Original paper

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The frequency and factors affecting anxiety and depression in patients with rheumatoid arthritis

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Abstract

Introduction: Rheumatoid arthritis (RA) is a chronic inflammatory disease. Anxiety and depression are important problems in patients with RA. The aim of this study was to determine the frequency and the factors affecting depression and anxiety in patients with RA.

Material and methods: One hundred and eighty-two patients with RA, aged 18–85 years, were included in this study. The diagnosis of RA was established according to ACR/EULAR RA classification criteria from 2010. Psychosis, pregnancy, breastfeeding and malignancy were exclusion criteria. The demographic data as well as disease duration, educational status, Disease Activity Score with 28-joint counts (DAS28), Health Assessment Questionnaire (HAQ) score and the Hospital Anxiety and Depression Scale (HADS) were the parameters used in the analysis.

Results: Depression symptoms were present in 50.3%, anxiety in 25.3% of the studied patients. In patients with depression and/or anxiety HAQ and DAS28 scores were higher than other studied RA patients. Depression was determined at significantly higher rates in females, housewives and those with a low education level. Anxiety was determined significantly more often in blue-collar workers.

Conclusions: In the present study, depression and anxiety were observed at high rates in patients with RA. These results confirm the real problem in RA patients in comparison to the general population. This points to the relationship between inflammation and depression and anxiety. Psychiatric evaluations and mental status assessment should not be forgotten together with physical examinations of RA patients.

Key words: depression, anxiety, rheumatoid arthritis, disease activity.

Introduction

Depression is extremely common in patients with rheumatoid arthritis (RA), with an incidence 1.7-fold greater than in individuals without RA [1]. The rate of major depression diagnosed in clinical interviews of RA patients is 16.8%, and the rate of depression in RA patients screened with the Hospital Anxiety and Depression Scale (HADS) has been reported to be between 14.8% and 48% [2].

Hospitalization, loss of workforce, healthcare costs, and mortality are higher in patients with depression and RA compared to those with RA only [3, 4]. Anxiety in RA patients has been reported at the rate of 25.1%. In 16.3% of RA patients, anxiety and depression are seen together [5].

Patients with depression and anxiety symptoms show a reduced response to disease-modifying antirheumatic drugs (DMARDs) and glucocorticosteroids, and there is worsening of physical function and disease activity. Depression symptoms may be a prognostic marker of poor rheumatological outcomes [6, 7].

The presence of depression at the start of treatment has been shown to reduce the response to treatment by 30% [8]. Depression symptoms have also been determined to reduce remission rates [9, 10].

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Material and methods

Participants

This study included patients aged 18–85 years, who presented at our Rheumatology Polyclinic and were diagnosed with RA according to the ACR 2010 diagnostic criteria [11]. Patients were excluded from the study if they had psychosis, were pregnant or breastfeeding, were receiving psychiatric treatment, or had a diagnosis of malignancy.

A record was made for each patient of age, sex, marital status, employment status, body mass index (BMI), disease duration, comorbidities, drugs used in treatment, the Disease Activity Score in 28 joints based on erythrocyte sedimentation rate (DAS28–ESR), the Health Assessment Questionnaire (HAQ) score and the Hospital Anxiety and Depression Scale (HADS) score.

The HADS is used to determine the risk of anxiety and depression in a patient, the level, and severity of change. There are two subscales that separately evaluate anxiety and depression. In the Turkish version of the scale the cut-off points have been determined as 10 for the anxiety subscale, and 7 for the depression subscale [12].

The study protocol was approved by the Ethics Committee of Akdeniz University Faculty of Medicine (07.02.2018 decision number: 150).

Statistical analysis

Descriptive information was presented as means, standard deviations, frequencies, and ranges as appropriate. The χ^2 test for categorical data, Student's *t*-test or the Mann-Whitney *U* test for continuous data was performed for comparisons between demographic and clinical characteristics of patients with or without anxiety and depression.

Multivariate logistic regression analyses were performed to evaluate the relationship of demographic and clinical factors with anxiety or depression in patients with rheumatoid arthritis.

