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ORIGINAL ARTICLE

# Psychological Aspects of Rheumatoid Arthritis: The Role of Depression in Pain Management

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## Abstract

**Background/Aim:** Rheumatoid arthritis (RA) is a chronic autoimmune disorder that primarily affects the joints, leading to stiffness, swelling and persistent pain. Pain in these patients is not only a physical symptom but also a complex experience shaped by biological, psychological and social influences. Depression and anxiety frequently occur alongside the disease, further contributing to greater pain perception, reduced functional ability and diminished quality of life. Aim of this study was to highlight the impact of depression on functional status and pain intensity in female patients with rheumatoid arthritis.

**Methods:** A descriptive analytical study involving 50 female patients diagnosed with RA according to ACR/EULAR criteria followed patients during inpatient rehabilitation at the Institute for Physical Medicine, Rehabilitation and Orthopaedic Surgery "Dr Miroslav Zotović" was performed. The study examined the relationship between pain (VAS), functionality (HAQ), depression (BDI) and personality disorders (MMPI).

**Results:** The average age of participants was 63.8 years. The most common comorbidities were hypertension (64 %) and hypothyroidism (30 %). Of the total 50 patients, 23 (46 %) were smokers. The mean VAS pain scale value was 6.59, while the HAQ questionnaire average value was 0.811. Depression was identified in 17 patients (12 mild, 4 moderate and 1 severe depression). Patients with depression had higher pain intensity and poorer function.

**Conclusion:** Psychosocial factors, including anxiety and depression, are important predictors of functional status and pain in RA. For effective pain management, it is important to identify, through a biopsychosocial approach, all factors that influence subjective pain perception.

**Key words:** Arthritis, rheumatoid; Depression; Pain.

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## Introduction

Rheumatoid arthritis (RA) is a chronic progressive condition, immunologically mediated, with inflammation starting in the synovium and advancing to joint damage and extra-articular manifestations. The prevalence in most countries according to epidemiological studies ranges around 1 %, the disease occurs 2-3 times more frequently in females and most commonly manifests between ages 40 and 50. Joint damage often advances quickly after disease onset, leading to deformities, making proper diagnosis and treatment in early disease stages critically important.[1] The disease course is variable, ranging from mild oligoarthritis to severely progressive polyarthritis with severe damage.[2]

Given that the disease leads to significantly reduced work capacity and severe disability in patients, it has both significant social and medical importance. Patients being treated for RA report that pain is their greatest problem, causing psychological disturbances and sleep difficulties. Along with all associated conditions and symptoms, it leads to poorer quality of life and functional disability, more so than joint damage and deformities alone.[3-6]

Previously, RA was considered an inflammatory disorder affecting peripheral joints, driven by local immunological mechanisms that trigger cytokine activation.[4] Today, it is recognised that pain in RA is not solely the consequence of joint inflammation. It is believed that central disorders play a significant role, including central sensitisation, altered pain perception in the CNS, as well as psychological factors such as anxiety and depression.[7-9]

Modern approaches recognise pain as a complex phenomenon that cannot be fully explained by inflammation alone, but also by neurobiological and psychosocial components. Acute pain aims to prevent the action of harmful stimuli and thus has a protective function. In contrast to acute pain, which signals potential tissue damage, chronic pain lacks a clear physiological function and persists beyond the normal healing period, even after the initial painful stimulus has ceased.[10] After cessation of harmful stimuli, in inflammatory arthritis after inflammation subsides, pain may still persist.[7-10]

Longitudinal studies support the fact that central sensitisation can contribute to pain persistence in RA, which may explain why some patients, despite controlled inflammatory processes and low disease activity, experience severe pain and have significantly reduced functionality.[11, 12] Numerous studies indicate that patients with chronic pain have changes in brain regions involved in cognitive and emotional pain modulation.[13]

Proinflammatory cytokines originating from the periphery can affect central brain structures, influencing regions implicated in depression such as the prefrontal cortex, hippocampus, anterior cingulate cortex and basal ganglia. These changes are associated with alterations in neuroendocrine activity and neurotransmitter metabolism.[14] Along with other chronic conditions, female gender and psychosocial factors including anxiety and depression are important predictive factors for pain prognosis in RA.[15]

This complex interaction may help explain why individuals with persistent pain are more susceptible to developing anxiety and depression and conversely, why patients with cognitive dysfunction or psychological stress are predisposed to chronic pain. Persistent pain contributes to central mechanisms of pain amplification.[16] Several factors may account for the high prevalence of depression in RA patients, including the burden of living with a chronic disease with no complete cure, loss of social or occupational roles and even potential side effects of pharmacological treatment.[17]

