

CLINICAL CHARACTERISTICS OF PATIENTS WITH PRIMARY AND SECONDARY FIBROMYALGIA IN BULGARIA

Valentina Reshkova^{1✉}, Rasho Rashkov¹, Ivan Milanov²

Received on August 23, 2021

Accepted on September 29, 2021

Abstract

Fibromyalgia (FM) is characterized by a chronic widespread pain, general fatigue, anxiety, depression, sleep disturbances and functional disorders. FM affects both women and men in 9:1 to 20:1 ratio. The purpose of this clinical study is to analyze clinical manifestations in patients with primary and secondary fibromyalgia. Eighty-three patients with primary FM, 39 patients with FM and osteoarthritis (OA), 23 patients with FM and systemic lupus erythematosus (SLE), 27 patients with SLE, and 36 healthy subjects were included. The present study compared chronic pain, fatigue, depression and anxiety in patients with primary FM, patients with SLE, FM + OA, FM + SLE and healthy subjects. Based on the 2016 criteria for number of chronic widespread pain areas, there is a statistically significant difference of the control group compared to the patients with primary FM ($p = 0.001$), FM + OA ($p = 0.001$), FM + SLE ($p = 0.001$), SLE ($p = 0.001$). Based on the MFIS fatigue scale, the chronic fatigue is a statistically significant difference of the control group, as compared to patients with primary FM ($p = 0.004$), FM + OA ($p = 0.02$), FM + SLE ($p = 0.001$). Based on the HADS clinical parameter, anxiety and depression are a statistically significant difference of the control group, as compared to patients with primary FM ($p = 0.01$), FM + OA ($p = 0.01$), FM + SLE ($p = 0.01$), and no difference in patients with SLE ($p = 0.77$). The comparison between the patient groups is important to evaluate the disease activity and the treatment to be recommended.

Key words: fibromyalgia, pain, fatigue, depression, anxiety

<https://doi.org/10.7546/CRABS.2024.07.12>

Introduction. Fibromyalgia (FM) is characterized by a chronic widespread pain, general fatigue, anxiety, depression, sleep disturbances, and functional disorders. FM affects both women and men in 9:1 to 20:1 ratio. It affects 7 to 10 million people in the USA, which accounts for 3 to 6% of the population. There is no definite ethnic predisposition. There are no epidemiological data on the prevalence of FM in Bulgaria [1].

In 1990, a new group of criteria was published under the aegis of ACR (American College of Rheumatology). The association of generalized pain and at least 11 tender points sensitive to digital pressure out of 18 possible locations was found to be conclusive in identifying fibromyalgia patients, with a sensitivity of 88.4%, a specificity of 81.1% and a precision of 84.9% [1].

In 2016, ACR developed new diagnostic criteria based on the presence of chronic widespread pain in more than 7 out of 19 body areas over the past 3 months and accompanying clinical symptoms (severity scale (SS) – fatigue, unrefreshing sleep, cognitive symptoms) [2].

The diagnosis of primary fibromyalgia implied the presence of clinical characteristics of fibromyalgia with no recognizable cause. The diagnosis of secondary fibromyalgia was established when the clinical symptoms of FM were secondary to a subjacent rheumatologic disease or when it coexisted with another disorder. Osteoarthritis, systemic lupus erythematosus and other diseases have often been and continue to be associated with fibromyalgia.

The association of FM with SLE has been investigated by several authors. The incidence rate of secondary FM in SLE patients is around 20%. This number is much greater than in the general population.

According to DE ARAUJO et al. [3], there is a significant difference in the number of chronic pain areas between the FM-only group and the combined FM and SLE group. More tender points (15.05) are found in the FM group, and in the FM and SLE group they are 11.75 ($p = 0.0001$) [3].

DI FRANCO et al. [4] demonstrated a clear association between chronic pain in fibromyalgia and SLE patients and assessed fatigue and quality of life in SLE patients.

According to MARCHIONE [5], 13% of patients with osteoarthritis suffer from FM. The treatment of FM costs 8453 USD, and 11 253 USD for OA, including healthcare, absence from work and medication.

Material/patients and methods. We present a prospective study in fibromyalgia patients conducted at the Clinic of Rheumatology of University Hospital “St. Ivan Rilski” and Medical center “Focus 5” in Sofia, between September 2013 and September 2017.

The aim of this study is to examine the main clinical characteristics, including pain, chronic fatigue, depression and anxiety of patients with primary and secondary fibromyalgia, compared to a control group of healthy subjects.