The associations between independent variables and anxiety/depression were expressed as the odds ratio (OR) with 95% confidence interval (CI). A *p*-value less than 0.05 was considered statistically significant. All analyses were done using IBM SPSS Statistics 20.

Results

One hundred and eighty-two patients with RA were included in this study. The mean age of the patients was 52.9 ±12.0 years (range 21–81 years), and the mean disease duration was 11.7 ±8.9 years (range 1–50 years). Seventy-five and three tenths percent of the patients were female. The mean DAS28 score was 2.8 ±1.1 and the mean HAQ score was 1.08 ±1.2.

Table I summarizes the descriptive statistics for age, BMI, disease duration, DAS28, HAQ, and HADS scores, sex, marital and working status, education level, comorbidities and drugs used for RA (conventional synthetic disease-modifying antirheumatic drugs [csDMARDs]

Table I. Demographic and clinical characteristics

Variable	Mean ±SD	Range
Age [years]	52.9 ±12.0	21–81
BMI [kg/m^2]	29.1 ±4.9	18.1–48.7
Disease duration [years]	11.7 ±8.9	1–50
DAS28	2.8 ±1.1	0.9–6.6
HAQ	1.08 ±1.2	0–3
HADS – anxiety	7.5 ±4.3	0–17
HADS – depression	7.2 ±4.0	0–19
	Number (%)	
Anxiety +	46 (25.3)	
Depression +	92 (50.3)	
Sex		
Women	137 (75.3)	
Men	45 (24.7)	
Marital status		
Married	149 (81.9)	
Single	33 (18.1)	
Working status		
Retired	47 (25.8)	
Housewife	102 (56)	
White-collar worker	19 (10.4)	
Blue-collar worker	14 (7.7)	
Education		
Uneducated	39 (21.4)	
Primary school	92 (50.5)	
High school	30 (16.5)	
University	21 (11.5)	
Comorbidities		
None	116 (63.7)	
Present	66 (36.3)	
Drugs		
csDMARD	127 (69.8)	
bDMARD	55 (30.2)	

BMI – body mass index, bDMARD – biologic disease-modifying antirheumatic drug, csDMARD – conventional synthetic disease-modifying antirheumatic drug, DAS28 – Disease Activity Score with 28-joint counts, HADS – Hospital Anxiety Depression Scale, HAQ – Health Assessment Questionnaire.

Table II. The χ^2 test results of demographic characteristics between patients with and without anxiety

Sex						$p = 0.182$
		Women	Men	Total		
Anxiety –	*n* (%)	99 (72.3)	37 (82.2)	136 (74.7)		
Anxiety +	*n* (%)	38 (27.7)	8 (17.8)	46 (25.3)		
Total	*n* (%)	137 (100)	45 (100)	182 (100)		
Marital status						$p = 0.239$
		Married	Single	Total		
Anxiety –	*n* (%)	114 (76.5)	22 (66.7)	136 (74.7)		
Anxiety +	*n* (%)	35 (23.5)	11 (33.3)	46 (25.3)		
Total	*n* (%)	149 (100)	33 (100)	182 (100)		
Education						$p = 0.108$
		Uneducated	Primary	High school	University	Total
Anxiety –	*n* (%)	26 (66.7)	68 (73.9)	22 (73.3)	20 (95.2)	136 (74.7)
Anxiety +	*n* (%)	13 (33.3)	24 (26.1)	8 (26.7)	1 (4.8)	46 (25.3)
Total	*n* (%)	39 (100)	92 (100)	30 (100)	21 (100)	182 (100)
Working status						$p = 0.019$
		Retired	Housewife	White-collar	Blue-collar	Total
Anxiety –	*n* (%)	42 (89.4)	71 (69.6)	15 (78.9)	8 (57.1)	136 (74.7)
Anxiety +	*n* (%)	5 (10.6)	31 (30.4)	4 (21.1)	6 (42.9)	46 (25.3)
Total	*n* (%)	47 (100)	102 (100)	19 (100)	14 (100)	182 (100)
Comorbidities						$p = 0.809$
		None	Present	Total		
Anxiety –	*n* (%)	86 (74.1)	50 (75.8)	136 (74.7)		
Anxiety +	*n* (%)	30 (25.9)	16 (24.2)	46 (25.3)		
Total	*n* (%)	116 (100)	66 (100)	182 (100)		
Drugs						$p = 0.281$
		DMARD	Biological	Total		
Anxiety –	*n* (%)	92 (72.4)	44 (80)	136 (74.7)		
Anxiety +	*n* (%)	35 (27.6)	11 (20)	46 (25.3)		
Total	*n* (%)	127 (100)	55 (100)	182 (100)		

