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Anxiety and Depression in Inflammatory Rheumatic Diseases

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Abstract

Objective: To compare the degree of anxiety and depression in patients suffering from rheumatoid arthritis (RA), systemic lupus erythematosus (SLE) and systemic sclerosis (SSc), also to determine the relationship between the duration of diseases and the symptoms of anxiety and depression.

Methods: We included 106 RA, 62 SLE and 28 SSc patients. Beck Anxiety Inventory (BAI) and Beck Depression Inventory (BDI) were used to assess anxiety and depression. Cut-off point was 14 for BAI, and 10 for BDI. According to the results of the questionnaire, respondents were categorized in: no, mild, moderate, and severe anxiety / depression group. Psychologists participated in analysis of the surveys.

Results: 49.5% of patients were anxious, and 52.0% were depressive. The highest median of BDI was found in SSc patients (11.5 for SSc, 10 for RA, 6.5 for SLE). Median values of BAI were approximately the same in all three diseases (14 for RA, 12.5 for SLE, 13 for SSc). Average disease durations were similar in RA (13.24 years) and SLE (12.78 years), and shorter in SSc (10.29 years) patients. The most common symptom of depression was fatigue.

Conclusion: The anxiety was similar in all studied diseases. The degree of depression was the highest in SSc patients, who also had the shortest disease duration average. The relationship between disease duration and the appearance of anxiety and depression was not significant. Depression in SSc may occur due to the pathophysiology of disease, or due to the worst prognosis compared with SLE and RA.

Keywords: Anxiety; Depression; Rheumatoid arthritis; Systemic lupus erythematosus; Systemic sclerosis

Introduction

Rheumatic diseases affect many organ systems and usually have chronic course. Painful sensations, engaging of internal organs and skin, and hand and foot deformities in patients with systemic lupus erythematosus (SLE), systemic sclerosis (SSc) and rheumatoid arthritis (RA) can lead to the development of anxiety and depression. Furthermore, low quality of life and psychosocial status can cause anxiety and depression in patients suffering from inflammatory rheumatic diseases [1,2]. Prevalences of anxiety and mainly depression increase in patients suffering of RA over time, due to more psychological distress compared with healthy individuals [3-5]. In SLE, most common cause of depression is pain, although newer studies stress neuroimmunological role of neurotransmitters and cytokines [6,7]. In SSc, depression and anxiety correlate with local and global disabilities and psychological characteristics, so with the time, patients have more difficulties to cope with disease [8,9]. There are only few articles in the literature which compared anxiety and depression between RA, SLE and SSc, but neither one analyzed which disease has the highest incidence or degree of anxiety/depression.

Anxiety and depression are also associated with rheumatic diseases in some other ways, such as time of appearance and gender engaging. They are more often in females, what is similar with rheumatic diseases [10-14]. There is no significant difference in peak prevalence of major depression and SLE [11,15]. Anxiety and depression are common in many chronic diseases, such as diabetes mellitus or chronic renal failure, and they occur due to complications of the main disease or type of applied therapy. Patients with psychosocial support have better therapy compliance and higher quality of life [16-19]. Considering most common used therapy, there is evidence that corticosteroids lower serotonin level, what can also cause depression [20]. After all, there is a projection from 1997 which had foreseen that major depression will be second cause of disability by 2020, after ischemic heart diseases and before some other common conditions such as road-traffic accidents, cerebrovascular diseases or chronic obstructive pulmonary diseases [21].

Our aim was to investigate incidence of symptoms of anxiety and depression in patients suffering from RA, SLE and SSc. We chose these three diseases because of their differences in pathophysiology and systemic impact on organism, so the whole rheumatology could be representatively presented. We also compared degree of anxiety and depression between studied diseases and determined correlation with duration of diseases. We hypothesized that degree of anxiety and depression is highest in patients with SSc, because SSc is poorly researched and has worse therapy options compared with RA and SLE. Our second hypothesis was that longer duration of rheumatic disease is associated with higher degree of anxiety and depression.

