity, disease activity, and sleep quality.

Methods

Patients with RA were recruited through the process of random cluster sampling from the inpatient and outpatient clinics of the Rheumatology and Rehabilitation Department of Al-Azhar University Hospitals. A total of 1200 patients were consecutively invited to participate in a single-center cross-sectional study over a period of

1 year starting in October 2017 and ending in October 2018, and the data analysis and explanation were done over another period of 6 months. To be included in the study, the patients had to be aged more than 18 years and fulfill the European League against Rheumatism/American College of Rheumatology (EULAR/ACR 2010) criteria for the diagnosis of RA [16]. According to the 2010 ACR/EULAR classification criteria for RA, the diagnosis of definite RA is determined by the presence of synovitis in at least one joint, the absence of a diagnosis that more adequately explains the synovitis, and the accomplishment of a total score of at least 6 (out of a possible 10) from the individual scores in four domains. For this calculation, the highest score obtained in a particular domain is considered.

Patients with other autoimmune rheumatic diseases, prior history, or current inflammatory joint disease other than RA (e.g., gout) were excluded from the study. The Disease Activity Score 28 (DAS28) was used for the assessment of RA disease activity [17].

The Arabic Version of Beck's Depression Inventory—II (BDI-II) is a 21-item questionnaire used to screen and evaluate the severity of depressive symptoms. The range from 0 to 13 is considered minor, 14 to 19 is mild, 20 to 28 is moderate, and 29 to 63 is severe [18]. Ghareeb [19] produced the Arabic version, and psychometric features were evaluated across 17 Arabic-speaking nations.

Patients with RA were screened for depressive symptoms and classified into two groups. Group 1 included patients with both RA and depressive symptoms of varying severity; group 2 included patients with RA but without depressive symptoms.

The HAQ-pain scale is a 15-cm visual analog scale with anchor points of 0 (no pain) and 100 (very severe pain) [20].

The Arabic version of the multidimensional assessment of fatigue (MAF) covers the 4 dimensions of fatigue: severity, distress, interference in activities of daily living, and frequency and change during the previous week [21]. The MAF's Arabic translation offers excellent validity and reliability [22].

The Pittsburgh Sleep Quality Index (PSQI) assesses self-reported sleep quality and disruptions during the previous month. Subjective sleep quality, sleep latency, sleep length, habitual sleep efficiency, sleep disruptions, use of sleeping medication, and daytime dysfunction are the seven components of sleep quality measured by the scale, which includes 19 items. The 7 component scores range from 0 to 21. The PSQI global score properly separates patients into "good sleepers" (PSQI total score ≤ 5) and "poor sleepers" (PSQI total

score > 5) [23]. This questionnaire has been validated in Arabic [24].

According to 1990 ACR diagnostic criteria, fibromyalgia was determined by the presence of widespread pain (axial plus upper and lower segment plus left and right-sided pain), as well as mild to moderate tenderness at more than or equal to 11 of the 18 tender point sites on digital palpation [25].

This study was approved by the Research Ethics Committee of the Rheumatology and Rehabilitation Department at Al-Azhar University Hospitals, and all patients signed a written informed consent before entering the study. It is in accordance with the Helsinki Declaration’s legal principles. The privacy of all details of patients was granted, as each medical file containing all inquiries contained a code number.

Analysis

Data were coded and entered using the statistical package for the Social Sciences (SPSS) version 26 (IBM Corp., Armonk, NY, USA).

Results

Among 1200 patients with RA, 1152 (96%) were suffering from depressive symptoms. On assessing the severity of depression using the Beck Depression Inventory-II scale, we found that 520 (43.3%) of our patients had minimal depression, 236 (19.7%) had mild depression, 232 (19.3%) had moderate depression, and 164 (13.7%) had severe depression (as shown in Fig. 1).

The demographic and clinical data of patients were summarized in Table 1.