Despite the prevalence and significance of mental health disorders, they are rarely investigated in rheumatological studies and research, as well as in clinical practice.[18] According to recent data, mental health has been investigated and observed in less than 8 % of published papers related to RA, while quality of life has been monitored in a somewhat higher percentage (around 19 %), mainly using the SF-36 test.[19]

As a common psychiatric comorbidity, depression impacts over 264 million individuals worldwide and contributes significantly to global disability. Its symptoms and consequences are very diverse, caused by a combination of different factors including individual sensitivity and the way the disease develops and responds to treatment.[20] One of the factors that further complicates depression diagnosis is the presence of chronic pain. Persons suffering from long-term pain are often medically examined for pain, but the broader context of their psychological and social condition is not considered.[16]

Depression and chronic pain, according to literature data, occur together in up to 60 % of cases.[16] Sociodemographic characteristics such as employment status and education can influence quality of life in female RA patients. Work activities and social status can affect the psychological state of female patients, with potential consequences on quality of life and functional status.

The prevalence of depression in RA ranges between 14 % and 41 %.[21] There are studies indicating that the level of depression in disease duration over 9 years is up to 40 %.[22] The correlation between depression and RA is multifactorial:

it can result from social and economic factors, functional disability and degree of inflammation. A range of depressive symptoms—including disturbances in sleep, fatigue and decreased appetite—are commonly observed in patients with RA.[19]

Understanding how chronic pain relates to psychological factors, fatigue and sleep disorders has great clinical and theoretical significance and leads to the need for an individual approach to treating these patients. Cognitive decline in RA patients is influenced by key symptoms, including chronic pain and psychological distress.[23]

Presented study aimed to investigate the relationship between somatic symptoms, functional disability and psychological deviations in female patients with RA. The focus was on assessing pain intensity, functional capacity and presence of depressive and anxiety symptoms using validated scales and questionnaires.

# Methods

A descriptive analytical study included 50 female patients diagnosed with RA according to current ACR/EULAR criteria.[24] The patients underwent inpatient physical therapy and medical rehabilitation at the Institute for Physical Medicine, Rehabilitation and Orthopaedic Surgery "Dr Miroslav Zotović".

Sociodemographic characteristics of patients (age, smoking status, occupation) were observed, as well as presence of comorbidities. During rehabilitation, patients were monitored for pain intensity using the visual analogue scale (VAS) pain scale, functional status assessment using the HAQ questionnaire, assessment of depression and anxiety presence using the Beck depression scale (BDI) and Minnesota multiphasic personality inventory (MMPI) personality test, as psychiatric comorbidities.[25-28] All assessment instruments were administered in the Serbian - language versions.

The study included females aged 18-70 years and all participants previously agreed to participate in the research. The study did not include female patients suffering from diabetes, those who had cerebrovascular stroke, malignancy, alcoholism, pregnancy, peripheral nervous system diseases, surgical intervention performed in the previous 6 months, patients on antidepressant therapy, pregabalin/gabapentin.

All female patients were treated with physical therapy modalities (individual kinesiotherapy program, functional occupational therapy, analgesic electro-procedures and hydrokinesiotherapy in thermos-mineral water) as standard protocol during medical rehabilitation. All female patients underwent pain intensity assessment (VAS scale), functional status (Health Assessment Questionnaire - HAQ index) and psychometric tests that are in standardised use at the institution where the research was conducted.

## Statistical methods

Results are presented as number (%) or mean ± SD, or median (interquartile range), depending on data type and distribution. Groups were compared using parametric (Student t-test) and non-parametric (Mann-Whitney U test) tests. Pearson and Spearman correlations were used to assess correlations between variables. All p-values less than 0.05 were considered statistically significant. All data were analysed using SPSS 29.0 (IBM Corp. Released 2023. IBM SPSS Statistics for Windows, Version 29.0. Armonk, NY: IBM Corp.) and R 4.1.0. (R Core Team (2017). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria.

# Results

The study included 50 participants with RA as primary diagnosis. The average age of participants was in the seventh decade; all were female and half were smokers (46 %) (Table 1). Descriptive statistics found that unemployed (housewives) comprised 37.7 %, administrative workers 24.44 %, merchants 11.1 % and agricultural workers 6.66 % (Figure 1).

Almost all participants had significant comorbidities, most commonly hypertension, hypothyroidism and osteoporosis. All female participants except one used csDMARD therapy, while only 14 % were on biological therapy. Taking data on associated diseases, 64 % of female patients were taking hypertension therapy, 30 % hypothyroidism therapy and 28 % had verified osteoporosis (Figure 2).