and biological disease-modifying antirheumatic drugs [bDMARDs]).

According to the Turkish validation scores of HADS with a cut-off value of 10 for anxiety and cut-off value of 7 for depression, anxiety was detected in 25.3% of the patients, and depression was detected in 50.3% of the patients.

Tables II and III present the comparisons of sex, marital and working status, education level, comorbidities and drugs used between the patients with or without anxiety and depression. There was a statistically significant difference in working status between patients with or without anxiety and in sex education level and working status between patients with or without depression ($p < 0.05$).

In blue-collar workers presence of anxiety was significantly higher than in retired patients. The depression rate was significantly higher in women compared to men, in uneducated patients compared to patients who are high school or university graduates and in housewives than retired patients. Biological disease-modifying antirheumatic drug and csDMARD users were compared; no statistically significant difference was found in terms of anxiety and depression (Tables II and III).

Tables IV and V present the comparisons of age, disease duration, BMI, DAS28 and HAQ scores. Both patients with anxiety and depression have significantly higher scores of DAS28 and HAQ compared to patients without anxiety and depression ($p < 0.05$), indicating higher disease activity and worse functional status.

Table III. The χ^2 test results of demographic characteristics between patients with and without depression

Sex						p = 0.008
		Women	Men	Total		
Depression –	*n* (%)	60 (43.8)	30 (66.7)	90 (49.5)		
Depression +	*n* (%)	77 (56.2)	15 (33.3)	92 (50.5)		
Total	*n* (%)	137 (100)	45 (100)	182 (100)		
Marital status						p = 0.902
		Married	Single	Total		
Depression –	*n* (%)	74 (49.7)	16 (48.5)	90 (49.5)		
Depression +	*n* (%)	75 (50.3)	17 (51.5)	92 (50.5)		
Total	*n* (%)	149 (100)	33 (100)	182 (100)		
Education						p = 0.002
		Uneducated	Primary	High school	University	Total
Depression –	*n* (%)	13 (33.3)	41 (44.6)	20 (66.7)	16 (76.2)	90 (49.5)
Depression +	*n* (%)	26 (66.7)	51 (55.4)	10 (33.3)	5 (23.8)	92 (50.5)
Total	*n* (%)	39 (100)	92 8100)	30 (100)	21 (100)	182 (100)
Working status						p = 0.006
		Retired	Housewife	White-collar	Blue-collar	Total
Depression –	*n* (%)	32 (68.1)	40 (39.2)	12 (63.2)	6 (42.9)	90 (49.5)
Depression +	*n* (%)	15 (31.9)	62 (60.8)	7 (36.8)	8 (57.1)	92 (50.5)
Total	*n* (%)	47 (100)	102 (100)	19 (100)	14 (100)	182 (100)
Comorbidities						p = 0.082
		None	Present	Total		
Depression –	*n* (%)	63 (54.3)	27 (40.9)	90 (49.5)		
Depression +	*n* (%)	53 (45.7)	39 (59.1)	92 (50.5)		
Total	*n* (%)	116 (100)	66 (100)	182 (100)		
Drugs						p = 0.949
		DMARD	Biological	Total		
Depression –	*n* (%)	63 (49.6)	27 (49.1)	90 (49.5)		
Depression +	*n* (%)	64 (50.4)	28 (50.9)	92 (50.5)		
Total	*n* (%)	127 (100)	55 (100)	182 (100)		

The multivariate logistic regression analysis using anxiety and depression as dependent variables is presented in Table VI. The Health Assessment Questionnaire score was significantly associated with both presence of anxiety (OR = 1.04, 95% CI: 1.00–1.09, p = 0.041) and depression (OR = 1.10, 95% CI: 1.04–1.16, p = 0.000). Being a university graduate was significantly associated with decreased risk of depression (OR = 0.16, 95% CI: 0.02–0.94, p = 0.043).