Both groups had no statistically significant differences concerning age or sex, whilst a small but significant

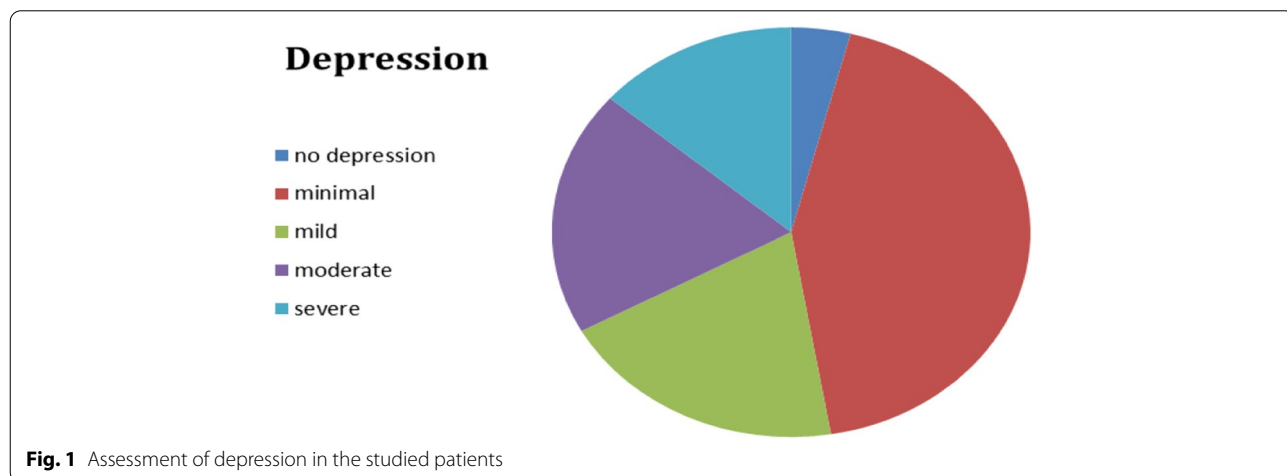


Fig. 1 Assessment of depression in the studied patients

Table 1 Demographic and clinical characteristics of RA patients with and without depression

	RA with depression (n:1152)	RA without depression (n:48)	P value
Age in years, mean ± SD	38.47 ± 8.71 (20–50)	35.75 ± 10.50 (20–49)	0.051
Disease duration in years, mean ± SD	4.40 ± 3.78 (0.17–20)	3.01 ± 2.86 (0.33–8)	0.003
Sex			
Male	92 (8.0%)	4 (8.3%)	0.790
Female	1060 (92.0%)	44 (91.7%)	
Marital status			
Married	980 (85.1%)	36 (75.0%)	0.020
Widow	60 (5.2%)	4 (8.3%)	
Divorced	40 (3.5%)	0 (0.0%)	
Single	72 (6.3%)	8 (16.7%)	
Current methotrexate use	888 (77.1%)	36 (75.0%)	0.737
Current use of steroids	640 (55.6%)	32 (66.7%)	0.129
RF positive	936 (81.3%)	32 (66.7%)	0.012
Larsen score, mean ± SD	10.63 ± 13.36	6.33 ± 7.19	0.009
Morning stiffness for ≥60 minutes, mean ± SD	38.87 ± 46.03	6.25 ± 14.46	< 0.001

Table 2 The DAS28 (and related components) and HAQ in both RA groups

	RA with depression (n:1152)	RA without depression (n:48)	P value
DAS28, mean ± SD	4.99 ± 1.34	3.43 ± 1.06	< 0.001
ESR, mean ± SD	47.48 ± 24.92	32.58 ± 19.57	< 0.001
Swollen joints, mean ± SD	5.91 ± 5.62	1.33 ± 1.86	< 0.001
Tender joints, mean ± SD	8.21 ± 6.59	2.00 ± 1.98	< 0.001
DAS28			
High (DAS28>5.1)	580 (50.3%)	4 (8.3%)	< 0.001
Moderate (DAS28>3.2 to ≤5.1)	420 (36.5%)	20 (41.7%)	
Low (DAS28≤3.2)	100 (8.7%)	12 (25.0%)	
Remission (DAS28<2.6)	52 (4.5%)	12 (25.0%)	
HAQ-pain score, mean ± SD	47.64 ± 26.01	19.17 ± 12.69	< 0.001

