

# Psychological affection in rheumatoid arthritis patients in relation to disease activity

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## Abstract

Rheumatoid arthritis (RA) is a common, systemic autoimmune disease characterized by persistent symmetric polyarthritis (synovitis). Anxiety and depression are common among patients with RA, compared to the general population and have been associated with increased pain, fatigue, physical disability and health care costs, and an overall reduced health-related quality of life. The aim of the present study was to assess the relation between psychological factors (anxiety and depression) and disease activity (and severity) parameters in RA patients.

This national, single-center, cross-sectional study recruited over 6 months 25 patients with RA diagnosed according to the 2010 American College of Rheumatology/European League Against Rheumatism classification criteria, and 25 healthy control individuals. All participants were subjected to the clinical and laboratory evaluation of disease activity and psychological assessment according to the International Classification of Mental and Behavioral Disorders tenth revision. Significance and regression analyses were performed to determine disease activity and severity predictors.

80% of RA patients had depression and 52% anxiety symptoms, while only 8% of healthy controls reported mild depression ( $P < .001$ ). Data also found highly significant correlation between depressive symptoms and RA disease activity ( $P < .05$ ).

Psychiatric manifestations are common in RA and they strongly correlate with severity of the disease.

**Abbreviations:** ACR = American College of Rheumatology, CRP = C reactive protein, DAS28 = disease activity score in 28 joints, ESR = erythrocyte sedimentation rate, HAQ-DI = health assessment questionnaire disability index, ICD-10 = the International Classification of Mental and Behavioral Disorders tenth revision, RA = rheumatoid arthritis, RF = rheumatoid factor, SD = standard deviation, VAS = visual analog scale.

**Keywords:** anxiety, depression, disease activity, disease severity, rheumatoid arthritis

## 1. Introduction

Rheumatoid arthritis (RA) is an autoimmune disease that results in a chronic, systemic inflammatory disorder that may affect many tissues and organs, but principally attacks synovial joints. It can be a disabling and painful condition, which can lead to substantial loss of functioning and mobility if not treated.<sup>[1]</sup> Severity of RA is assessed using the disease activity score in 28 joints (DAS28),<sup>[2]</sup> which is a composite score comprising clinician report of signs, patient self-report, and biochemical measures. It was developed originally to enable the monitoring of RA activity and is the standard measure used to gauge response to therapy.

Editor: Fumio Tsuji.

The authors have no funding and conflicts of interest to disclose.

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Medicine (2019) 98:19(e15373)

Received: 19 November 2018 / Received in final form: 7 March 2019 /

Accepted: 26 March 2019

<http://dx.doi.org/10.1097/MD.00000000000015373>

Anxiety and depression are higher in patients with chronic medical diseases than general population (15%–23% vs 6.6%).<sup>[3]</sup> Given that RA is a chronic disease, anxiety and depression are more common among patients with RA, compared with the general population (28%–44% vs 6.6%)<sup>[3–5]</sup> and the condition has been associated with increased pain, fatigue, physical disability and healthcare costs, and overall reduced health-related quality of life. They have poorer long-term outcomes, including increased pain, comorbidities, and mortality levels.<sup>[6]</sup> The literature is rich with studies concerning psychological affection in RA patients and correlating it to disease activity and severity parameters. However, these studies showed markedly variable results due to different study designs and different methods for assessment. This study aimed at assessing the prevalence of psychological affection in RA patients, using the International Classification of Mental and Behavioral Disorders tenth revision (ICD-10) criteria as standard method for assessment, in addition to its relationship to disease activity parameters.

## 2. Methods

Twenty-five patients who fulfilled the 2010 RA classification criteria<sup>[7]</sup> by the American College of Rheumatology (ACR)/European League Against Rheumatism were included in this national, cross-sectional, single-center study. These patients were recruited from rheumatology outpatient clinics consecutively over the 6-month study duration. Twenty-five healthy age and sex-matched individuals constituted the control group. Signed

informed consent form was taken for every patient and control subject, and the study was approved by the Ethics Committee at Minya University. Were excluded from the study population, patients with depressive episode attributable to psychoactive substance use or to any organic mental disorder or with psychotic symptoms as hallucinations, delusions, or depressive stupor also anxiety sustained by a physical disorder, such as hyperthyroidism, an organic mental disorder or psychoactive substance-related disorder.

