

## Research Article

# The effect of depression and related psychosocial factors on disease activity in rheumatoid arthritis

Depresyon ve ilişkili psikososyal faktörlerin romatoid artrit aktivitesine etkisi

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## Abstract

**Introduction:** Rheumatoid arthritis is one of the most common inflammatory chronic diseases worldwide. Depression is common in patients with rheumatoid arthritis. The relationship between depression and rheumatoid arthritis is a matter of curiosity, and it is thought that there is a bidirectional interaction between them. Depression is an important health problem that requires treatment. Therefore, it is essential to determine the conditions that call for more attention in terms of depression when following rheumatoid arthritis patients in primary care.

**Methods:** Patients who applied to the rheumatology outpatient clinic, followed up for at least 1 year, and were diagnosed with rheumatoid arthritis according to the American College of Rheumatology (ACR) criteria were consecutively invited to the study. A total of 110 people, 18 men and 92 women, accepted the invitation. Beck Depression Inventory (BDI), Health Assessment Questionnaire (HAQ), and visual analogue scale (VAS) were filled together with the questionnaire developed by the researcher. In the joint examination of the patients, the number of tender joints and swollen joints were noted. Disease Activity Score (DAS28) was calculated and noted by measuring C Reactive Protein and erythrocyte sedimentation rates (ESR) in earlier tests performed on the patients. Rheumatoid factor status was recorded at the time of diagnosis or by checking the follow-up records.

**Results:** In rheumatoid arthritis (RA) patients, the BDI score was higher in people with other chronic diseases and those who felt the need to apply to a psychiatry clinic. The BDI score was higher in patients with other chronic diseases and those who felt the need to apply to a psychiatry clinic for rheumatoid arthritis. RA patients with high BDI scores also had high DAS28 and HAQ scores. In addition, disease activity was significantly correlated with RF positivity.

**Conclusion:** Rheumatoid arthritis patients should be evaluated for depression. Depression evaluation should be done more carefully in cases with high disease activity, other chronic diseases, and those who feel the need to apply to a psychiatry clinic.

**Keywords:** Rheumatoid arthritis, depression, visual analogue scale, chronic disease

## Öz

**Giriş:** Romatoid artrit dünyada sık görülen inflamatuvar kronik hastalıklardandır. Romatoid artrit hastalarında depresyon sık rastlanır. Depresyon ile romatoid artritin ilişkisi merak konusu olup, aralarında çift yönlü bir etkileşim olduğu düşünülmektedir. Depresyon tedavisi gereken önemli bir sağlık sorunudur. Birinci basamakta romatoid artrit hastalarını takip ederken depresyon açısından daha dikkatli olunması gereken durumları belirlemek önemlidir.

**Yöntem:** Romatoloji polikliniğine başvuran en az 1 yıldır takipli ve Amerikan Romatizma Cemiyeti (ACR) kriterlerine göre romatoid artrit tanısı almış hastalar sırasıyla çalışmaya davet edildi. Daveti kabul eden 18'i erkek, 92'si kadın toplam 110 kişiydi. Araştırmacı tarafından geliştirilen anket formunun yanında Beck Depresyon Envanteri (BDE), Sağlık Değerlendirme Anketi (HAQ) ve görsel analog skala (VAS) dolduruldu. Hasta eklem muayenesinde hassas eklem sayısı ve şiş eklem sayısı not edildi. Hastanın yaptırmış olduğu tetkiklerdeki C reaktif protein, eritrosit sedimentasyon hızı (ESH) kaydedilerek Hastalık Aktivite Skoru (DAS28) hesaplandı ve not edildi. Romatoid faktör durumu hastanın tanı esnasında ya da sonraki tetkiklerine bakılarak kaydedildi.

**Bulgular:** Romatoid artrit (RA) hastalarında ek kronik hastalığı olanlarda, psikiyatri kliniğine başvuru ihtiyacı hissedenlerde BDE skoru daha yüksek bulundu. Ayrıca BDE skoru yüksek olan RA hastalarının DAS28 ve HAQ skorlarının da yüksek olduğu saptandı. Hastalık aktivitesinin ayrıca RF pozitifliği ile istatistiksel olarak anlamlı bir ilişki içinde olduğu görüldü.