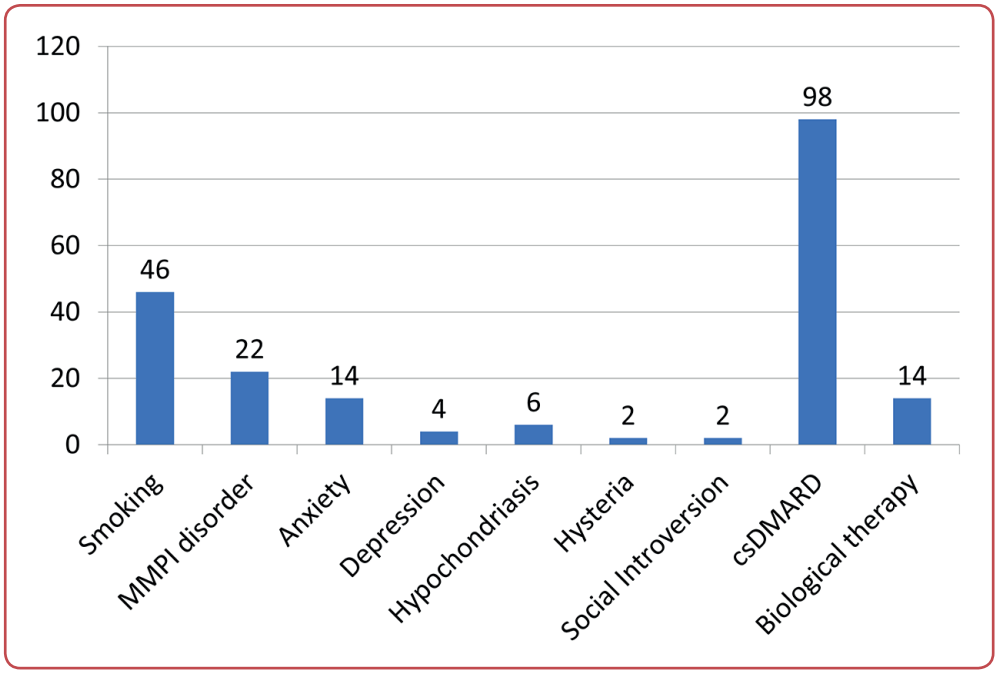


*Figure 1: Demographic characteristics of patients*

*MMPI – Minnesota multiphasic personality inventory; csDMARD – conventional synthetic disease-modifying anti-rheumatic drug;*

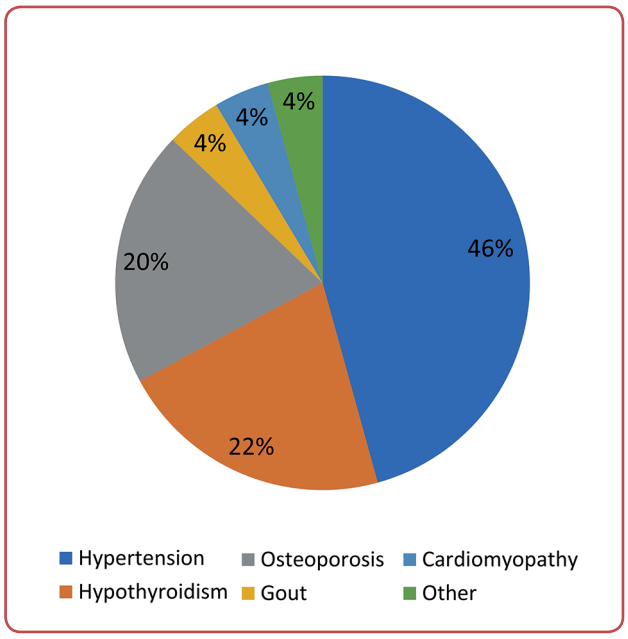


*Figure 2: Comorbidities of patients with rheumatoid arthritis*

*Table 1: Participants characteristics*

| Characteristics | Value |
|---|---|
| Age (N ± SD) | 63.8 ± 9.3 |
| Gender, female (N (%)) | 50 (100 %) |

*SD - standard deviation;*

The average pain intensity value, measured on the VAS scale, was 6.59 ± 1.47. In functional status and disability assessment, the HAQ index was 0.811 ± 0.284. In psychometric test assessment using the MMPI personality test, 14 % of female patients had anxiety, 2 % had elements of hysteria and on the BDI 38.88 % of female patients had depression symptoms - 26.66 % were mildly depressed patients, 8.88 % moderate depression, while one patient (2.22 %) had verified severe depression.