All patients were subjected to clinical evaluation (full history and examination including Ritchie articular index 28 tender and swollen joint count), laboratory evaluation (erythrocyte sedimentation rate [ESR], C reactive protein [CRP] and rheumatoid factor [RF]), in addition to assessment of disease activity and outcome measures (disease activity score in 28 joints [DAS28]-ESR,<sup>[2]</sup> health assessment questionnaire disability index [HAQ-DI]<sup>[8]</sup> and the 10-Likert visual analog scale [VAS]<sup>[9]</sup>). Psychological assessment was performed according to the ICD-10.<sup>[10]</sup>

### 2.1. Statistical analysis

Quantitative variables were summarized by number of observed values, mean, standard deviation, range, and median. Chi-square and 2-tailed tests were used throughout to analyze correlation between disease activity scores and psychological signs, as well as significance of differences between RA patient group and their healthy counterparts; statistical significance was set at the conventional level of  $P$  value  $< .05$ . Regression analysis was used to determine activity and severity predictors. The SPSS software version 16.0 was used for statistical analyses.

## 3. Results

### 3.1. Demographic characteristics of patients

The group of RA patients included 23 female (92%) and 2 male (8%) patients, with a mean age of  $41.32 \pm 10.74$  years. Control group included 22 female (88%) and 3 male (12%) patients, with a mean age of  $36.92 \pm 10.65$  years.

### 3.2. Disease characteristics

Regarding clinical and laboratory disease activity measurements in the RA patients, 24 (96%) patients had arthritis, while 14 (56%) patients had arthralgia, 19 (76%) patients had morning stiffness more than 1 hour, 6 (24%) patients had fever, 21 (84%) patients had myalgia, 24 (96%) of patients were receiving drugs, 16 (64%) were on nonsteroidal anti-inflammatory drugs, while 19 (76%) were on methotrexate, 23 (92%) on antimalarial medication, 7 (28%) on leflunomide, and 11 (44%) patients on steroids. ESR levels were at  $45.24 \pm 21.55$  with a median of 40 (range 11–100) and 80% of RA patients were positive for CRP and 84% for RF.

### 3.3. Disease activity and disability indices in RA group

Table 1 shows that only 1 patient (4%) had mild DAS28 score ( $>2.6$ – $\leq 3.2$ ), 7 patients (28%) had moderate disease activity with a DAS28 score ( $>3.2$ – $\leq 5.1$ ), and 13 (52%) patients had high disease activity according to a DAS28 score  $>5.1$ . Four patients (16%) were in remission (DAS28  $\leq 2.6$ ). The HAQ-DI score ranged from 0 to 3 with median of 3 and mean of  $20.96 \pm 0.84$ ; 14 (56%) patients had mild impairment according to their

**Table 1**

#### Disease activity and disability indices.

	RA patients (N = 25)
<b>DAS28</b>	
Score	
Mean $\pm$ SD	2.16 $\pm$ 1.10
Median (range)	3 (0–3)
Remission	4 (16%)
Mild	1 (4%)
Moderate	7 (28%)
High	13 (52%)
<b>HAQ-DI</b>	
Score	
Mean $\pm$ SD	0.96 $\pm$ 0.84
Median (range)	1 (0–3)
No impairment	7 (28%)
Mild impairment	14 (56%)
Moderate impairment	2 (8%)
Complete impairment	2 (8%)
<b>VAS</b>	
Score	
Mean $\pm$ SD	1.72 $\pm$ 0.84
Median (range)	2 (0–3)
No pain	2 (8%)
Mild	7 (28%)
Moderate	12 (48%)
Severe	4 (16%)
<b>Articular index</b>	
Mean $\pm$ SD	12.36 $\pm$ 9.46
Median (range)	11 (0–46)

DAS28 = disease activity score-28 items, HAQ-DI = health assessment questionnaire disability index, SD = standard deviation, VAS = visual analog scale.

