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The prevalence of depression/anxiety among patients with rheumatoid arthritis and its relationship with quality of life

Učestalost depresije/anksioznosti i njena povezanost sa kvalitetom života kod bolesnika sa reumatoidnim artritisom

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Abstract

Background/Aim. Rheumatoid arthritis (RA) is accompanied by numerous comorbidities, among which depression and anxiety (D/A) occupy a significant place. The aim of the study was to determine the prevalence of D/A in RA patients and the relationship with their quality of life (QoL). **Methods.** The study included RA patients treated at the Rheumatology Clinic of the Military Medical Academy in Belgrade, Serbia in the period from May to November 2016. Disease activity was assessed by the Disease Activity Score 28-SE (DAS28-SE). D/A was determined using the Hospital Anxiety and Depression Scale (HADS) questionnaire and European Quality of Life 5 Dimensions 3 Level Version (EQ-5D-3L) questionnaire Question 5. Three questionnaires were used to assess QoL: the general RAND 36-item Health Survey 1.0 (RAND36), the specific Rheumatoid Arthritis Quality of Life Questionnaire (RAQoL) and EQ-5D-3L. **Results.** Based on the HADS questionnaire, the prevalence of depression was 52% with the average HADS score value of 7.6 ± 3.2, while the prevalence of anxiety was 32% with the mean HADS score value of 5.8 ± 3.8. Question 5 of the EQ-5D questionnaire showed that the prevalence of D/A was 77.4%, of which 71.7% of patients had moderate D/A, while 5.7% of patients had severe D/A. Impairment in all the domains of QoL was found in tested patients, as assessed by all three questionnaires. The RAQoL questionnaire showed moderate QoL impairment, with a score value of 15.5 ± 7.9. The EQ-VAS score value was 58.6 ± 16.0, while the EQ-5D index was 0.6 ± 0.3. Univariate linear regression produced a statistically significant negative predictive value of QoL for the presence of D/A. Multivariate linear regression showed a statistically significant independent negative predictive value of QoL, as assessed by the RAQoL questionnaire (p = 0.010) and the mental QoL component of the RAND 36 questionnaire (p = 0.030) for the degree of depression. **Conclusion.** In RA patients, there is a significant prevalence of D/A as well as impairment of QoL in all domains. The tests performed have shown that QoL has a statistically significant negative predictive value for the presence of D/A.

Key words:
anxiety; arthritis, rheumatoid; depression; prevalence; prognosis; quality of life; surveys and questionnaires.

Apstrakt

Uvod/Cilj. Reumatoidni artritis (RA) praćen je mnogobrojnim komorbiditetima među kojima depresija i anksioznost (D/A) zauzimaju značajno mesto. Cilj rada bio je da se proceni učestalost D/A kod bolesnika sa RA i njena povezanost sa kvalitetom života (KŽ). **Metode.** Ispitivanjem su obuhvaćeni bolesnici sa RA, lečeni na Klinici za reumatologiju Vojnomedicinske akademije u Beogradu, Srbija, u periodu od maja do novembra 2016. godine. Aktivnost bolesti je procenjivana pomoću *Disease Activity Score* 28-SE (DAS28-SE). Pomoću *Hospital Anxiety and Depression Scale* (HADS) i petog pitanja *European Quality of Life 5 Dimensions 3 Level Version* (EQ-5D-3L) upitnika određivani su D/A. Za procenu KŽ korišćena su tri upitnika: opšti *RAND 36-item Health Survey* 1.0 (RAND36), specifični upitnik KŽ osoba obolelih od RA (RAQoL) i upitnik EQ-5D-3L. **Rezultati.** Na osnovu HADS upitnika, učestalost depresije iznosila je 52%, sa prosečnom vrednošću HADS skora 7,6 ± 3,2, dok je učestalost anksioznosti iznosila 32%, sa srednjom vrednošću HADS skora 5,8 ± 3,8. Pomoću petog pitanja EQ-5D upitnika nađena je učestalost D/A od 77,4%, od čega je umerenu D/A imalo 71,7%, a izraženu 5,7% bolesnika. Kod