Discussion

In this study, depression was determined in 50.3% of the patients and anxiety in 25.3%. The DAS28–ESR and HAQ scores were determined to be significantly higher in patients with depression and anxiety compared to those without. Depression was determined at a higher rate in females, those with a low level of education, and housewives. A university level of education was found to reduce the risk of depression. Anxiety was determined at higher rates in blue-collar workers.

In a systematic review of 21 studies that included 4,447 RA patients, the prevalence of depression was found to be 48% [13]. Altan et al. [14] reported a 54% rate of depression and 38% of anxiety in patients with RA, using cut-off points of 10 for anxiety and 7 for depression in the current study, according to HADS. Isık et al. [15] used HADS-A and HADS-D scales and

Table IV. Comparison of demographic and clinical characteristics between patients with and without anxiety

Variable	Anxiety –	Anxiety +	*p*-value
Age	53.3 ±12.6	51.8 ±10.1	0.452
Body mass index	29.0 ±4.6	29.3 ±5.6	0.744
Disease duration	12.3 ±9.0	10.1 ±8.5	0.093
DAS28	2.6 ±1.0	3.3 ±1.2	0.002
HAQ	0.9 ±1.1	1.7 ±1.4	< 0.001

DAS28 – Disease Activity Score with 28-joint counts, HAQ – Health Assessment Questionnaire.
Statistical significance was calculated using the Mann-Whitney U test.

Table V. Comparison of demographic and clinical characteristics between patients with and without depression

Variable	Depression –	Depression +	*p*-value
Age	51.6 ±12.1	54.2 ±11.9	0.152
Body mass index	28.6 ±4.8	29.6 ±4.9	0.194
Disease duration	11.5 ±9.1	11.9 ±8.8	0.735
DAS28	2.5 ±0.9	3.1 ±1.2	0.001
HAQ	0.6 ±0.75	1.6 ±1.47	< 0.001

DAS28 – Disease Activity Score with 28-joint counts, HAQ – Health Assessment Questionnaire.
Statistical significance was calculated using the Mann-Whitney U test.

Table VI. Multivariate analysis for demographic and clinical factors associated with anxiety and depression in patients with rheumatoid arthritis

Variable	Anxiety		Depression	
Factors	RR (95% CI)	*p*-value	RR (95% CI)	*p*-value
Age	0.99 (0.95–1.03)	0.991	1.02 (0.97–1.06)	0.347
Body mass index	1.02 (0.94–1.10)	0.562	1.05 (0.98–1.13)	0.148
Disease duration	0.96 (0.91–1.01)	0.200	0.99 (0.95–1.04)	0.854
DAS28	1.37 (0.94–1.99)	0.095	1.31 (0.92–1.87)	0.124
HAQ	1.04 (1.00–1.09)	0.041	1.10 (1.04–1.16)	0.000
Sex	2.12 (0.49–9.07)	0.308	3.15 (0.94–10.61)	0.063
Marital status	1.31 (0.47–3.58)	0.599	0.52 (0.19–1.43)	0.209
Education				
Uneducated		0.275		0.063
Primary school	1.17 (0.45–3.04)	0.735	1.27 (0.49–3.26)	0.612
High school	1.05 (0.27–4.09)	0.934	0.55 (0.14–2.12)	0.393
University	0.11 (0.00–1.37)	0.087	0.16 (0.02–0.94)	0.043
Working status				
Retired		0.592		0.251
Housewife	1.27 (0.30–5.38)	0.741	1.04 (0.29–3.68)	0.946
White-collar worker	2.00 (0.34–11.76)	0.442	3.48 (0.74–16.39)	0.113
Blue-collar worker	3.25 (0.57–18.41)	0.181	3.62 (0.66–19.68)	0.136
Comorbidities	1.09 (0.47–2.50)	0.832	1.70 (0.79–3.64)	0.171
Drugs	1.77 (0.73–4.28)	0.199	1.40 (0.64–3.05)	0.390

DAS28 – Disease Activity Score with 28-joint counts, HAQ – Health Assessment Questionnaire.

found 41.5% depression and 13.4% anxiety in patients with RA, and these rates were found to be significantly higher than in the control group.

