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Depression in Rheumatoid Arthritis: Association with Quality of Life, Function and Disease Activity

Romatoid Artritte Depresyon: Yaşam Kalitesi, Fonksiyon ve Hastalık Aktivitesi ile İlişkisi

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Abstract
Objectives: The aim of our study is to evaluate the depression rate in patients with rheumatoid arthritis (RA) and its association with pain, disease activity, functional status, and various health related quality of life (HRQoL) domains in terms of functional status, vitality, social and emotional functioning.
Materials and Methods: A total of 90 RA patients and 50 sex and age matched controls were included in the study. Demographic characteristics, erythrocyte sedimentation rates, C-reactive protein, tender and swollen joint count, patient and physician global assessment of disease activity were recorded. Disease Activity Score-28 (DAS28) was used for measuring disease activity. The severity of pain was determined by using 10 cm Visual Analog Scale-Pain (VAS-pain). HRQoL was evaluated by using Short Form 36 (SF 36).
HAQ (Health Assessment Questionnaire) was used for evaluation of the functional status. Depression was evaluated by using Beck Depression Scale (BDS).
Results: Mean age was 54.51±12.54 in RA (75 women, 15 men) group and 51.94±9.69 in the control group (41 women, 9 men). Mean VAS-pain was 55.85±26.24; HAQ was 1.27±0.81 and DAS28 was 5.04 ±2.44 in RA patients. The mean BDS was 19.67±13.11 in RA group and 6.64±6.73 in the control group. RA patients scored significantly higher in BDS when compared with the controls (p<0.001). BDS was linearly related with DAS28 and VAS-pain at a high level and negatively correlated with physical function, physical role, bodily pain, general health, vitality, mental health, social functioning and emotional role subgroups of SF36 (p<0.001). There was no statistically significant relation between BDS and HAQ (*p*=0.431)
Conclusion: Depression is common in the patients with RA and associated with disease activity and pain. It negatively affects HRQoL in terms of vitality, and physical, social and emotional functioning.
Key words: Arthritis, rheumatoid; depression; quality of life

Öz
Amaç: Çalışmamızın amacı romatoid artritli (RA) hastalarda ağrı, hastalık aktivitesi, fonksiyonel durum ve vitalite, fonksiyonellik, sosyal ve duygusal işlevsellik gibi sağlıkla ilişkili yaşam kalitesi (HRQoL) alanları arasındaki ilişkiyi değerlendirmektir.
Materyal ve Metot: Çalışmaya toplam 90 RA hastası ve 50 cinsiyet ve yaş uyumlu kontrol dahil edildi. Demografik özellikler, eritrosit sedimantasyon oranları, C-reaktif protein, hassas ve şiş eklem sayısı, hasta ve hekimin global değerlendirmesi kaydedildi. Hastalık aktivitesini ölçmek için Hastalık Aktivite Skoru-28 (DAS28) kullanıldı. Ağrının şiddeti, 10 cm Görsel Analog Skala-Ağrı (VAS-ağrı) kullanılarak belirlendi. HRQoL, Kısa Form 36 (SF 36) kullanılarak değerlendirildi. Fonksiyonel durumun değerlendirilmesi için HAQ (Sağlık Değerlendirme Anketi) kullanıldı. Depresyon, Beck Depresyon Ölçeği (BDS) kullanılarak değerlendirildi.
Bulgular: Yaş ortalaması RA'da (54 kadın, 15 erkek) 54,51 ± 12,54; kontrol grubunda (41 kadın, 9 erkek) 51,94 ± 9,69 idi. RA'lı hastalarda ortalama VAS 55,85 ± 26,24 idi; HAQ 1,27 ± 0,81, DAS28 ise 5,04 ± 2,44 idi. RA grubunda ortalama BDS 19,67 ± 13,11 ve kontrol grubunda 6,64 ± 6,73 idi. RA hastalar kontrol grubu ile karşılaştırıldığında, BDS'de anlamlı olarak daha yüksek puan aldı (p <0,001). BDS ile DAS28 ve VAS-ağrı arasında doğrusal ilişki vardı ve SF36'nın fiziksel işlev, fiziksel rol, vücut ağrısı, genel sağlık, vitalite, zihinsel sağlık, sosyal işlevsellik ve duygusal rol alt grupları ile negatif korelasyon gösterdi (p <0,001). BDS ve HAQ arasında istatistiksel olarak anlamlı bir ilişki bulunmadı (p=0,431).