**Sonuç:** Romatoid artrit hastaları depresyon açısından değerlendirilmelidir. Hastalık aktivitesi yüksek olan, ek hastalığı olan, psikiyatri kliniğine başvurma ihtiyacı hisseden olgularda depresyon değerlendirmesi daha hassasiyetle yapılmalıdır.

**Anahtar kelimeler:** Romatoid artrit, Depresyon, Görsel Analog Skala, Kronik Hastalık

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## Introduction

Although the etiology of rheumatoid arthritis (RA) is not exactly known, it is a multisystemic, chronic, autoimmune, and inflammatory disease affected by genetic factors, infectious agents, sex, hormonal factors, and environmental factors that progresses with synovial cell proliferation and inflammation that can cause damage to the joints. RA tends to involve the peripheral joints symmetrically. It can lead to cartilage destruction, bone erosion, and integrity deterioration in the joints, causing shape and function disorders and reducing the patient's quality of life. The disease affects women more than men, and is one of the most common inflammatory diseases, with a worldwide prevalence of approximately 1%. The severity of the disease may differ from person to person. While it can be silent and asymptomatic for a long time in some people, it can rapidly progress in others and cause serious joint disorders [1, 2].

Depression is an important health problem that negatively affects physical and mental health and interpersonal relationships, causes economic problems and job losses, reduces the quality of life, and even leads to suicide. The World Health Organization (WHO) reported the average rate of depression worldwide in 2015 as 4.4% in its 2017 report. According to sex, it was seen at a rate of 5.1% in women and 3.6% in men [3]. Depression is common worldwide, including in Turkey. In Turkey, the frequency of depressive symptoms was 9% at the national level in 2012, and it was twice higher in women than in men [4].

RA is a chronic disease, and many studies show the relationship of chronic diseases with depression [5,6]. For example, in a meta-analysis examining the prevalence of depression in patients with rheumatoid arthritis, 72 studies and 13189 patients were reviewed and showed a worldwide prevalence of 38.8% [7]. In another study, Fakra et al. reported that depression rates in RA patients were between 14-48% [8].

It is known that primary care physicians frequently encounter patients with RA and depression, which are diseases with high incidences. The relationship between chronic diseases and depression has been the subject of research. As RA is a chronic disease, it is a significant health issue investigated for its relationship with depression. The answer to whether chronic diseases affect depression or vice versa is sought. Although finding this answer is complicated, considering the necessity of treating both diseases, revealing other factors that increase depression in RA patients will remind primary care physicians to be more careful when screening depression. Our study aimed to determine the important conditions in terms of depression in RA patients and define the situations that physicians should consider.

## Methods

Patients who applied to the rheumatology outpatient clinic of a state hospital, were diagnosed with RA according to the revised 1987 criteria of the American College of Rheumatology [9] and were followed up for at least one year were consecutively invited to the study. Patients who did not have the mental ability to understand and answer questions during the study and eight patients who did not volunteer to participate in the study (lack of time, unwillingness, etc.) were excluded. Demographic and psychosocial characteristics, educational status, chronic diseases, and diagnostic processes of the patients were queried with a questionnaire developed by the researcher.

Beck Depression Inventory (BDI) [10] was used for evaluating depression, Health Assessment Questionnaire (HAQ) [11] was used to determine functional status, and the visual analog scale patient global assessment (VAS) was used for global assessment. Swollen joint count (SJC), tender joint count (TJC), patient global assessment (VAS), erythrocyte sedimentation rate (ESR), and C reactive protein (CRP) values were recorded by joint examination and used to calculate disease activity scores (DAS28). In addition, rheumatoid factor (RF) was noted as a positive or negative evaluation based on the routine laboratory tests of the patients for follow-up by considering the laboratory parameters tested during or after the diagnosis.

**BDI:** The BDI was applied to all patients. In the validity and reliability article of the Turkish inventory, a cut-off points of 17 is suggested [10]. Therefore, patients with a score of 17 and above were considered to have a high BDI score.

**HAQ:** The HAQ consisted of eight activities (items) containing 20 questions: dressing, standing, eating, walking, hygiene, grip, and daily activities [11]. Each answer is graded from 0 to 3. The HAQ is a questionnaire reflecting functional status, and its score has been shown to correlate with disease activity indicators.