1. *Mean age and gender distribution of patients from all groups and healthy individuals.*

- ▷ 83 patients, 78 women and 5 men, with primary FM, mean age 40.67 ± 11.15 years;
- ▷ 39 women with fibromyalgia and osteoarthritis, mean age 50.77 ± 10.73 years;
- ▷ 23 patients, 22 women and one man with SLE and fibromyalgia, mean age 47.9 ± 8.86 years, with SLEDAI activity score of 4–6 points, without involvement of vital organs and systems and without neurolupus;
- ▷ 27 patients, 25 women and 2 men with SLE, mean age 46.96 ± 11.7 years with SLEDAI activity score of 4–6 points without involvement of vital organs and systems and without neurolupus;
- ▷ 36 healthy individuals, 30 women and 6 men, mean age 46.53 ± 9.9 years.

Additional information about patient groups included etiological factors for disease occurrence and duration of FM.

2. *Distribution of patients from all groups per FM etiology.*

Statistically significant difference for etiological factors for FM was found between the individual underlying causes ($p < 0.05$), but not between patient groups ($p > 0.05$). A total of 29 patients reported exercise as the underlying cause for FM, 13 patients with primary fibromyalgia, 12 subjects with secondary fibromyalgia in osteoarthritis, and 4 patients with secondary fibromyalgia in SLE. The most prevalent underlying cause for FM was psychological stress, which was reported by a total of 113 patients, 68 patients with primary fibromyalgia, 27 subjects with secondary fibromyalgia in osteoarthritis, and 19 patients with secondary fibromyalgia in SLE. Only two patients with primary fibromyalgia reported unemployment as the underlying cause for FM.

3. *Distribution of patients per FM duration.*

The duration of FM was 4.18 years in the group of patients with primary FM, 6.77 years in patients with FM + OA, and 5.17 years in patients with SLE + FM. The lowest fibromyalgia onset mean age of 36.71 years was found in patients with primary FM with a statistically significant difference ($p < 0.05$) both between patients with OA + FM (44.15 years) and SLE + FM (42.01 years). Summarized data is presented in Table. 1.

Table 1 presents demographic and clinical variables of the study population.

Clinical methods:

1. *Evaluation of the diagnosis of fibromyalgia according to the 2016 ACR criteria.*

2. *Evaluation of the fibromyalgia diagnosis according to the 1990 ACR criteria based assessment of the fibromyalgia tender points.*

The study looked at changes in the pain threshold measured in kg/cm^2 at all trigger points by using Fisher dolorimeter. The pain scores and the changes occurring in a 3-month period were assessed by an exact figure. The only known objective method for assessment of the pain threshold is the Fisher dolorimeter.

T a b l e 1
Demographic and clinical variables of the study population

Patient group	Primary fibromyalgia	Fibromyalgia and osteoarthritis	Fibromyalgia and SLE	SLE	Healthy subjects
Number of patients	83	39	23	27	36
Number / % female	78 / 94%	39 / 100%	22 / 95.7%	25 / 92.6%	30 / 83.3%
Number / % male	5 / 6%	0 / 0%	1 / 4.3%	2 / 7.4%	6 / 16.7%
Patient age (years), mean $\pm$ SD (range)	40.68 $\pm$ 11.15	50.77 $\pm$ 10.73	47.9 $\pm$ 8.86	46.96 $\pm$ 11.7	46.53 $\pm$ 9.9
Duration of FM	4.2 $\pm$ 3.2	7 $\pm$ 4.9	5.17 $\pm$ 3.38	–	–
Mean age in beginning of FM (years) $\pm$ SD (range)	36.53 $\pm$ 10.32	43.2 $\pm$ 10.0	42.9 $\pm$ 7.58	–	–
Reason for FM					
Mental reason	81.9	69.2	82.6	–	–
Physical reason	15.7	30.8	17.4	–	–
Lack of work	2.4	0	0	–	–
Summary	100	100	100	–	–
Education					
Elementary education	2	3	2	2	2
Average education	36	15	10	14	15
Higher education	42	18	8	8	18
Professional education	3	3	3	0	1

It is a device for measuring the pressure in tender trigger points by a probe of 1 cm². The scale of the device is up to 9 kg/cm². Pressure is applied at a speed of 1 kg/cm²/sec. The patient had to indicate at what time the pressure grows into a feeling of pain. The following tender points were measured: Occiput (left, right), Low cervical (left, right), Supraspinatus (left, right), left and right second rib, Trapezius (left, right), Lateral epicondyle (left, right), Greater trochanter (left, right), Gluteal (left, right), and Knee (left, right).

All fibromyalgia symptoms were present for at least 3 months prior to assessment. Patients were assessed between September 2013 and September 2017.

All patients met the criteria for fibromyalgia. In both groups, SLE and osteoarthritis were coexisting with FM.