Different rates have been reported in various studies on the subject of the frequency of depression and anxiety, and these differences have been attributed to the design of the study, the scales used, and a possible relationship with geography and socioeconomic status [13].

In a study of German and Brazilian patients with RA, depression was determined at a higher rate in the Brazilians. High disease activity has been found to be associated with depression [16].

In an Italian cohort of 490 patients, depression was determined in 14.3%. There was determined to be a significant increase in the risk of depression with male sex, a high HAQ score, patient global evaluation and the use of antidepressants [17].

It is accepted that there is a two-way relationship between RA and depression [18, 19]. Depression is seen more in RA patients, and there has been found to be an increased risk of RA development in individuals with depression. There are increased proinflammatory cytokines in depression similar to in RA, and these cytokines are reduced with antidepressant treatment [20].

In patients with major depressive disorder, the risk of developing RA is increased by 38% compared to the normal population and the risk of RA development has been reported to be reduced in those using antidepressants compared to non-users [21]. Some anticytokine treatments used in RA have been determined to have positive effects on depression [22].

In a study by Ng et al. [23], depression and anxiety were found to be strongly correlated with DAS28–ESR. Depression has been determined to be significantly low in patients using etanercept. It has been reported that female sex and disease activity are strong predictors for depression.

In a study of 18,421 RA patients taking biological treatment, Matcham et al. [8] determined that the response to treatment in 1 year decreased by 20–40% when depression was present at the start of biological treatment.

Fragoulis et al. [24] examined 848 early RA patients and reported the prevalence of anxiety and depression to be 19.0% and 12.2%, respectively. A relationship was found between depression and anxiety, disease activity and a poor functional result. A relationship was also found between CRP levels and depression but not with anxiety.

In a meta-analysis, Zhang et al. [25] determined higher disease activity and lower quality of life in RA patients with depression compared to those without depression, but no difference was determined with respect to pain and functional disability. A low socioeconomic status, female sex, young age, and functional limitations have been reported to be factors associated with depression in RA patients [26]. Depression is generally associated with the severe form of RA [27].

Watad et al. [28] determined a higher rate of anxiety in RA patients than in a control group. Female sex, young age, smoking, and low socioeconomic status were reported to be independent factors associated with anxiety. In another study, low socioeconomic status and high DAS28 scores were determined to be associated with anxiety [24].

In our study, when bDMARD and csDMARD users were compared, no statistically significant difference was found in terms of anxiety and depression. In our study, we found a significant difference between the patients' DAS28 and HAQ scores and the presence of anxiety and depression.

Similarly, in a study, bDMARDs and cDMARDs were not found to be superior to each other in terms of depression [29]. There is a need for further studies specifically investigating the effects of bDMARDs on depression and anxiety.

Depression was determined to be related to the global health score in a study of 464 RA patients, and anxiety was determined to be related to being married and functional disability [30]. In another study, it was reported that the presence of anxiety and depression in patients with RA can cause suicide and diminished quality of life and can worsen the prognosis of RA [31].

Study limitations

The study had a relatively low number of patients, a cross-sectional design, was conducted in a single center, and it lacked a control group.

In addition, the socioeconomic status of the patients was not examined. As the study included patients who were being followed up in a tertiary level center, the results may not be generalizable to all RA patients.

Conclusions

Depression and anxiety are observed extremely frequently in RA patients. It should be taken into consideration that this may affect the remission response of patients, the prognosis, and even mortality, and there should be collaboration with the psychiatry department in these cases.

The authors declare no conflict of interest.