**DAS28:** DAS28 was calculated with the  $(0.56 \times TJC^{1/2}) + (0.28 \times SJC^{1/2}) + (0.7 \times \ln[ESR]) + (0.014 \times HGD[VAS-mm])$  formula. A special calculator was used for these calculations. Evaluation of the obtained values: the remission value was 2.4 and below; the low disease activity value was between 2.4 and 3.6; the moderate disease activity value was between 3.6 and 5.5, and the high activity value was above 5.5. Visual Analog Scale, CRP, ESR, TJC, and SJC were used for DAS28 calculation [12].

**VAS:** The VAS has traditionally been used as a grading tool that aims to determine the degree of pain subjectively by the patient. One end of the 10-centimeter line is based on the principle that the patient has no pain, and the other end is for the worst pain state, and the current pain level is marked and measured in millimeters. The VAS is a tool used to monitor the course of pain during the disease process and to calculate the DAS28 score in RA patients [12].

## Statistical analysis

The SPSS (Statistical Package for Social Sciences) software program version 19.0 (SPSS Inc., Chicago, IL) was used for statistical analysis. In addition to descriptive statistical methods (mean, standard deviation, frequency), the Student's t-test was used to compare normally distributed variables between two groups, and the Mann Whitney U test for comparisons between two groups with skewed distributions.

The Kruskal Wallis test was used to compare skewed numerical variables between more than two groups, and the Mann Whitney U test was used to determine the groups causing the difference. A Chi-square test was applied to compare qualitative data. The results were evaluated at a 95% confidence interval, and the significance level was  $p < 0.05$ .

### Ethical Approval

Before starting the study, permission from the local ethics committee and a written informed consent form were obtained from the patients. The principles of the Declaration of Helsinki were followed throughout the study. Our study was carried out with the permission of the hospital's local ethics committee as a specialty thesis research.

### Results

The study was conducted with 110 patients, 18 males (16.4%) and 92 females (83.6%). The patients were between 26 and 81 years old, and the mean age was  $52.95 \pm 11.62$  years. The onset times of RA (first joint swelling) ranged from one to 37 years (mean  $12.97 \pm 9.42$  years). The duration of follow-up due to RA in the rheumatology outpatient clinic was between one year and 24 years (mean  $6.39 \pm 4.42$ ).

The HAQ levels of the cases ranged from 0 to 39, with a mean of  $12.10 \pm 10.32$ . The number of tender joints in the cases ranged from 0 to 20, with a mean of  $5.31 \pm 4.83$ . The number of swollen joints in the cases ranged from 0 to 10, with a mean of  $1.84 \pm 2.57$ . The VAS levels of the cases ranged from 10 to 100, with a mean of  $45.29 \pm 19.20$  (Table 1).

**Table 1.** HAQ, tender joint, swollen joint, and VAS Averages

	Min-Max	Mean±SD
HAQ	0-39	12.10±10.32
Tender Joint Count	0-20	5.31±4.83
Swollen Joint Count	0-10	1.84±2.57
Visual Analog Scale	10-100	45.29±19.20

According to the BDI score, there was no significant difference between the patients' mean age, education level, need for help from others due to RA in daily life, and rheumatoid factor (RF) positivity. There was no significant relationship between the BDI score and sex ( $p=0.057$ ). Although there is no significant relationship, it is noteworthy that the rate of those with high BDI scores in females (40.2%) is higher than in males (16.7%). There is a significant correlation between BDI scores and feeling the need to apply to a psychiatry clinic ( $p=0.001$ ) (Table 2).

**Table 2.** Evaluations of the BDI scores

		BDI Score		p*
		High	Low	
		Mean±SD	Mean±SD	
Age		$52.95 \pm 11.74$	$52.94 \pm 11.63$	0.998**
Gender	Female	37 (40.2%)	55 (59.8%)	0.057
	Male	3 (16.7%)	15 (83.3%)	
Educational Status	Illiterate	5 (25.0%)	15 (75.0%)	0.439
	Primary school	25 (37.3%)	42 (62.7%)	
	Highschool and above	10 (43.5%)	13 (56.5%)	
Needing Assistance in Daily Life Due to RA	Yes	28 (40.6%)	41 (59.4%)	0.233
	No	12 (29.3%)	29 (70.7%)	
Feeling the Need to Apply to the Psychiatry Clinic	Yes	22 (56.4%)	17 (43.6%)	<b>0.001</b>
	No	18 (25.4%)	53 (74.6%)	
Rheumatoid Factor	Positive	27 (35.1%)	50 (64.9%)	0.665
	Negative	13 (39.4%)	20 (60.6%)	

\*Chi-square test \*\*Student t test

When we compared disease activity with sex and disease duration, no significant correlation was found, while it was highly correlated in patients with positive rheumatoid factor and high BDI scores ( $p=0.034$ ) ( $p=0.008$ ) (Table 3).