DAS28 Disease Activity Score in 28 joints, HAQ Health Assessment Questionnaire, ESR erythrocyte sedimentation rate

Table 3 Symptoms related to depression in the 2 patient groups

	RA with depression (n:1152)	RA without depression (n:48)	P value
Sleep quality			
Good sleep	376 (32.6%)	40 (83.3%)	< 0.001
Poor sleep	776 (67.4%)	8 (16.7%)	
Fatigue	972 (84.4%)	12 (25.0%)	< 0.001
Fibromyalgia	444 (38.5%)	0 (0.0%)	< 0.001

difference in marital status was found. Patients with RA and depression had a longer disease duration, more erosive joint changes, more morning stiffness, and were more likely to have rheumatoid factors than RA patients without depression.

The DAS28 score showed a statistically significant difference between the groups. It was higher in the group with RA and depression than in the RA-only group (Table 2). This difference was related to the subjective components of the DAS28 (ESR, tender joints, and swollen joints), which were also statistically higher in the RA group than in the depression group. Additionally, high disease activity was more prevalent in the RA with depression group, together with a very small prevalence of low disease activity or remission. The mean HAQ-pain score was higher among patients with RA and concomitant depression (47.64 ± 26.01).

There was significantly lower sleep quality in the RA with depression group as 67.4% of this group were poor sleepers. Higher rates of fatigue and fibromyalgia were also present in the RA with the depression group (Table 3).

Regarding sleep quality assessment in our patients, all components of the PASQI score showed a highly

Table 4 Global PSQI and its component scores in the 2 groups

	RA with depression mean ± SD	RA without depression mean ± SD	P value
Comp 1	1.45 ± 0.81	0.33 ± 0.48	< 0.001
Comp 2	1.29 ± 1.18	0.58 ± 0.96	< 0.001
Comp 3	1.90 ± 1.08	1.17 ± 1.00	< 0.001
Comp 4	2.01 ± 1.18	0.50 ± 0.65	< 0.001
Comp 5	0.67 ± 0.61	0.08 ± 0.28	< 0.001
Comp 6	0.20 ± 0.66	0.00 ± 0.00	0.026
Comp 7	1.15 ± 1.08	0.33 ± 0.63	< 0.001
Total PSQI	8.67 ± 4.90	3.08 ± 2.28	< 0.001

Comp1 subjective sleep quality, comp2 sleep latency, comp3 sleep duration, comp4 Habitual sleep efficiency, comp5 sleep disturbance, comp6 use of sleep medication, comp7 daytime dysfunction

statistically significant difference between groups (Table 4). The group of RA with depression showed higher scores (indicating worse sleep quality) in all components as well as the total PASQI score.

Discussion

Depression, a common disorder among patients with RA, has been shown to be frequently underestimated [26] and is considered a major cause of mortality [27]. A higher rate of depression is noticed among Egyptian patients with RA, and clinicians must keep an eye on this often-overlooked comorbidity [28]. In our sample, depressive symptoms were observed in 1152 (96%) of patients affected by RA, which emerged to be significantly greater than the earlier published prevalence. Although severe depression was noticed in 13.7% of patients, the majority (43.3%) had minimal depression, which came in line with Sruamsiri et al. [29].

Depression has been shown to afflict 9.5 to 41.5% of patients with RA [30], which is up to three times the general population [31] and is by far the most prevalent condition in RA [32]. Three Egyptian studies found varying

rates of depression among patients with RA, with two of them reporting depression rates of 15.3% and 23%, respectively [33, 34], and the third, done by Elsherbiny et al. [35], revealing a prevalence of 45%, which was close to the percentage reported in several cohorts [7, 36]. These differences in frequency between studies, particularly among Egyptian patients with RA, could be attributed to differences in research methodology, sample size, depression detection methods, and/or the type of medical institutions involved in each study.