Materials and Methods

Our research was designed as cross-sectional study. It was performed at Department of Clinical Immunology and Rheumatology. Data collection lasted from August 2012 to April 2014. We included 106 patients with RA, 62 with SLE and 28 with SSc. All patients were

diagnosed by licensed rheumatologist, according ARA criteria from 1987 and revised ACR/EULAR criteria from 2010 for RA, ACR criteria from 1997 (Hochberg MC) for SLE, and diagnostic criteria from 1980 and revised ACR/EULAR criteria from 2013 for SSc [22-26]. We excluded patients with CNS lupus, psycho-organic syndrome and daily dose of prednisolone higher more than 10 mg from the study because of the potential impact to BAI/BDI results.

We got information about disease onset and duration during anamnesis and, after that, patients fulfilled their questionnaires. Beck Anxiety Inventory (BAI) and Beck Depression Inventory (BDI) were used to assess anxiety and depression. These inventories are in use for many years as helpful diagnostic tool [27,28]. They are designed as 21-question self-report inventory, and for each question respondents had to pick one of four offered answers scored 0 to 3. The sum of these points is between 0 and 63, and it makes BAI/BDI total score. BAI describes prevalence of: numbness, hot sensations, wobbliness in legs, inability to relax, fear of worst happening, dizziness, heart pounding/racing, unsteadiness, feeling terrified, nervous, choking, hands trembling, body trembling, fear of losing control, difficulties in breathing, fear of dying, panic attacks, discomforts in abdomen, faintness, face flushing and sweating. BDI assesses respondents': mood, pessimism, sense of failure, lack of satisfaction, feeling guilty, feeling punished, self hate, self-accusation, suicidal ideas, prevalence of crying, irritability, social withdrawal, indecisiveness, body image, work inhibition, sleep disturbances, fatigue, appetite, weight loss, somatic preoccupations and loss of libido. BAI and BDI suffer from the same problems as other self-report inventories, in that scores can be easily exaggerated or minimized by the person completing them. To minimize this bias, private and quiet ambience was provided for fulfilling questionnaires. We also included psychologist in our work. Very high total scores were suspect of aggravation and symptom simulation, so these respondents were excluded from further analysis. We did not include patients with disease duration shorter than one month, because reaction to diagnosis report could increase BAI and BDI scores.

According to BAI/BDI total score respondents were categorized in one of four groups: without, mild, moderate or severe anxiety/depression. By this point, we want to stress that there are no universal referent values for BAI/BDI scores. Interpretation of these scores mostly depend on respondents' environment and community, so many geographic areas have their own local referent values [29-32]. Questionnaires and their referent values were obtained from the hospital psychologist who works at Department of Psychiatry. Cut-off point was 14 or higher for BAI, and 10 or higher for BDI. Respondents with BAI total score up to 19 were classified as mildly anxious, from 20 to 28 as moderately anxious, and 29 and higher as severely anxious. BDI total scores up to 16 were considered as mild depression, between 17 and 29 as moderate depression, and over 29 as severe depression.

Statistical analyses were performed using statistical software MedCalc for Windows, version 11.5.1.0 (MedCalc Software, Mariakerke, Belgium). Descriptive statistics were provided using the mean, S.D., median (Mdn) and range of values between minimum and maximum. Data were assessed for normality of distribution using Kolmogorov-Smirnov test. When assessing the statistical significance of degree of anxiety and depression between studied diseases, Kruskal-Wallis test for independent samples was used. Frequency of categorical data was compared by the chi-square tests. Spearman's correlation coefficients were calculated to examine the associations of disease durations and anxiety/depression, because many measures were found to be non-normally distributed. The significance threshold for P-value was established at 5%.

Results

Finally, 196 patients were included. Their demographics according studied diseases are shown in Table 1. As expected almost 90% of our cohort was female. Mean age of SLE patients was over 10 years lower than mean age of RA and SSc patients. The shortest disease duration was found in SSc patients.

Characteristics	RA	SLE	SSc	Overall
Males	17(16.04)	3(4.84)	1(3.57)	21(10.71)
Females	89(83.96)	59(95.16)	27(96.43)	175(89.29)
Age, mean (S.D.), years	63.05(14.45)	48.94(14.08)	59.46(11.48)	57.07(15.26)
Disease duration, mean (S.D.), years	13.24(11.15)	12.78(8.01)	10.29(8.67)	12.69(9.87)
Without immunosuppressive therapy[a]	11(10.38)	4(6.45)	3(10.71)	18(9.18)

Data are expressed as n(%) unless otherwise noted. [a]Immunosuppressive therapy: glucocorticoids and DMARDs (MTX, SSZ, HCQ, AZA, LEF and CYC); We did not consider biological drugs.