HAQ-DI score, 2 (8%) patients had moderate impairment, 2 (8%) patients had complete impairment, and 7 (28%) patients presented no impairment. The VAS score ranged from 0 to 3 with median of 2 and mean of  $1.72 \pm 0.84$ ; 7 (28%) patients had mild pain, 12 (48%) had moderate pain, 4 (16%) had severe pain, and only 2 (8%) patients had no pain. The articular index of RA group ranged from 0 to 46 with median of 11 and mean of  $12.36 \pm 9.46$ .

### 3.4. Psychological status of RA patients

Psychological evaluation of RA patients found that over 50% of patients had severe depressive symptoms (14 [56%] patients), while only 2 (8%) patients displayed mild symptoms and 4 (16%) patients had moderate symptoms. Table 2 also shows that 16 (64%) patients had recurrent depression, another 16 had somatic symptoms, and 13 (52%) patients had anxiety. In the control group, on the other hand, only 2 (8%) subjects reported mild depressive symptoms, 1 (4%) had somatic symptoms, and 2 (8%) had anxiety symptoms. Psychological disorders were, therefore, more frequent among RA patients, compared to control subjects (Table 2,  $P < .001$ ). Figure 1 displays the correlation of disease activity with depression and anxiety.

### 3.5. Correlation between RA disease parameters and psychological manifestations

Table 3 shows that depressive symptoms ( $P = .002$ ), recurrent depression ( $P = .02$ ), and somatic manifestation ( $P = .002$ ) were mostly associated with moderate to severe disease activity;

**Table 2**  
**Comparison of psychological data in RA and control groups.**

	RA patients (N = 25)	Control subjects (N = 25)	Chi-Square, P-value
Depressive symptoms			
Mild	2 (8%)	2 (8%)	29.57, .0001*
Moderate	4 (16%)	0 (0%)	
Severe	14 (56%)	0 (0%)	
Recurrent depression	16 (64%)	0 (0%)	23.52, .0001*
Somatic symptoms	16 (64%)	1 (4%)	20.05, .0001*
Anxiety	13 (52%)	2 (8%)	4.52, .0006*

RA = rheumatoid arthritis.

\* A P-value < .05 indicates statistical significance.

anxiety was also only reported among RA patients with elevated DAS28 scores, but correlation did not reach statistical significance ( $P=.09$ ). Patients who were in remission reported no psychological manifestations. CRP levels did not correlate with any of the psychological factors; ESR was used to calculate DAS28, and was not correlated with any psychological factor neither.

This table also shows that all patients with complete impairment had severe depression ( $P=.08$ ), recurrent depression ( $P=.37$ ), and somatic symptoms ( $P=.01$ ).

All patients with severe pain, as evaluated by the VAS, had severe depression ( $P=.01$ ), recurrent depressive episodes ( $P=.02$ ), and most of them had anxiety (3 out of 4 patients [75%]) though not to a significant extent.

#### 4. Discussion

The present study aimed primarily at evaluating prevalence of psychological affection in RA patients, in a specialized center in Upper Egypt.

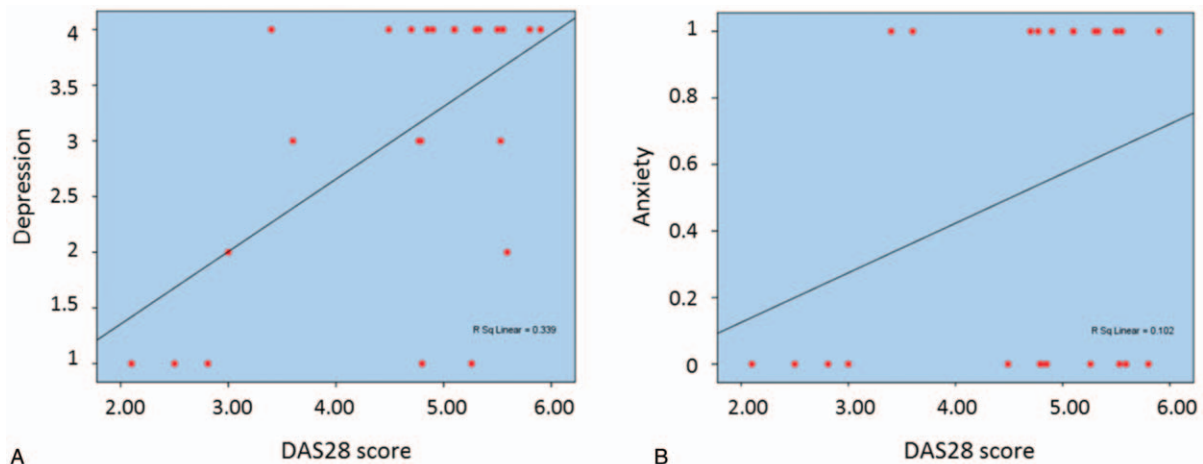
It included 23 female (92%) and 2 male (8%) patients who had had RA for  $3.68 \pm 2.32$  years and 25 healthy subjects. Though the sample size was quite limited with a total of 50 participants, it compares to a recent study performed on RA patients in the same Egyptian region of Minya.<sup>[11]</sup> The large prevalence of RA among women in our study also matched the gender imbalance reported by the same study on RA patients in Minya.<sup>[11]</sup> This