Low economic income, unemployment, low educational level, RA disability, and other comorbidities, on the other hand, may explain the high prevalence of depression among our patients with RA.

According to Karpouzas et al. [37], longer disease duration, more erosive joint changes, longer morning stiffness, and rheumatoid factor positivity were all associated with depression in patients with RA.

In individuals with RA, the Larsen score, which evaluates erosive joint damage, has been linked to depression. This is most likely because the significant erosive joint changes associated with RA can lead to decreased physical ability and impaired function, which can affect a person's psychological health and, as a result, the likelihood of depression.

DAS28 and related variables were found to be significantly related to depression in patients with RA; this was confirmed by Kwiatkowska et al. [38]. Furthermore, Li et al. [39] discovered a link between depression and disease activity, demonstrating that higher levels of inflammatory cytokines implicated in disease activity such as interleukin-6 (IL-6) may have an impact on depression, implying that pro-inflammatory cytokines may play a role in the development of this condition.

Patients with RA and concurrent depression had significantly higher HAQ-pain and lower QoL scores, confirming the findings of a prior study [40].

This study showed that depression among patients with RA was associated with poor sleep quality, worsening fatigue scores, and an increased rate of FM. We found that 38.3% of our patients with RA and depression also had FM. Depression is one of the most frequent comorbidities in the FM population, with an average lifetime incidence of approximately 63% [41]. Furthermore, depressive disorders are three times more common in FM patients than in the general population [42] and FM patients show a higher incidence of depression than people with other chronic pain disorders [43]. In RA, pro-inflammatory cytokines including TNF and IL-6 have been implicated in central sensitization and the development of FM [44].

Sleep deprivation or discontinuity has been shown to influence sleep quality in patients with RA, and poor

sleep quality has been linked to depression, high disease activity, a high pain threshold, and fatigue [45]. According to the current study's findings, 67.4% of patients with RA and concurrent depression were shown to have poor sleep quality and worsening of all sleep components as measured by the PASQL. Past research by Rezaei et al. [46] confirmed our findings, stating that sleep difficulties may be more common in RA patients due to disease activity, pain chronicity, fatigue, and depression.

According to Irwin et al. [45], the pathophysiology of sleep problems may be explained by increased nuclear factor kappa-B (NF- κ B) signaling, resulting in persistent hyperalgesia; thus, the link between sleep problems and pain is reciprocal.

Despite the fact that a few previous studies in Egyptian patients with RA investigated the prevalence of depression and its association with disease activity [33, 34, 47–49], neither of these patients with RA had been assessed or treated for depression, nor had their symptoms been addressed during follow-up evaluations. This exemplifies how depression is frequently overlooked in patients with RA.

The study's main limitation was the lack of a non-RA healthy control group with which to compare results. Because we intend to screen for and correlate depressive symptoms in patients with RA, we anticipated that the proposed study design would provide potentially useful information regarding this patient population. Future research may address the research issue more effectively by employing a different or more robust methodology.

Conclusions

Depression is a common psychiatric disorder among patients with RA and needs to be assessed as part of the disease management process. Depression was associated with worsened HAQ-pain, PASQL, and fatigue ratings, as well as an increase in DAS28. Screening for depression in patients with RA should be done on a regular basis in order to help patients achieve significant improvement or remission.

Abbreviations

PASQL: Pittsburgh Sleep Quality Index; HAQ: Health Assessment Questioner; DAS28: Disease activity score in 28 joints; ESR: Erythrocyte sedimentation rate; IL-6: Interleukin-6.

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Authors' contributions

A.I.A. conceived and designed the analysis and supervision of the work, and A.M.K. contributed to the manuscript writing. M.L. contributed to the data collection and aided in the result interpretation. The authors read and approved the final manuscript.

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Availability of data and materials

The data will be available upon reasonable request.

Declarations

Ethics approval and consent to participate

The Rheumatology Department ethical committee, Faculty of Medicine, Al-Azhar University, approved this study. It adheres to the legal principles outlined in the Helsinki declaration. Each participant provided written informed consent. Because each medical file containing all inquiries contained a code number, all patient details were kept private.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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