3. Assessment of fatigue on the physical, cognitive and psychosocial MFIS subscales.

Fatigue in FM patients was assessed by the Fatigue Severity Scale (FSS) and Modified Fatigue Impact Scale (MFIS). The scales have physical, cognitive and psychosocial subscales with questions related to change in physical activity, cognitive function and social contacts. Patients answered the scales using scores within a range.

4. Assessment of anxiety and depression on the HADS scale for anxiety and depression.

HADS focuses on non-physical symptoms so that it can be used to diagnose anxiety and depression in people with significant physical ill-health. Any overlap, for instance impaired concentration secondary to pain rather than depression, is usually easy to separate on an individual basis. The questionnaire comprises seven questions for anxiety and seven questions for depression, and it takes 5–10 min to complete. The Hospital Anxiety and Depression Scale (HADS) is a self-assessment questionnaire that has been found to be a reliable instrument for detecting states of anxiety and depression in the setting of hospital outpatient clinic. The HADS questionnaire has seven items each for depression and anxiety subscales. Scoring for each item ranges from zero to three, with three denoting highest anxiety or depression level. A total subscale score of >8 points out of a possible 21 denotes considerable symptoms of anxiety or depression.

5. Assessment of SLEDAI-2K.

The SLEDAI-2K includes evaluation of specific manifestations in nine organ systems. Weighting is used, resulting in individual item scores ranging from 1 to 8, which are simply added to give a global score ranging from 0 to 105. Lupus HDA (high disease activity) has been defined as an SLEDAI-2K score, 2K score greater than 6. Similarly, lupus LDA (low disease activity) state has been defined using the following criteria less than or equal to 4, with no activity in major organ systems [6, 7].

Statistical methods. The data was analyzed using the Windows SPSS 16.0 statistical software platform. For all comparisons, a significance level of $p < 0.05$

was chosen at which the null hypothesis was rejected. The quantitative values are presented as arithmetic mean $\pm$ SD.

A non-parametric Kolmogorov–Smirnov test was used to determine the type of distribution. For a correct distribution, parametric methods were used, including Student’s *t*-test, variance analysis, correlation analysis. In case of incorrect distribution or homogeneity of variables, non-parametric methods were used, including Mann–Whitney test, Kruskal–Wallis test, and Chi-square test.

Results. Assessment of the number of chronic widespread pain areas in the three FM groups (primary, FM + OA and FM + SLE), healthy individuals and SLE results. Figure 1 shows a significant difference according to the 2016 criteria for diagnosing FM for chronic widespread pain areas in the arithmetic mean values of the control group, compared to the number of chronic widespread pain areas in patients with primary FM ($p = 0.001$), FM + OA ($p = 0.001$), FM + SLE ($p = 0.001$), SLE ($p = 0.001$).

The mean number of chronic widespread pain areas in all patients of the respective group, compared to healthy individuals and SLE patients, is presented in Fig. 1. The most chronic widespread pain areas were reported in patients with FM+OA (14.05, arithmetic mean $\pm$ standard deviation: 14.05 ± 2.75); followed by the FM + SLE group (13.96, 13.96 ± 1.8). Patients with primary FM had a mean number of chronic widespread pain areas of 13.8 (13.8 ± 2.1). Healthy individuals had 7.47 chronic widespread pain areas (7.47 ± 3.57). In SLE patients, the chronic widespread pain areas were 4.56 (4.56 ± 1.63) (Fig. 1).

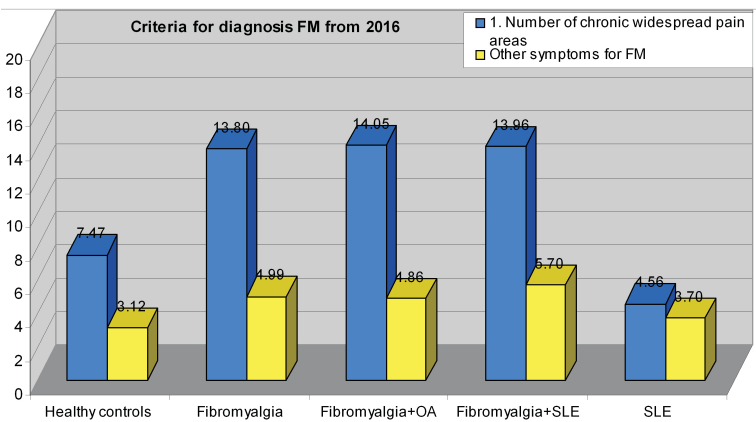


Fig. 1. Criteria for diagnosis FM from 2016 – comparison between all groups of patients and the groups of healthy controls and SLE patients ($p < 0.05$)

Assessment of the numbers of tender points in the three groups of FM patients (primary FM, FM + OA, and FM + SLE), healthy individuals and SLE patients. The mean value of the pain threshold from all tender points in all patients of the respective group, compared to healthy

individuals and patients with SLE, is presented in Fig. 2. Patients with FM + SLE had the highest average number of tender points of 15.4, (15.4 ± 1.9); followed by the group of FM + OA patients with 14.3 (14.3 ± 2.1). Patients with primary FM had a mean tender points score of 14.1 (14.1 ± 1.88). Healthy individuals had 6.4 tender points (arithmetic mean $\pm$ standard deviation 6.4 ± 3.79 , min; 5.06, maximum 7.7 at 95% confidence interval, standard error 0.65). Patients with SLE had 4.8 tender points (4.8 ± 2.4) (Fig. 2).