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ispitivanih bolesnika je pomoću sva tri upitnika utvrđena narušenost u svim domenima KŽ. Upitnikom RAQoL pokazana je umerena narušenost KŽ, sa vrednošću skora 15,5 ± 7,9. Vrednost EQ-VAS skora iznosila je 58,6 ± 16,0, dok je EQ-5D indeks iznosio 0,6 ± 0,3. Univarijantnom linearnom regresijom dobijena je statistički značajna negativna prediktivna vrednost KŽ za prisustvo D/A. Multivarijantnom linearnom regresijom pokazana je statistički značajna nezavisna negativna prediktivna vrednost KŽ, procenjena pomoću RAQoL upitnika (p = 0,010) i mentalne komponente KŽ RAND 36 upitnika (p = 0,030) za stepen depresije. **Zaključak.** Kod bolesnika sa RA postoji značajna učestalost D/A kao i narušenost KŽ u svim domenima. Sprovedenim ispitivanjima je pokazano da KŽ ima statistički značajnu negativnu prediktivnu vrednost za prisustvo D/A.

Ključne reči:
anksioznost; artritis, reumatoidni; depresija; prevalenca; prognoza; kvalitet života; ankete i upitnici.

Introduction

Rheumatoid arthritis (RA) is a chronic disease characterized by persistent synovitis and systemic inflammation leading to joint destruction, functional disability, and premature mortality. The disease is accompanied by numerous comorbidities that significantly impair quality of life (QoL). According to the results of the large multicenter COMOrbidities in Rheumatoid Arthritis (COMORA) study, which determined the prevalence of comorbidities in RA, depression was most common with 15%, followed by asthma with 6.6%, cardiovascular events (myocardial infarction, cerebrovascular insult) with 6%, solid tumors (except for basal cell carcinoma) with 4.5%, and chronic obstructive pulmonary disease (COPD) with 3.5% [1].

Despite the prevalence and significance of mental health disorders, they have been rarely investigated in rheumatology studies and clinical practice. Reports show that mental health has been studied in less than 8% of published works dealing with RA, while QoL is studied somewhat more frequently (in 19% of studies), mostly using the SF-36 questionnaire [2].

The prevalence of depression in RA ranges between 9.5% [3] and 41.5% [4], while the prevalence of anxiety ranges from 21% to 70% [5]. Follow-up studies have indicated that the cumulative risk of the occurrence of depression after 9 years of RA is 40% [6]. Depression and anxiety (D/A) in RA are associated with a higher degree of disease activity, reduced QoL, increased use of healthcare services, as well as reduced adherence to therapy. The correlation between depression and RA is multifactorial: it may be a result of social and economic factors, functional disability, and/or inflammation. There are various reasons for the large variation in the prevalence. It is very difficult to distinguish between patients with depressive disorder and those with a normal reaction since they live with a chronic, functionally limiting condition. Further, numerous symptoms of depression, such as fatigue, poor sleep, and loss of appetite, can be part of the clinical picture of RA itself. In addition to the foregoing, the prevalence is also affected by different methods used for diagnosing depression. A gold standard is a psychiatric interview and diagnosis through the Diagnostic and Statistical Manual (DSM) or International Classification of Diseases (ICD) criteria. However, alternative self-report questionnaires can also be useful due to their practicality in everyday work. Previous research has indicated that the recognition and appropriate treatment of D/A improve the response to treatment and considerably reduce symptoms associated with RA, improving the functional status and QoL [7]. That is why the aim of the study was to determine the prevalence of D/A in patients with RA and the correlation with their QoL.