overrepresentation of women was also underlined in a 2009 review, which discussed the potential involvement of sex hormones in RA onset and evolution.<sup>[12]</sup> In this study, patients were relatively young, with an average age of 41 years; which also could explain female gender prevalence, in accordance with a 2006 study which reported that below the age of 50, females have a 4 to 5 times higher incidence rate of RA than their male counterparts, while the female/male ratio above the age of 60 to 70 years goes to only about 2.<sup>[13]</sup>

The vast majority of patients (80%) had depression, whether mild (2 patients), moderate (4 patients), or severe (16 patients), classified according to ICD-10 classification of Mental and Behavioral Disorders.

Findings demonstrated a highly significant correlation between occurrence of depressive symptoms, recurrent depressive episodes, and somatic manifestation (marked loss of interest in regular activities, appetite, libido, and lack of emotional reaction) with severity of disease activity in RA patients as assessed by the DAS28 tool.

The results of the present study were in agreement with Muhammad et al who studied 102 RA patients diagnosed according to the 1987 ACR criteria.<sup>[14]</sup> Though disease duration reported in that study was longer than reports of the present study, gender distribution, and average age of patients were closely comparable. Importantly, over 70% of RA patients were found to have depression (over 40% reported moderate-to-severe cases), significantly correlated with the severity of disease.



**Figure 1.** Correlation between disease activity score and (A) depression and (B) anxiety. DAS28 = disease activity score-28 items.

**Table 3**  
**Correlation between RA disease parameters and psychological data.**

	DAS28				Correlation ( <i>r</i> ), <i>P</i> -value
	Remission <i>n</i> =4	Mild <i>n</i> =1	Moderate <i>n</i> =7	High <i>n</i> =13	
Depressive symptoms					
Absent	4 (100%)	0 (0%)	0 (0%)	1 (7.7%)	0.594, .002*
Mild	0 (0%)	1 (100%)	0 (0%)	1 (7.7%)	
Moderate	0 (0%)	0 (0%)	3 (42.9%)	1 (7.7%)	
Severe	0 (0%)	0 (0%)	4 (57.1%)	10 (76.9%)	
Recurrent depression	0 (0%)	0 (0%)	6 (85.7%)	10 (76.9%)	-0.455, .02*
Somatic symptoms	0 (0%)	0 (0%)	5 (71.4%)	11 (84.6%)	-0.582, .002*
Anxiety	0 (0%)	0 (0%)	5 (71.4%)	8 (61.5%)	0.340, .09

	HAQ-DI – Presence of impairment				Correlation, <i>P</i> -value
	None <i>n</i> =7	Mild <i>n</i> =14	Moderate <i>n</i> =2	Complete <i>n</i> =2	
Depressive symptoms					
Absent	3 (42.9%)	1 (7.1%)	1 (50%)	0 (0%)	0.351, .08
Mild	0 (0%)	2 (14.3%)	0 (0%)	0 (0%)	
Moderate	1 (14.3%)	3 (21.4%)	0 (0%)	0 (0%)	
Severe	3 (42.9%)	8 (57.1%)	1 (50%)	2 (100%)	
Recurrent depression	4 (57.1%)	9 (64.3%)	1 (50%)	2 (100%)	-0.186, .37
Somatic symptoms	2 (28.6%)	11 (78.6%)	1 (50%)	2 (100%)	-0.499, .01*
Anxiety	3 (42.9%)	8 (57.1%)	1 (50%)	1 (50%)	0.190, .36