RA: Rheumatoid Arthritis; SLE: Systemic Lupus Erythematosus; Ssc: Systemic Sclerosis; DMARD: Disease-Modifying Anti-Rheumatic Drug; MTX: Methotrexate; SSZ: Sulphasalazine; HCQ: Hydroxychloroquine; AZA: Azathioprine; LEF: Leflunomide; CYC: Cyclophosphamide

Table 1: Demographic and clinical characteristics of respondents.

We finished our study with 192 completed BAIs and 196 completed BDIs. Four missing BAIs were lost during data collection. 12 patients with RA, 2 with SLE and 4 with SSc could not remember how long their disease lasted. We did not exclude these patients with missing data from study because their questionnaires were relevant for our research. There is large disproportion in number of patients between studied diseases due to difference in prevalences of diseases, but our sample was eligible for statistical analysis.

Descriptive statistical data for BAI and BDI total scores are shown in Table 2. Median values of BAI were approximately the same in all three studied diseases, and the highest median of BDI was found in SSc patients. There were no significant difference in degree of anxiety between studied diseases, but we found statistically significant

difference in degree of depression between RA and SLE patients, and SSc and SLE patients (Table 2).

	Anxiety		Depression	
	BAI score[a]	Average rank[b](n)	BDI score[a]	Average rank[b](n)
RA	14(0-39)	98.76(102)	10(0-39)	107.41(106)
SLE	12.5(1-51)	89.92(62)	6.5 (0-32)	79.32(62)
SSc	13(4-35)	102.84(28)	11.5(0-31)	107.23(28)
P-value	NS	0.4954	NS	0.0055

[a]Data are expressed as Mdn (range of values between minimum and maximum) unless otherwise noted; [b]Kruskal-Wallis test was used; NS: Not Stated; RA: Rheumatoid Arthritis; SLE: Systemic Lupus Erythematosus; Ssc: Systemic Sclerosis; BAI: Beck Anxiety Inventory; BDI: Beck Depression Inventory.

Table 2: Difference in degree of anxiety and depression between studied diseases.

According to cut-off point 14 or higher for BAI, 49.5% respondents had some kind of anxiety disorder (mild to severe). 52% respondents were classified as depressive, considering BDI cut-off point 10 or higher. The majority of respondents were classified as without anxiety (50.5%) / depression (48.0%) or with mild anxiety (22.4%)/depression (34.2%). The highest incidence of moderate anxiety (20.59%) and depression (19.81%) was found in RA patients. SLE patients had the highest incidence of severe anxiety (11.67%) and the highest incidence of severe depression was found in SSc patients (3.7%) (Figure 1).

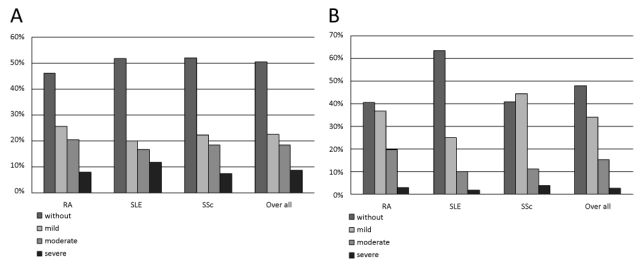

Figure1: Incidence of anxiety (A) and depression (B) in inflammatory rheumatic diseases.

Differences in frequencies of anxiety and depression subgroups between studied diseases were not statistically significant (P=0.941 for anxiety and P=0.134 for depression). According to studied disease, the most common BAI symptoms with incidence over 75% were: faintness, unsteadiness and nervousness in RA, nervousness and hot sensations in SLE, and faintness, numbness and dizziness in SSc patients. Overall, nervousness, faintness and hot sensations were the most common BAI symptoms among 192 respondents (Figure 2).