Sonuç: RA'lı hastalarda depresyon yaygındır ve hastalık aktivitesi ve ağrı ile ilişkilidir. Depresyon, vitalite fiziksel, sosyal ve duygusal işlevler açısından HRQoL'yi olumsuz yönde etkilemektedir.
Anahtar kelimeler: Artrit, romatoid, depresyon, yaşam kalitesi

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Introduction

Mood disorders are common in the general population, with 12-month prevalence rate of 9.5%.[1] The rate of depression is higher among individuals suffering from chronic medical conditions. As with any chronic condition, there is a high rate of depression in the patients with autoimmune disorders compared to the general population.[2]

Rheumatoid arthritis (RA) is a chronic autoimmune disease characterized by persistent synovitis and systemic inflammation.[3] Chronic inflammation and pain may cause decreased physical activity, functional deficiencies, impaired quality of life, and psychological disturbances. RA has a significant effect on patients' lives, being ranked among the highest of all chronic diseases in terms of physical, social and emotional functions.[4]

The aim of our study is to evaluate depression and its association with disease activity, functional status and pain, and as well as to determine its impact on various health related quality of life (HRQoL) domains in terms of functional status, vitality, social and emotional functioning.

Materials and Methods

This cross-sectional study was conducted at the physical medicine and rehabilitation clinic of a training and research hospital between January and April 2018. All of the patients gave their informed consent prior to their inclusion in the study. The study protocol was approved by the Medical Research Ethics Committee of the hospital. The study conforms to the provisions of the World Medical Association's Declaration of Helsinki.

A total of 90 RA patients (75 women, 15 men) who met the American College of Rheumatology (ACR) and European League Against Rheumatology (EULAR) 2010 classification criteria for RA and 50 sex and age matched controls (41 women, 9 men) were included in the study[5]. Exclusion criteria were: < 18 years old, severe cognitive and neurological problems (stroke, multiple sclerosis, amyotrophic lateral sclerosis etc.), active cancer, and receiving any antidepressant medication in the last year.

Demographic characteristics, erythrocyte sedimentation rates, C-reactive protein, tender and swollen joint count, patient and physician global assessment of disease activity (PGA and PhGA) were recorded.

Disease Activity Score-28 (DAS28) was used for measuring disease activity.[6] The severity of pain was determined by using 10 cm Visual Analog Scale-Pain (VAS-pain).[7]

HRQoL was evaluated by using Short Form 36 (SF 36).[8] HAQ was used for evaluation of the functional status.[9]

Depression was evaluated by using Beck Depression Scale (BDS).[10] BDS is a self-rated questionnaire which includes 21 items where each item is scored between 0 and 3. Cut off values are 0-10 for normal, 11-16 for mild to moderate depression, 17-20 for borderline clinical depression, 21-29 for moderate to severe depression and 30-63 for severe depression.

Examination and questionnaires of all the individuals involved in the study were made performed by the same physician.

Statistical Analysis

Descriptive statistics [mean, median, SD (Standard deviation), minimum, maximum and frequencies] were used for assessing the demographics and clinical parameters. Differences between patients and controls were compared using Mann-Whitney U test. The presence of correlation was evaluated by Pearson's or Spearman's correlation coefficient according to test of normality results. A value of $p<0.05$ was considered statistically significant. All analyses were performed using Statistical Package for the Social Sciences-21.0 (SPSS 21.0) software. Post hoc power analysis was made by using G power 3.1.9.2 program. Analysis showed that power of the study (1-β err prob) was 0.86 for our sample size (group 1 =90; group 2=50).

Results

Demographic characteristics

A total of 90 patients with RA (75 women, 15 men) and 50 healthy controls (41 women, 9 men) were included. Mean age was 54.51±12.54 in RA group and 51.94±9.69 in the control group. Age and gender did not significantly differ among the groups (p=0.212, p=0.841 respectively).

Clinical findings, disease activity and functional status of the patients

Mean VAS-pain was 55.85±26.24; HAQ was 1.27±0.81 and DAS28 was 5.04 ±2.44 in RA patients. According to DAS28, 2.22% of the patients (2 patients) were in remission. 16.66% of the patients (15 patients) had mild, 65.55% (59 patients) moderate and 15.55% (14 patients) severe disease activity.