	VAS – Presence of pain				Correlation ( <i>r</i> ), <i>P</i> -value
	None	Mild	Moderate	Severe	
Depressive symptoms					
Absent	2 (100%)	2 (28.6%)	1 (8.3%)	0 (0%)	-0.562, .01*
Mild	0 (0%)	2 (28.6%)	0 (0%)	0 (0%)	
Moderate	0 (0%)	0 (0%)	4 (33.3%)	0 (0%)	
Severe	0 (0%)	3 (42.9%)	7 (58.3%)	4 (100%)	
Recurrent depression	2 (100%)	4 (57.1%)	3 (25%)	4 (100%)	-0.541, .02*
Somatic symptoms	2 (100%)	3 (42.9%)	4 (33.3%)	0 (0%)	-0.423, .06
Anxiety	0 (0%)	3 (42.9%)	7 (58.3%)	3 (75%)	0.334, .08

DAS28 = disease activity score-28 items, HAQ-DI = health assessment questionnaire disability index, VAS = visual analog scale.

\* A *P*-value < .05 indicates statistical significance.

In addition, the study by Mostafa et al on 170 RA patients found a positive significant correlation between depressive symptoms and disease activity of patients.<sup>[15]</sup>

There is in disagreement with Cordingley et al who studied 322 RA patients with active disease (mean DAS28 = 6.0) and found that there was no significant correlation between depression and disease activity<sup>[16]</sup>; this discrepancy may be due to the use of hospital anxiety and depression scale in assessing depression instead of the ICD-10 international classification of Mental and Behavioral Disorders.

On the other hand and comparing with the same study,<sup>[16]</sup> our data also showed no significant correlation between anxiety symptoms and disease activity of RA patients assessed by DAS28, also matching findings by Khedr et al.<sup>[17]</sup>

In our study, we found that the frequency of psychological disorders in RA patients was 80%, compared with 20% in controls. Specifically, RA patients displayed a significantly higher frequency of psychological disorders (depression: *P* = .0001 and somatic manifestations: *P* = .0006), when compared to their RA-free counterparts. These results were in agreement with Khedr et al where frequency of psychological disorders in RA patients was 60.8%, compared with 12% in controls (anxiety, somatoform disorder, and depression).<sup>[17]</sup> The present study found a significant correlation between somatic manifestations and HAQ-DI score of RA patients (*P* = .01), in accordance with Muhammad et al,<sup>[14]</sup> but no significant correlation existed

between depressive symptoms, recurrent depressive episodes and anxiety symptoms, and extent of impairment among RA patients.

In our study, depression correlated significantly with VAS pain score (*P* = .01), matching results by 2 studies.<sup>[17,18]</sup>

## 5. Limitations

This work explores a small sample of patients and control subjects; in fact, no sample size calculation was performed, and this study serves as an exploratory investigation of the problem, which warrants a larger study and follow-up over time.

## 6. Conclusion

Psychological manifestations are common in RA and they positively correlate with severity of disease activity.

## 7. Recommendations

Psychological examination should be routinely undertaken in patients with rheumatic diseases, and special attention should be given to depression and anxiety, given their strong relationship to severity of the disease.

As psychological affectation in RA patients affects disease outcome and increases morbidity psychological evaluation would provide a more accurate and earlier diagnosis, which

would lead to better clinical care and preventing debilitating changes and subsequent physical dysfunctions and impairment of the quality of life of RA patients.

### Author contributions

Amal Ali Hassan, Mona Hamdy Nasr, and Ahmed Mustafa Kamal designed the study. Alyaa Daa Elmoghazy, Mona Hamdy Nasr, and Ahmed Lotfi Mohamed were responsible for proposal/study protocol writing. Aliya Daa Elmoghazy also collected data and performed the statistical analyses. Ahmed Lotfi Mohamed wrote the manuscript, which was read and approved by all authors.

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