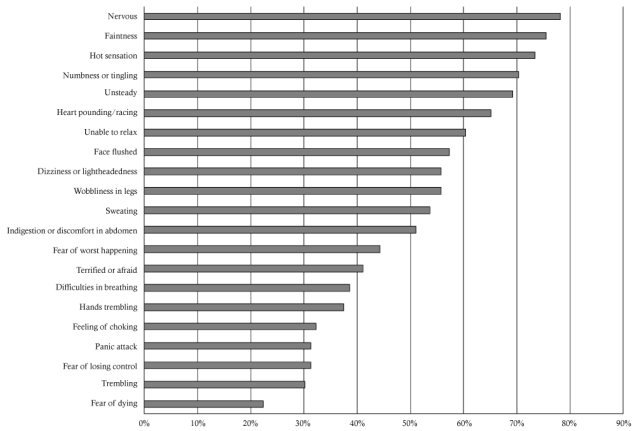

Figure 2: Percentage of respondents with positive BAI symptoms.

Only three BDI symptoms were present in more than a half of respondents (n=196): fatigue, work inhibition and sleep disturbance (Figure 3). The same distribution was found between studied diseases, but incidences of the symptoms were different. The highest incidence of fatigue was in SSc patients (89.29%), and the highest incidences of work inhibition (76.42%) and sleep disturbance (57.55%) were in RA patients. SLE patients had the lowest incidences in the all three previously mentioned symptoms.

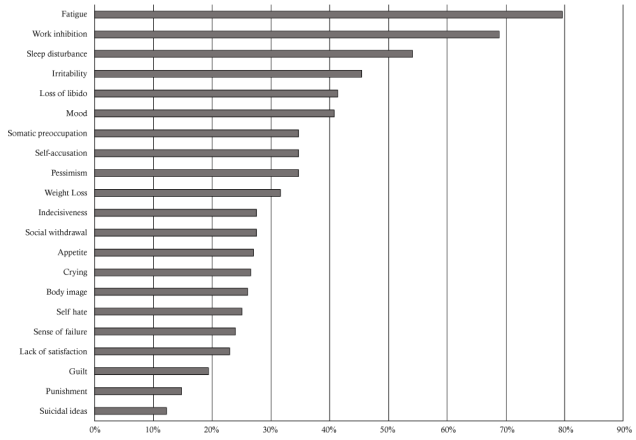

Figure 3: Percentage of respondents with positive BAI symptoms.

Longer duration of rheumatic disease was not associated with higher BAI total score (P=0.1465, r=0.1096). Also, we did not find statistically significant correlation between disease durations and BDI total scores (P=0.7532, r=-0.0237). Interesting fact is that SSc patients had the shortest disease duration (Table 1) and the highest BDI Mdn (Table 2).

	Anxiety		Depression	
	BAI score[a]	Average rank[b] (n)	BDI score[a]	Average rank[b] (n)
RA	14(0-39)	98.76(102)	10(0-39)	107.41(106)

SLE	12.5(1-51)	89.92(62)	6.5(0-32)	79.32(62)
SSc	13(4-35)	102.84(28)	11.5(0-31)	107.23(28)
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[a]Data are expressed as Mdn (range of values between minimum and maximum) unless otherwise noted. [b]Kruskal-Wallis test was used. NS: Not Stated; RA: Rheumatoid Arthritis; SLE: Systemic Lupus Erythematosus; Ssc: Systemic Sclerosis; BAI: Beck Anxiety Inventory; BDI: Beck Depression Inventory

Table 2: Difference in degree of anxiety and depression between studied diseases.

Discussion

In our observational study, we established that RA and SSc patients are more often depressed than SLE patients. SSc patients have a highest degree of depression compared with SLE and RA patients. These patients had the highest BDI Mdn and the highest incidence of mild and severe depression. The level and incidence of anxiety was similar in all studied diseases. These results may occur to imperfections of BAI and BDI. Waheed et al. [33] investigated anxiety and depression in these three diseases, but they did not exactly compare degree of anxiety and depression. Demographics of their respondents were similar to ours, but they used different questionnaires and had different results. Their incidence of anxiety and depression was 65.8%, what is higher than ours and can be consequence of frequent riots in Pakistan's society.