Methods

The study included RA patients treated at the Rheumatology Clinic of the Military Medical Academy in Belgrade, Serbia from May to November 2016. The enrolment criteria were the following: RA diagnosis based on the American College of Rheumatology (ACR) 1987 classification criteria and ACR/European European Alliance of Associations for Rheumatology (EULAR) 2010, age ≥ 18 years. Patients with other systemic connective tissue diseases, fibromyalgia, previously verified cognitive disorder and psychiatric disease, and those who had used antidepressants in the previous month were excluded from the study. Structured questionnaires compiled based on literature data were used for the collection of information regarding subject and disease characteristics. The first part of the questionnaires included social and demographic characteristics of subjects: gender, age, place of residence (rural/urban environment), employment status, and level of education. The second part of the questionnaires referred to the clinical characteristics of RA: disease duration, therapy [use of methotrexate (MTX), other disease-modifying antirheumatic drugs (DMARDs), corticosteroids, and biological therapy].

To assess the activity of RA, the Disease Activity Score 28 (DAS 28-SE) was determined for all patients based on the total number of tender and swollen joints, the patient's assessment of disease activity on the VAS scale, and erythrocyte sedimentation rate (ESR) (mm/h). The assessment of the patient's functional ability was performed using the Health Assessment Questionnaire – Disability Index (HAQ DI), which contains a total of 20 questions scored from 0 to 3 (0 = without difficulties, 3 = I cannot do it).

When it comes to inflammation markers, the following tests were performed: ESR rate by Westergren (SE) and C-reactive protein (CRP) using the nephelometric method. D/A were diagnosed using two questionnaires: Hospital Anxiety and Depression Scale (HADS) and Question 5 of the

European Quality of Life 5 Dimensions 3 Level Version (EQ-5D-3L). The HADS [8] questionnaire contains 14 questions (7 for depression and 7 for anxiety). The patient assesses the degree of agreement using the Likert scale, from 0 to 3. The total score for each scale is from 0 to 21. A score exceeding 11 indicates the presence of D/A; 8-10 indicates borderline cases; 0-7 is a normal finding. The EQ-5D-3L [9] questionnaire contains five questions regarding various dimensions of health: mobility, self-care, usual activities, pain/discomfort, and D/A.

Three questionnaires were used for the assessment of QoL: general – the RAND 36-item Health Survey 1.0 (RAND36), specific – the Rheumatoid Arthritis Quality of Life (RAQoL), and EQ-5D-3L. The RAND contains 36 questions scored in 8 domains (physical functioning, social functioning, limitations due to physical problems, limitations due to emotional problems, mental health, vitality, pain, and general health perception). Each subscale is ranked from 0 to 100, where a higher score indicates better QoL. The RAND can be converted into two composite scores: physical health composite score (PCS) and mental health composite score (MCS) [10]. The RAQoL contains 30 questions regarding the mental and physical domains, which are answered with yes and no (1/0). The total score is 30, and a lower score indicates a better QoL [11]. The EQ-5D-3L comprises two parts – a descriptive system and a visual analog scale (VAS). The EQ-5D-3L descriptive system measures five dimensions of health: mobility, self-care, usual activities, pain/discomfort, and D/A. Each dimension has 3 levels: without problems (1), there are some problems (2), and severe problems (3). The EQ VAS represents a self-assessment of health on a vertical analog scale from the worst (0) to the best possible health (100). All five dimensions of the EQ-5D-3L questionnaire are converted into a general health index using scores derived from a general population sample. The German time-trade-off (TTO) was used in this research as this European population is most similar to the studied population in Serbia.

Statistical analysis

The correlation analysis was assessed based on Spearman's rank correlation coefficient. The investigation of the predictive value of inflammation parameters and main disease characteristics as the selected variables in the assessment of depression and QoL was carried out using linear and logistic regression analysis methods. Values of $p < 0.05$ were considered statistically significant differences. The obtained results were statistically processed using a statistical program for Windows, version 20.0 (Statistical Package for Social Science-SPSS Inc.).