**Table 3.** Evaluations of the DAS-28 Scores

		Based on DAS 28 Scores				p*
		Remission	Low Activity	Moderate Activity	High Activity	
		n (%)	n (%)	n (%)	n (%)	
<b>Sex</b>	<b>Female</b>	10 (10.9%)	18 (19.6%)	47 (51.1%)	17 (18.5%)	0.333
	<b>Male</b>	2 (11.1%)	7 (38.9%)	7 (38.9%)	2 (11.1%)	
<b>Disease Duration</b>	<b>1-5 Years</b>	3 (13.0%)	2 (8.7%)	15 (65.2%)	3 (13.0%)	0.214
	<b>≥ 5 Years</b>	9 (10.3%)	23 (26.4%)	39 (44.8%)	16 (18.4%)	
<b>Rheumatoid Factor</b>	<b>Positive</b>	7 (9.1%)	14 (18.2%)	38 (49.4%)	18 (23.4%)	<b>0.034</b>
	<b>Negative</b>	5 (15.2%)	11 (33.3%)	16 (48.5%)	1 (3.0%)	
<b>BDI Score</b>	<b>High</b>	0	6 (15.0%)	25 (62.5%)	9 (22.5%)	<b>0.008</b>
	<b>Low</b>	12 (17.1%)	19 (27.1%)	29 (41.4%)	10 (14.3%)	
	<b>Interrupted</b>	6 (12.2%)	11 (22.4%)	24 (49.0%)	8 (16.3%)	

\*Chi-square test

BDI scores were significantly higher in patients with comorbidity (44%) than in cases without comorbidity (20%) (p=0.015) (Table 4).

**Table 4.** The relationship between Comorbidity and BDI Scores

		Comorbidity		p
		Present	Not Present	
		n (%)	n (%)	
<b>BDI Score</b>	<b>High</b>	33 (44.0%)	7 (20.0%)	0.015*
	<b>Low</b>	42 (56.0%)	28 (80.0%)	

\* Chi-square test (p<0.05)

HAQ scores of patients with high BDI scores were significantly higher than those with low BDI scores (p=0.001) (Table-5).

**Table 5.** The relationship between BDI and HAQ scores

		HAQ Score		p
		Mean±SD	Median	
<b>BDI Score</b>	<b>High</b>	17.85±10.22	18	0.001**
	<b>Low</b>	8.81±8.90	6	

\*\* Mann Whitney U test (p<0.05)

## Discussion

Our study aimed to determine the features that affect depression in patients with RA. When we look at the statistically significant findings, BDI scores were higher in those who felt the need to apply to the psychiatry clinic and those with comorbidities. In addition, the DAS28 and HAQ scores of RA patients with high BDI scores were also significantly higher. There was also a significant relationship between disease activity and RF (+) and BDI scores.

Many studies on patients with RA have shown that depression is more common than in the general population [7,8]. This led to research questions about whether depression causes RA or whether RA causes depression. Many studies relate depression to chronic diseases and RA. In a cohort study of 403932 patients with major depressive disorder (MDD) and 5339399 control patients (non-MDD), Vallerand et al. found that developing RA in MDD increased by 38% compared to the control group. In the MDD group, the risk of developing RA decreased in those using antidepressants. However, in the non-MDD group, the risk of developing RA was increased in those using antidepressants [13]. The effect of antidepressant use may be confusing, but there appears to be a bidirectional relationship between MDD and RA.

The gold standard in diagnosing depression is a diagnosis made in line with a psychiatrist's interview and guidelines. Since each patient couldn't meet with a psychiatrist in our hospital conditions, depression scoring was performed using the inventories. In our study, 40 of 110 patients (36.36%) had a higher score as to BDI (cut-off point 17). This rate was close to other studies. In the meta-analysis conducted by Matcham et al., 72 studies and 13189 patients were evaluated. When depression in RA was evaluated worldwide, the rate was 16.8% for major depression, 38.8% according to the Patient Health Questionnaire-9, and 34.2% according to the Hospital Anxiety and Depression Scale with a threshold of 8 (it was 14.8% using a threshold of 11) [14]. In another meta-analysis by Abdel-Ahad et al., 47 studies were evaluated, and the prevalence of depression was reported as 48% [15]. In the study of Yurdakul et al. in Turkey, the rate of RA with a score of 17 or higher on the BDI was 42.21% [16]. From this point of view, our study's BDI high scores were similar to other studies.