References

1. Lin MC, Guo HR, Lu MC, et al. Increased risk of depression in patients with rheumatoid arthritis: a seven-year population-based cohort study. Clinics (Sao Paulo) 2015; 70: 91–96, DOI: 10.6061/clinics/2015(02)04.
2. Matcham F, Rayner L, Steer S, Hotopf M. The prevalence of depression in rheumatoid arthritis: a systematic review and meta-analysis. Rheumatology (Oxford) 2013; 52: 2136–2148, DOI: 10.1093/rheumatology/ket169.
3. Li N, Chan E, Peterson S. The economic burden of depression among adults with rheumatoid arthritis in the United States. J Med Econ 2019; 22: 372–378, DOI: 10.1080/13696998.2019.1572015.
4. Marrie RA, Walld R, Bolton JM, et al. Psychiatric comorbidity increases mortality in immune-mediated inflammatory diseases. Gen Hosp Psychiatry 2018; 53: 65–72, DOI: 10.1016/j.genhosppsych.2018.06.001.
5. Rayner L, Matcham F, Hutton J, et al. Embedding integrated mental health assessment and management in general hospital settings: feasibility, acceptability and the prevalence of common mental disorder. Gen Hosp Psychiatry 2014; 36: 318–324, DOI: 10.1016/j.genhosppsych.2013.12.004.
6. Matcham F, Norton S, Scott DL, et al. Symptoms of depression and anxiety predict treatment response and long-term physical health outcomes in rheumatoid arthritis: a secondary analysis of a randomised controlled trial. Rheumatology (Oxford) 2016; 55: 268–278, DOI: 10.1093/rheumatology/kev306.
7. Rathbun AM, Reed GW, Harrold LR. The temporal relationship between depression and rheumatoid arthritis disease activity, treatment persistence and response: a systematic review. Rheumatology (Oxford) 2013; 52: 1785–1794, DOI: 10.1093/rheumatology/kes356.
8. Matcham F, Davies R, Hotopf M, et al. The relationship between depression and biologic treatment response in rheumatoid arthritis: an analysis of the British Society for Rheumatology Biologics Register. Rheumatology (Oxford) 2018; 57: 835–843, DOI: 10.1093/rheumatology/kex528.
9. Rathbun AM, Harrold LR, Reed GW. A prospective evaluation of the effects of prevalent depressive symptoms on disease activity in rheumatoid arthritis patients treated with biologic response modifiers. Clin Ther 2016; 38: 1759–1772.e3, DOI: 10.1016/j.clinthera.2016.06.007.
10. Michelsen B, Kristianslund EK, Sexton J, et al. Do depression and anxiety reduce the likelihood of remission in rheumatoid arthritis and psoriatic arthritis? Data from the prospective multicentre NOR-DMARD study. Ann Rheum Dis 2017; 76: 1906–1910, DOI: 10.1136/annrheumdis-2017-211284.
11. Aletaha D, Neogi T, Silman AJ, et al. 2010 rheumatoid arthritis classification criteria: an American College of Rheumatology/European League Against Rheumatism collaborative initiative. Ann Rheum Dis 2010; 69: 1580–1588, DOI: 10.1136/ard.2010.138461.
12. Aydemir Ö, Güvenir T, Küey L, Kültür S. Hastane anksiyete ve depresyon ölçeği Türkçe formunun geçerlilik ve güvenilirliği. Türk Psikiyatri Dergisi 1977; 8: 280–287.
13. Fu X, Li ZJ, Yang CJ, et al. The prevalence of depression in rheumatoid arthritis in China: a systematic review. Oncotarget 2017; 8: 53623–53630, DOI: 10.18632/oncotarget.17323.
14. Altan L, Bingöl Ü, Sağırkaya Z, et al. Romatoid artritli hastalarda anksiyete ve depresyon. Romatizma 2004; 19: 7–13.
15. Isık A, Koca SS, Ozturk A, Mermi O. Anxiety and depression in patients with rheumatoid arthritis. Clin Rheumatol 2007; 26: 872–878, DOI: 10.1007/s10067-006-0407-y.