Results

The study included 53 patients with RA with an average age of 54.6 ± 9.8 years. Women accounted for 86.8% (53/46). There were 35.8% of employed patients (53/19), while 42 patients (79.2%) had primary and secondary education. The main characteristics of subjects and RA are presented in Table 1. Regarding the treatment, 79.2% of patients (42/53) were treated with MTX, while 64.2% (34/53) received glucocorticoids. Biological therapy, mainly tocilizumab (61%), was given to 37.7% of patients (20/53). The average DAS 28 score was 4.0 ± 1.8. About a third of patients (26.4%) were in remission, and slightly more of them had high disease activity (34%). The functional status of the investigated group (HAQ DI) was mildly impaired, and the average value was 0.77 ± 0.77.

Table 1

Clinical features and antirheumatic treatment in patients with rheumatoid arthritis (n = 53)

Parameter (characteristics)	Values
Disease duration (years)	8.0 ± 7.2
Presence of RF and/or anti-CCP	46 (86.8)
Methotrexate use	42 (79.2)
Therapy corticosteroids	34 (64.2)
Therapy another BMD	11 (20.8)
Any biological therapy	20 (37.7)
Tender joint count TJC	5.8 ± 5.7
Swollen joint count SJC	2.2 ± 3.3
VAS	43.5 ± 18.9
DAS28-ESR	4.04 ± 1.79
DAS 28 < 2.6	14 (26.4)
DAS28 2.6–3.1	3 (5.7)
DAS28 > 3.1	15 (28.3)
DAS28 > 5.1	18 (34)
HAQ DI	0.77 ± 0.77

The values represent mean value ± standard deviation (SD) or number (percentages).
RF – rheumatoid factor; VAS – visual analog scale (0–10 cm); HAQ DI (Health Assessment Questionnaire); DAS28 – Disease Activity Score using 28 joints; ESR – erythrocyte sedimentation rate; TJC– tender joint count; SJC – swollen joint count; anti-CCP – anti-cyclic citrullinated peptides; BMD – bone mineral density.

The prevalence of D/A in patients with RA is shown in Table 2.

The prevalence of depression assessed by the HADS questionnaire was 52%. The average value of the HADS score for depression was 7.6 ± 3.2. As assessed by the same questionnaire, the prevalence of anxiety was 32%, with the average HADS score value of 5.8 ± 3.8.

The prevalence of D/A assessed by Question 5 of the EQ-5D questionnaire was 77.4%, of which 38 (71.7%) patients had D/A and 3 (5.7%) patients had severe D/A.

The RAQoL questionnaire indicated moderately impaired QoL with an average score value of 15.5 ± 7.9. A significant percentage of patients had difficulties in all the five QoL domains when the EQ-5D questionnaire was used, mainly in the domain of the presence of pain/discomfort and everyday functioning. The same questionnaire was used to analyze the impact of emotional problems on QoL. It was established that 77.4% (41/53) of patients had problems due to the presence of D/A. As part of the mentioned questionnaire, based on the personal QoL assessment by the patient, the average value on the VAS score of 58.6 ± 16.0 was obtained, while the average value of the general health index (EQ-5D index) was 0.6 ± 0.3 (Table 3).

The RAND36 questionnaire was used for an additional QoL assessment, and the values are presented in Table 4.

An analysis of the QoL and D/A degree ratio revealed a statistically significant negative predictive value of QoL, as assessed by the RAQoL and RAND36 questionnaires, with the presence of D/A (Table 5).

Multivariate linear regression showed statistically significant independent negative predictive value of QoL, as assessed by the RAQoL questionnaire and the mental QoL component of the RAND 36 questionnaire for the degree of depression (Table 6).

Table 2

Prevalence of depression/anxiety (D/A) in patients with rheumatoid arthritis (n = 53)

Parameter	Values
HADS	
depression score	7.6 ± 3.2
0–7	24 (48)
8–10	18 (36)
> 11	8 (16)
anxiety score	5.8 ± 3.8
0–7	34 (68)
8–10	11 (22)
> 11	5 (10)
EQ-5D-3L	
number of patients with D/A	41 (77.4)
number of patients with moderate D/A	38 (71.7)
number of patients with severe D/A	3 (5.7)

The values represent mean value ± standard deviation (SD) or number (percentages).