Level of depression and health-related quality of life of the patients

The mean BDS was 19.67±13.11. Of the patients; 26.66% (24 patients) were normal, 18.88% (17 patients) had mild to moderate depression; 12.22% (11 patients) had borderline clinical depression, 35.55% (32 patients) had moderate to severe depression and 6.66% (6 patients) had severe depression. In the control group, 96.00% (48 patients) were normal and 4.00% (2 patients) had mild to moderate depression. The mean±SD HRQoL scores of the patients were 47.67±27.15, 37.22±42.93, 44.61±21.41, 40.97±22.52, 43.56±23.89, 56.53±25.84, 48.14±45.28, and 56.47±21.36 in the physical functioning, role-physical, bodily pain, general health, vitality, social functioning, role-emotional, and mental health subgroups of SF36, respectively.

Demographics and clinical data are summarized in Table 1.

Table 1. Demographic and Clinic Patient Data

	Minimum	Maximum	Median	Mean	Standard deviation
Age (years)				54.51	12.54
VAS-pain	0.00	10.00	4.00	5.04	2.44
Patient Global Assessment	0.00	9.00	3.00	3.50	2.64
Physican Global Assessment	0.00	8.00	3.00	2.88	2.01
DAS 28	2.55	6.39	3.34	4.11	0.98
HAQ	0.00	3.00	0.62	1.27	0.81
BDS				19.67	13.11
SF36- physical function	0.00	100.00	62.50	47.67	27.15
SF36- physical role	0.00	100.00	75.00	37.22	42.93
SF36- pain	0.00	100.00	51.00	44.61	21.41
SF36- general health	0,00	92.00	52.00	40.97	22.52
SF36- energy	0.00	95.00	55.00	43.56	23.89
SF36- social functions	0.00	100.00	62.50	56.53	25.84
SF36- emotional role	0.00	100.00	83.35	48.14	45.28
SF36- mental health	4.00	96.00	68.00	56.47	21.36

VAS:Visual Analog Scale; DAS 28: Disease Activity Score 28; HAQ: Health Assessment Questionnaire, BDS: Beck Depression Scale; SF-36: Short Form 36.

Comparison of level of depression of the patients and the controls

The mean BDS was 19.67±13.11 in RA group and 6.64±6.73 in the control group. RA patients scored significantly higher in BDS when compared with the controls ($p<0.001$) (Table 2).

The relation of depression with clinical parameters and health related quality of life parameters

BDS was linearly related with DAS28 and VAS-pain at a high level ($p<0.001$, $p=0.005$ respectively). There was no statistically significant relation between BDS and HAQ ($p=0.431$) (Table 3).

BDS was found to be negatively correlated with physical function, physical role, bodily pain, general health, vitality, mental health, social functioning and emotional role subgroups of SF36 ($p<0.001$). When the correlation coefficients were analyzed, mental health showed the highest negative correlation with BDS ($r=-0.770$). It was followed by

vitality and social functioning subgroups of SF36 (r=-0.710 and 0.620, respectively) (Table 3).

Table 2. The comparison of depression of the patients and the control group

	RA group (n=90) mean±standard deviation	**Control group (n=50) mean±standard deviation**	***p* value**
BDS	15.00±8.42	6.21±9.26	<0.001**

*BDS: Beck Depression Scale, *: p<0.05 (significant), **: p<0.01 (highly significant)*

Table 3. The relation of depression with clinical variables and health-related quality of life

Clinical Variables		**BDS**
VAS-pain	r	0.292
	p	0.005**
DAS28	r	0.389
	p	<0.001**
HAQ	r	0.081
	p	0.431
SF36-physical function	r	-0.371
	p	<0.001**
SF36-physical role	r	-0.395
	p	<0.001**
SF36-bodily pain	r	-0.407
	p	<0.001**
SF36-general health	r	-0.534
	p	<0.001**
SF36-vitality	r	-0.710
	p	<0.001**
SF36-social functioning	r	-0.620
	p	<0.001**
SF36-emotional role	r	-0.577
	p	<0.001**
SF36-mental	r	-0.770
	p	<0.001**

*VAS: Visual analog scale, SF36: Short form-36, BDS: Beck Depression Scale, *: p<0.05 (significant), **: p<0.01 (highly significant)*