16. Morf H, da Rocha Castelar-Pinheiro G, Vargas-Santos AB, et al. Impact of clinical and psychological factors associated with depression in patients with rheumatoid arthritis: comparative study between Germany and Brazil. Clin Rheumatol 2021; 40: 1779–1787, DOI: 10.1007/s10067-020-05470-0.
17. Pezzato S, Bonetto C, Caimmi C, et al. Depression is associated with increased disease activity and higher disability in a large Italian cohort of patients with rheumatoid arthritis. Adv Rheumatol 2021; 61: 57, DOI: 10.1186/s42358-021-00214-3.
18. Nerurkar L, Siebert S, McInnes I, Cavanagh J. Rheumatoid arthritis and depression: an inflammatory perspective. Lancet Psychiatry 2019; 6: 164–173, DOI: 10.1016/S2215-0366(18)30255-4.
19. Vallerand IA, Patten SB, Barnabe C. Depression and the risk of rheumatoid arthritis. Curr Opin Rheumatol 2019; 31: 279–284, DOI: 10.1097/BOR.0000000000000597.
20. Wiedlocha M, Marcinowicz P, Krupa R, et al. Effect of antidepressant treatment on peripheral inflammation markers: a meta-analysis. Prog Neuropsychopharmacol Biol Psychiatry 2018; 80: 217–226, DOI: 10.1016/j.pnpbp.2017.04.026.
21. Vallerand IA, Lewinson RT, Frolkis AD, et al. Original article: depression as a risk factor for the development of rheumatoid arthritis: a population-based cohort study. RMD Open 2018; 4: e000670, DOI: 10.1136/rmdopen-2018-000670.
22. Fakra E, Marotte H. Rheumatoid arthritis and depression. Joint Bone Spine 2021; 88: 105200, DOI: 10.1016/j.jbspin.2021.105200.
23. Ng KJ, Huang KY, Tung CH, et al. Risk factors, including different biologics, associated with depression and anxiety in patients with rheumatoid arthritis: a cross-sectional observational study. Clin Rheumatol 2020; 39: 737–746, DOI: 10.1007/s10067-019-04820-x.
24. Fragoulis GE, Cavanagh J, Tindell A, et al. Depression and anxiety in an early rheumatoid arthritis inception cohort. associations with demographic, socioeconomic and disease features. RMD Open 2020; 6: e001376, DOI: 10.1136/rmdopen-2020-001376.
25. Zhang L, Cai P, Zhu W. Depression has an impact on disease activity and health-related quality of life in rheumatoid arthritis: a systematic review and meta-analysis. Int J Rheum Dis 2020; 23: 285–293, DOI: 10.1111/1756-185X.13774.
26. Jacob L, Rockel T, Kostev K. Depression risk in patients with rheumatoid arthritis in the United Kingdom. Rheumatol Ther 2017; 4: 195–200, DOI: 10.1007/s40744-017-0058-2.
27. Godha D, Shi L, Mavronicolas H. Association between tendency towards depression and severity of rheumatoid arthritis from a national represen-tative sample: the Medical Expenditure Panel Survey. Curr Med Res Opin 2010; 26: 1685–1690, DOI: 10.1185/03007991003795808.

28. Watad A, Bragazzi NL, Adawi M, et al. Anxiety disorder among rheumatoid arthritis patients: insights from real-life data. J Affect Disord 2017; 213: 30–34, DOI: 10.1016/j.jad.2017.02.007.
29. Yayikci YI, Karadag A. Effects of conventional and biological drugs used for the treatment of rheumatoid arthritis on the quality of life and depression. Euras J Med 2019; 51: 12–16, DOI: 10.5152/eurasianjmed.2018.18018.
30. Katchamart W, Narongroeknawin P, Chanapai W, et al. Prevalence of and factors associated with depression and anxiety in patients with rheumatoid arthritis: a multicenter prospective cross-sectional study. Int J Rheum Dis 2020; 23: 302–308, DOI: 10.1111/1756-185X.13781.
31. Beşirli A, Alptekin JÖ, Kaymak D, Özer ÖA. The relationship between anxiety, depression, suicidal ideation and quality of life in patients with rheumatoid arthritis. Psychiatr 2020; 91: 53–64, DOI: 10.1007/s11126-019-09680-x.