HADS – Hospital Anxiety and Depression Scale; EQ-5D-3L – European Quality of Life 5 Dimensions 3 Level Version.

Table 3

Quality of life (QoL) assessment using RAQoL and EQ-5D-3L questionnaires

Parameter	Values
RAQoL	15.5 ± 7.9
Present state of health (EQ-5D-3L), any problem	
mobility	41 (77.4)
self-care	34 (64.2)
usual activities	44 (83.0)
pain/discomfort	51 (96.2)
anxiety/depression	41 (77.4)
EQ VAS	58.6 ± 16.0
EQ-5D index value	0.6 ± 0.3

The values represent mean value ± standard deviation (SD) or number (percentages).

RAQoL – Rheumatoid Arthritis Quality of Life; EQ-5D-3L – European Quality of Life 5 Dimensions 3 Level Version; EQ-5D index – general health index derived from all the five categories of the EQ-5D questionnaire; EQ VAS – Visual Analog Scale for the assessment of general health as part of the EQ-5D questionnaire.

Table 4

Quality of life (QoL) assessment using RAND36 questionnaires

Parameter	Values
Physical functioning	45.12 ± 19.20
Role limitations due to physical health	21.63 ± 30.13
Role limitations due to emotional problems	38.44 ± 37.63
Energy/fatigue	39.71 ± 22.83
Emotional well-being	59.62 ± 20.06
Social functioning	53.04 ± 24.82
Pain	40.19 ± 23.41
General health	46.83 ± 16.59
Health change	49.04 ± 29.69
PCS	38.44 ± 22.35
MCS	47.70 ± 26.33

The values represent mean value ± standard deviation.
PCS – Physical Component Summary (PCS) score RAND 36;
MCS – Mental Component Summary (MCS) score RAND 36.

Table 5

Univariate linear regression of the impact of (QoL) on the degree of depression (D)/anxiety (A)

Variables	RAQoL	EQ-5D	PCS RAND36	MCS RAND 36
D score (HADS)	0.596 (p = 0.000)	ns	-0.442 (p = 0.001)	-0.594 (p = 0.000)
A score (HADS)	0.379 (p = 0.008)	ns	-0.308 (p = 0.032)	-0.442 (p = 0.001)
EQ-5D (A/D)	ns		ns	ns

The given values represent the standardized regression coefficient β; ns – nonsignificant.
RAQoL – Rheumatoid Arthritis Quality of Life; HADS – Hospital Anxiety and Depression Scale; PCS – Physical Component Summary (PCS) score RAND 36; MCS – Mental Component Summary (MCS) score RAND36.

Table 6

Multivariate linear regression of quality of life (QoL) for the degree of depression*

Independent variables	Score D (HADS)	p
RAQoL	0.502	0.010
PSC RAND36	0.278	0.173
MCS RAND36	-0.426	0.030

The given values represent the standardized regression coefficient β.
RAQoL – Rheumatoid Arthritis Quality of Life; HADS - Hospital Anxiety and Depression Scale; PCS – Physical Component Summary (PCS) score RAND 36; MCS – Mental Component Summary (MCS) score RAND36.

Discussion

RA is a chronic inflammatory disease accompanied by numerous comorbidities, among which depression and anxiety occupy a significant place.

The results of our study based on the HADS questionnaire show that 52% of patients have some depression symptoms. This result complies with the previous studies in which the same questionnaire was used and which showed that more than 50% of RA patients had depressive disorders [4]. In other studies, the prevalence of depression in RA patients was 14-46%, depending on measuring instruments [12, 13]. In our study, it was found using Question 5 of the EQ-5D-3L questionnaire that even 77.4% of patients had D/A. With the same questionnaire, Arne et al. [14] obtained the prevalence of D/A of 48% in patients with RA. A possible reason for the lower presence of D/A could be the fact that in the said study, more patients (74.4%) had low disease activity in comparison with 32% of our subjects. Rathbun et al. [15], in their research, found a correlation between depression and the patient's assessment on the VAS and pain. Patient global VAS correlated with anxiety levels, which could partially explain the association between anxiety and worse disease activity outcomes in RA [16]. Numerous authors have shown that the correlation between depression and disease activity is bidirectional – active RA leads to the occurrence of depression, while depression impacts the activity of RA. In the work of Hider et al. [17], patients with depression had a higher DAS28 score, while patients with chronic depression had a slight decrease in the DAS28 score despite treatment with TNF inhibitors.