The most important disease-specific factors affecting the degree of RA, as well as depression, are shown in Table 2. As shown in the table, age had weak correlation with HAQ and BDI (HAQ was very close to conventional significance level, while BDI was not). Patients with osteoporosis had significantly higher VAS scores, while HAQ and BDI medians differ but not significantly. BDI was higher in smokers, lower in participants with hypertension and osteoporosis, but without statistically significant differences.

BDI correlated with VAS and HAQ, with only HAQ showing positive correlation at the border of statistical significance (Table 3, Figure 3). Additionally, BDI showed negative correlation with HAQ change (higher BDI corresponds to greater HAQ reduction), but without statistical significance.

*Table 2: VAS, HAQ and BDI in correlation with disease-specific factors*

| Factor | VAS | HAQ | BDI |
|---|---|---|---|
| Age [coef. (p)][a] | -0.109 (0.452) | 0.264 (0.064) | -0.220 (0.129) |
| **Smoking** | | | |
| Yes | 6.7 ± 1.4 | 0.70 (0.40) | 14 (12) |
| No | 6.5 ± 1.6 | 0.75 (0.25) | 8 (8) |
| p-value[b] | 0.643 | 0.860 | 0.335 |
| **Hypothyroidism** | | | |
| Yes | 6.7 ± 1.9 | 0.80 (0.35) | 8 (4) |
| No | 6.6 ± 1.2 | 0.70 (0.40) | 13 (12) |
| p-value[c] | 0.812 | 0.323 | 0.194 |

*[a] Pearson correlation coefficient (p-value); [b] t-test; [c] Mann-Whitney U test; Results are presented as mean ± standard deviation or median (interquartile range); VAS: visual analogue scale; HAQ: Health assessment questionnaire; BDI: Beck depression inventory;*

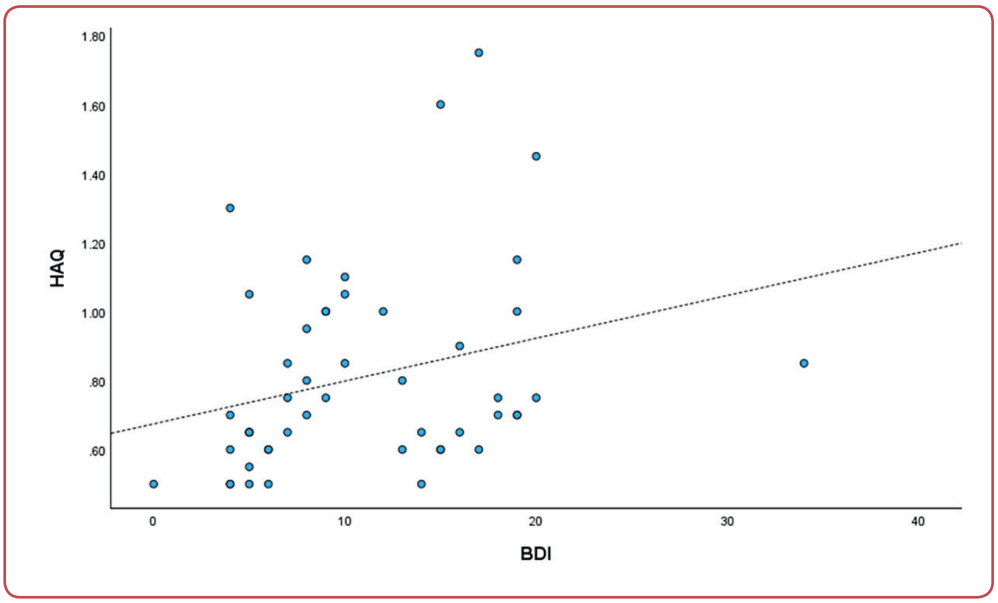


*Figure 3: Correlation between BDI and HAQ*

*BDI: Beck depression inventory; HAQ – Health assessment questionnaire*

# Discussion

RA is a complex chronic disease that significantly affects physical health, functional capacity and psychological state of patients. Understanding the interconnection between somatic symptoms and psychological problems in these patients is necessary for optimising their treatment and improving quality of life.

Presented study aimed to investigate the relationship between somatic symptoms, functional disability and psychological deviations in female patients with RA. The focus was on assessing pain intensity, functional capacity and presence of depressive and anxiety symptoms using validated scales and questionnaires.