In a Greek study by Anyfanti et al. [34] which is geographically closer, incidence of anxiety was 30.8% and incidence of depression was 21.8%. They used the Hamilton Anxiety Scale and Zung Self-Rating Depression Scale as tools for assessment of anxiety and depression. The main reason why they got lower incidences of anxiety and depression can be that around 13% of their patients were receiving antidepressants or antianxiety medication. Also, they include all patients who were attending rheumatology clinic.

The most common BDI symptom, present in approximately 80% of our respondents, was fatigue. Dupond in his review [35] is analyzing causes of fatigue in rheumatic diseases and he says that there are two kinds: physical and psychological fatigue. It is important to think about role of fatigue while analyzing BDI results of rheumatologic patients, because fatigue can occur due to activity of rheumatic disease (especially inflammation) or due to depressive episode. Karol et al. [6] and Melikoglu and Melikoglu [36] claim that the main cause of depression in rheumatic diseases is pain. Inflammation and pain could be the reason why a lot of patients in our cohort felt work inhibition or faintness. The weakness of our study is that we did not research role of pain, so we did not compare it with degrees of depression.

Our hypothesis that SSc patients would have the highest degree of depression was confirmed. Around 60% of our SSc patients were depressive and the most common reasons for depression was fatigue and work inhibition. Ostojic et al. [37] found that depressive symptoms depended mostly on socioeconomic factors, disease duration, and pain intensity, whereas disease severity had no significant impact on development of depressive symptoms and anxiety. They used BDI to assess depression, their cohort was a little bit larger than ours, and their research was located in Serbia. Incidence of depression in their patients was similar to ours (68.6%). Compared to our results, there are differences in incidences of anxiety and they found relationship between SSc duration and degree of depression, what is opposite to our findings (our SSc patients had the shortest disease duration). A slightly lower incidence of depression in SSc (46.2%) was found in study by Tedeschini E et al. [38] in hospital sample in Italy. They used BDI and their cohort size was twice as large as ours. Causes of depression in their study are similar to ones from Ostojic's study. Few other studies in different country confirmed depression in SSc. [8,39,40] Thombs BD et al. [41] in their systematic review established that incidence of depression in SSc is 36-65%. Almeida C et al. [42] in their review listed the causes of depression that may affect quality of life. They showed that development of strategies toward general SSc self-management, better handling with emotional distress, managing with body images, physical and occupational therapy for hands, fatigue and energy management, as well as managing sleep and sexual function problems can improve the quality of life in patients with SSc.

There was significant level of depression in RA patients, incidence was approximately 60%. Rathbun et al. [43] and Moll et al. [44] confirmed high frequency of depression in these patients in their systematic reviews. RA patients were the oldest in our cohort, so high incidence of depression can be caused by their age, because incidence of depression is getting higher as person grows older [45,46]. With this argument, we can explain the lowest incidence of depression in SLE patients, because they were younger than RA and SSc patients.

We did not prove correlation between disease duration and anxiety / depression, probably because most of our respondents learned how to cope with the disease through the time. Other authors got positive correlation between disease duration and anxiety/depression [5,37]. These differences can hardly be explained. Close and warm atmosphere between patients and personnel at our Department of Clinical Immunology and Rheumatology may be helpful in reduction of anxiety and depression. Furthermore, Mediterranean climate conditions and food lower incidence of depression [47].

More researches are needed to investigate correlation between depression and pathophysiology of SSc. For example, newer studies found relationships between serotonin and skin fibrosis [48,49]. It is proven that higher plasma levels of proinflammatory cytokines such as TNF-α affect serotonin metabolism causing the activation of neuronal serotonin transporters and depletion of serotonin precursors such as tryptophan [50]. Serotonin is a neurotransmitter with influence on patient's mood, so a close connection between rheumatologist and mental health professionals could prove beneficial for these patients.

Our study stressed that depression is more prominent in SSc comparing RA and SLE (excluding CNS SLE) what suggests new investigation related to cytokine alternations particularly about SSc. Interestingly, our study did not confirm that the degree of anxiety and depression in studied rheumatic diseases correlates with disease duration, so we presume that other contributors probably have a certain role in course of anxiety and depression in these rheumatic diseases.

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