When it comes to anxiety, our research using the HADS questionnaire (HADS score > 8) showed that 32% of patients were anxious. Using the same questionnaire and HADS score > 8, Yokogawa et al. [18] found that 29.3% of patients were anxious. El-Miedany and el-Rasheed [19] found that the prevalence of anxiety in RA was 70%. The study was conducted based on a clinical interview as an instrument for anxiety disorder measurement. In any case, our results comply with data from previous studies, which have demonstrated the level of anxiety in RA of 21–70%, as assessed by various measuring instruments [5].

The reason for the high level of D/A is multifactorial. Upon investigating the impact of social and demographic characteristics of subjects, it was observed that women accounted for 86.8% of the studied group, and it is known that depression is more frequent in the female than the male population.

Investigating the level of education, it was found that about 80% of patients had elementary and secondary education. Salaffi et al. [20] have established that a lower level of education represents a risk factor for chronic musculoskeletal pain and physical functioning, while Evers et al. [21] have pointed to a correlation between a lower level of education and the degree of D/A in RA patients.

A large number of previous studies have demonstrated that a particular level of functional limitation determined using the HAQ is a strong predictor of depression in RA patients [22]. Our study did not demonstrate a correlation between functional limitation and the degree of D/A, as the average HAQ score value in our patients was 0.77 ± 0.77, which was significantly lower than the average HAQ score in patients for whom a correlation with D/A has been found.

It is known that the QoL of RA patients is considerably reduced, which we also obtained in our study using all three questionnaires. The QoL of our patients was reduced in all domains of the EQ-5D-3L questionnaire as well as all physical and mental health domains of the RAND36 questionnaire. These results comply with the results of a study conducted by West and Jonsson [23], who have demonstrated an adverse effect of RA itself on the patient's physical, emotional, and social functioning. The study of Salaffi et al. [20] has demonstrated that the QoL components relating to the patient's physical and functional condition are the most frequently affected domains of the SF36 questionnaire. Our results comply with the said research as, according to the EQ-5D questionnaire, the highest percentage of patients had difficulties in the domain of pain/discomfort (96.2%) and everyday functioning (83%), while according to the RAND 36 questionnaire, the highest degree of impairment was in the domain of limitations in physical functioning (21.6 ± 30.1). The presence of pain is actually the main characteristic of RA, which represents an important factor for determining QoL in the early period of the disease [24].

A meta-analysis showed that patients with RA with depression tended to have lower QoL than patients without depression [25]. Depressed patients with RA have more pain [26], high disease activity [27], and reduced QoL. Our study demonstrated a significant correlation between QoL and the degree of D/A. The multivariate regression analysis showed that the QoL assessed using the RAQoL questionnaire, as well as the MCS score of the RAND 36 questionnaire, is an independent predictor of the degree of depression. That is also in compliance with the studies of Covic et al. [28], who have discovered that physical limitations affect the patient's emotional condition, primarily depression. Numerous cross-sectional and longitudinal studies have demonstrated a significant association of somatic symptoms with the occurrence of D/A [29, 30].

Routine detection and treatment of D/A should be part of a future strategy to improve the overall treatment of RA [2], which requires a multidisciplinary approach in RA treatment [31].

Conclusion

In RA patients, there is a high prevalence of D/A as well as considerable impairment of QoL. The degree of QoL impairment is an independent negative predictor for the degree of depression. The correlation between psychological disorders and somatic symptoms is actually bidirectional, indicating the need for discovering and treating psychological disorders simultaneously with somatic symptoms.

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