The prevalence of depression in participants was 38.88 %, which is consistent with literature data where depression prevalence in RA patients ranges between 14 % and 61 %.[29] A study conducted in Argentina that included 258 patients of both genders showed that severe depression prevalence was 33.8 %, while mild forms of depression were present in 25.6 % of patients, similar to presented

study where, of the total prevalence, most female patients (26.66 %) were in the mild depression category.[30]

All patients in presented group were women, which is consistent with literature data that often identifies female gender as a significant risk factor for developing depression in patients with RA.[31, 32] Studies have shown that hormonal, psychosocial and biological factors in women contribute to higher depression frequency compared to men.

Most female patients were on standard medication therapy based on csDMARDs (90.90 %), which includes methotrexate, prednisone and hydroxychloroquine. These medications usually help control inflammation and prevent disease progression, but long-term use can have side effects, including gastrointestinal disturbances, liver problems and potential immune system suppression.[33, 34]

Biological therapy (14 %) in this study indicates more severe disease form in those female patients. The advent of biological therapy (biological DMARDs) has drastically changed the therapeutic approach in RA treatment. Disease remission or low disease activity are now achievable goals for many patients who have access to these therapies, but although there are long-term data confirming biological drug efficacy, their use is not without risk.[35]

Smoking status is a significant risk factor for RA development, as 46 % of female patients in presented study were active smokers. Recently, Sugiyama and colleagues conducted the first meta-analysis suggesting that smoking is indeed a risk factor for RA in men with positive rheumatoid factor (RF) and in heavy smokers. In female smokers, the risk was approximately 1.3 times higher than in non-smokers.[36]

Research by Vellerant et al indicated a connection between obesity, depression and smoking status in female RA patients, in that BMI affects the relationship between oxidative stress and depressive symptoms. Smoking is one of the more significant risk factors as it enhances oxidative stress and causes epigenetic and immunological changes, considered a confirmed risk factor for RA while simultaneously increasing risk for depression development.

Pain remains one of the most dominant RA symptoms, even in patients in remission or with adequate therapy. Differences in pain perception may be related to factors such as disease duration, therapeutic response, but also presence of comorbidities, including depression and anxiety. Female patients with pronounced depressive symptoms in this study had higher pain intensity on the VAS scale (values between 7 and 9).[37]

Functional capacity in RA patients depends on factors such as disease duration, joint damage, pain presence and comorbidities. A study published in RMD Open (2020) examined depression and anxiety in patients who suffered from RA and found that higher HAQ scores were associated with depression, which positively correlates with presented results.[38] A 2018 study, confirms presented study findings, emphasising that subjective pain sensation, using VAS, has more significant impact on functional disability than objective disease activity parameters like DAS28, indicating that pain, as a subjective experience, directly reflects on functional abilities of patients with RA and emphasises the importance of its assessment and treatment in everyday clinical practice.[39]

Depression additionally worsens pain perception and functional disability, which is clearly seen in this study - female patients with depressive disturbances had higher pain intensity (7-9 on VAS scale) and worse HAQ index results. Although the study included a small sample, results show bidirectional connection between somatic symptoms (pain, functional disability) and psychological deviations (depression, anxiety).

This may be a consequence of several factors, including decreased motivation for physical activity, increased pain perception and lower tolerance threshold for disease symptoms. On the other hand, intense pain and functional limitations can contribute to development or worsening of depressive and anxiety symptoms, creating a vicious cycle that negatively affects quality of life.

This study has several limitations that should be considered when interpreting the results. First, the relatively small sample size, consisting exclusively of female patients, limits the generalisability of the findings to the broader population of individuals with RA. The study relied primarily on subjective measures of pain and functional disability, which are inherently influenced by in-

dividual patient perception and may introduce reporting bias. The absence of longitudinal follow-up prevented the assessment of changes in disease activity, functional status and treatment response over time. The wide age range of participants (18–70 years) may have introduced variability in clinical presentation and treatment outcomes that was not fully accounted for. The study did not control for or analyse the potential effects of different physical therapy modalities applied within the sample, which could have influenced the observed results.

## Conclusion

Many patients who were in remission and good disease control have pain and poorer functionality and this may be a result of non-inflammatory processes. The presence of depression as a comorbidity can significantly contribute to poorer condition in patients with RA, leading to worse quality of life. The connection between psychological deviations and somatic complaints is bidirectional and indicates the significance of a biopsychosocial approach in optimal treatment of patients with RA.

## Ethics

In accordance with Ethical Guidelines for Clinical Research in Healthcare, the study was conducted after approval by the Ethics Committee of the Institute for Physical Medicine, Rehabilitation and Orthopaedic Surgery "Dr Miroslav Zotović" with decision No 116-01-20348-2/22, dated 07 October 2022.

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## Conflicts of interest

The authors declare that there is no conflict of interest.

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## Data access

The data that support the findings of this study are available from the corresponding author upon reasonable individual request.

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