While 39 of 110 patients with RA stated that they needed to consult a psychiatrist (22 had high BDI scores and 17 had low scores), only 19 had applied to a psychiatrist, and 23 were using antidepressant medications. Also, BDI scores were high in 18 of 71 patients who stated that they did not feel the need to consult a psychiatrist. When investigating why patients did not go to a psychiatrist, Dalrymple et al. found that disease severity and disability were associated with not seeking support for psychiatric disorders [17]. If we deduce from this, the rate of applying to psychiatry remains low even if RA patients have depressive symptoms and feel the need to consult a psychiatrist.

In our study, RA patients with moderate and high activity (DAS28) had significant RF positivity and high BDI scores. A meta-analysis by Zhang et al. found that RA patients with depression tended to have higher disease activity and lower quality of life than patients without depression [18]. Also, Peck et al. found a significant relationship between HAQ scores and depression [19]. In the study by Gautam et al., the 8-week effect of yoga was investigated, and it was found that it led to a significant improvement in depression and HAQ scores in patients with RA [20]. When Fragoulis et al. followed newly diagnosed RA patients for 6 months to 1 year, they found that depression and DAS28 scores were associated over the entire time frame [21]. On the other hand, in the study of Jamshidi et al., no relationship was found between disease activity and depression, but a relationship was found between disability and depression [22]. While many studies found depression to be high in people with high disease activity according to the DAS28 score, few studies could not find such a relationship. A significant relationship was also found in our study.

According to the DAS 28 score, RF positivity was significantly higher in people with high disease activity. While there was a significant relationship between DAS28 scores and high BDI scores, there was no relationship between RF positivity and high BDI scores. In the study of Arman et al., the relationship between RF negativity and depression was determined, and they suggested that RF positivity has a protective effect against depression [23]. However, in our study, elevated BDI scores were not related to RF positivity. In the study by Tillmann et al., RA patients were compared with a healthy control group based on their personality traits. In their subgroup analysis, they found that RA patients with RF negativity had to receive longer depression treatments than patients with RF positivity, and they attributed this to the significantly higher psychological maladjustment of RF (-) patients [24].

In our study, no statistically significant result was found when age, sex, educational status, needing help from someone else in daily routine work, and duration of illness (below and above five years) were compared regarding depression. The difference between women (40%) and men (17%) was not statistically significant, but close to significance ( $p=0.057$ ). The fact that women show depressive symptoms at a higher rate than men in the general population explains this situation [3,4,25]. Furthermore, depression is more common in female RA patients [26]. The increase in depression proportions with education (25% in illiterates, 37% in primary school graduates, and 44% in high and above school graduates) was not statistically significant. Although it was expected that those who needed help from others in their daily routine work (41%) should have a higher proportion than those who did not (29%), this difference was not statistically significant either.

While the BDI score was 44% in those with an additional chronic disease, it was 20% in those who did not have an additional disease. Another factor that increases the frequency of depression in RA patients is the presence of additional chronic diseases.

## Limitations

A limitation of this study was the use of BDI. Although the BDI is a reliable tool for depression scoring, the gold standard for diagnosis is a psychiatric examination. Although our patients were referred to psychiatry depending on the BDI scores, it is a limitation that they did not undergo a psychiatric examination at the stage of depression diagnosis.

## Conclusion

Although rheumatoid arthritis patients are at increased risk for depression compared to the general population, this risk increases in some situations. Therefore, it is important to pay more attention when evaluating depression in patients with high HAQ scores, those with additional chronic diseases, and those who feel the need to apply to a psychiatry clinic.

**Conflict of Interest:** This article was compiled from the specialty thesis titled "Identification of factors affecting treatment compliance in patients with rheumatoid arthritis and recommendations to increase compliance".

Author Contributions		Author Initials
SCD	Study Conception and Design	MT, AO
AD	Acquisition of Data	MT,
AID	Analysis and Interpretation of Data	MT, AO
DM	Drafting of Manuscript	MT, AO
CR	Critical Revision	MT, AO

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