Discussion

Prevalence of depression in chronic diseases varies between 4.8% and 8.6%.[11] It is a major cause of morbidity in individuals with rheumatic disorders.[12,13] The major cause of depression in rheumatic diseases is that the patients have a chronic course which requires effective monitoring and management. Since clinical features of the disease may mimic depressive symptoms, it is difficult to detect and manage the depression.[14]

Depression is highly prevalent in RA patients. In a meta-analysis including 72 studies and 13189 patients, the prevalence of RA throughout the world was 38.8%.[15] Pu et al. evaluated depressive symptoms in 161 Chinese patients by using Hamilton Depression Scale and suggested that patients with RA had higher levels of depressive symptoms as compared to the healthy controls.[16] They reported the prevalence of depression as 62%. In a meta-analysis which was performed in the patients with RA in China, the prevalence rate of depression was 48%. It was suggested that clinicians should pay more attention to depression in the patients with RA.[17] In the study of Masood et al. where 128 patients with RA were evaluated with BDS at a tertiary care center in Pakistan, the rate of depression was 47.7%.[18] Jamshidi et al. reported the rate of depression in Iranian RA patients as 63.6%.[19] They measured the severity of depression using BDS. In our study, 26.66% of the patients were normal, 18.88% had mild to moderate depression; 12.22% borderline clinical depression, 35.55% moderate to severe depression and 6.66% severe depression. Also, RA patients scored significantly higher in BDS when compared with the controls. Estimates differ according to the way in which depression was measured. In our series, depression was more frequent when compared to the other trials. There may be three reasons for more frequent depression. The first one is the assessment method that we used. The second one is patient selection criteria. Since our group of patients was composed of mostly severe ones requiring regular follow-up in a tertiary hospital, there is a possibility for overestimating the frequency of depression when compared to RA patients in community.

In our study, severity of depression was positively correlated with disease activity. Association between depression and RA disease activity may be explained by immune and neurotransmitter disregulation. This disregulation may activate autoimmune mechanisms that play role in RA.[20] Also, Imran et al. reported that DAS 28 levels were correlated with BDS scores in Pakistani patients with RA.[21] They suggested that clinicians should screen RA patients for comorbid depression and manage it. On the other hand, Matcham et al. found a strong association between DAS28 and Hospital Anxiety Depression Scale scores in RA patients at 1-year follow-up.[22] They attributed this association to the subjective components of DAS 28 including tender joint count and patient global assessment. They suggested that depressive symptoms may cause high DAS28 levels and false positive disease activity despite well controlled inflammatory disease. Contrarily, Jamshidi et al. did not report any correlation between severity of depressive symptoms and disease activity in RA patients.[19] They assessed disease activity by using Disease Activity Score.

We found that depression was associated with severity of pain in our patients with RA. The same relation was reported in previous studies in the literature.[23] Psychological

processes have an influence on both the experience of pain and the treatment outcome.[24] Depression-pain link might be due to illness perception.[25] Illness perception is the cognitive and emotional representations that patients have about their diseases. It includes the emotional and behavioral responses, coping style and psychosocial reactions of the patient.[26] In this context, the patients' beliefs and emotional responses to their symptoms are key factors in the perception of pain.

There was no statistically significant relation between depression and functional status in our study. Contrarily, Imran et al. found that depression levels were positive correlate with HAQ scores in Pakistani.[21] Also Massod et al. reported that there was a strong association between BDI and HAQ scores.[18]

We investigated the impact of depression on various HRQoL domains. We found that depression levels were associated with HRQoL in terms of functional status, vitality, pain, mental health, and social and emotional functioning. Mental health was first in rank among the variables that influenced severity of depression. It was followed by vitality and social functioning. Previously, Ozcetin et al. found a strong negative correlation between BDS and all domains of SF36 in Turkish patients with RA.[27] Similarly, the same relationship was reported in a study conducted in United States of America.[28]

There are a few limitations in our study. Firstly, we used a screening tool for detecting depression. It might cause high rate of depression in our series. The 'gold standard' diagnosing method for depression is individual clinical interviews. Relatively small patient population and unbalanced patient and control groups may be regarded as another limitation.

In conclusion, depression is common in the patients with RA, and associated with disease activity and pain. It negatively affects HRQoL in terms of vitality, and physical, social and emotional functioning. Physicians should pay attention to depression in RA patients. Depressive symptoms should be screened in the routine controls and managed promptly.

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