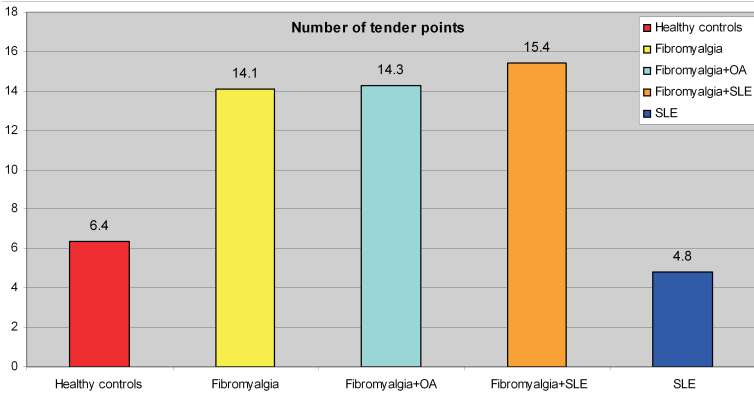


Fig. 2. Number of tender points – comparison between all groups of patients and the groups of healthy controls and SLE patients ($p < 0.05$)

There was a statistically significant difference of p of the number of tender points in the control group and patients with SLE, compared to patients with primary FM, FM + OA and FM + SLE. There was a significant difference in the number of tender points between primary fibromyalgia patients and patients with FM + SLE ($p = 0.001$), and between FM + SLE and FM + OA groups ($p = 0.001$).

The average number of tender points is an important parameter for diagnosis. It can be used in practice to compare patients, monitor the treatment effect and select the most adequate treatment for FM.

Assessment of MFIS fatigue results. The MFIS chronic fatigue score in patients with FM + SLE was 53.95 (53.95 ± 16.78), followed by the FM group with (44.25, 44.25 ± 17.31). Patients with FM + OA had a mean score for fatigue of 43.38 (43.38 ± 13.26). SLE patients had MFIS fatigue score of 36.41 points (36.41 ± 16.77). MFIS fatigue score in the healthy controls was 33.89 (33.89 ± 18.07). Based on the MFIS fatigue scale, there is a significant difference in chronic fatigue between the control group and patients with primary FM ($p = 0.004$), FM + OA ($p = 0.02$), FM + SLE ($p = 0.001$) (Fig. 3).

There was no significant difference for the clinical parameter fatigue between the groups of patients with FM and FM + OA, FM + OA and SLE. Increasing levels of stress and workload among the population and all risk factors for the

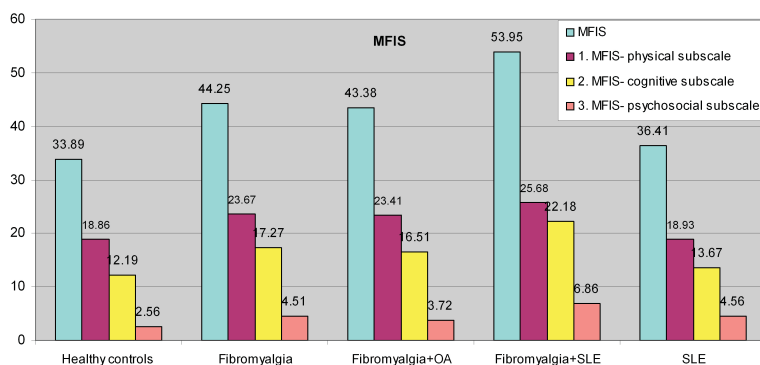


Fig. 3. MFIS chronic fatigue – comparison between all groups of patients and the groups of healthy controls and SLE patients ($p < 0.05$)

development of fibromyalgia are the underlying causes for the concomitant fatigue. Patients with SLE had similar results for chronic fatigue with healthy individuals and with statistically significant low-grade fatigue with the FM + SLE group.

Assessment of HADS anxiety results. The HADS anxiety score in patients with FM + SLE was 10.26 (10.26 ± 4.4), followed by the results in the FM + OA group (9.87, 9.87 ± 4.25). The mean value of HADS anxiety score in FM patients was 9.57 (9.57 ± 4.33). SLE patients had HADS anxiety score of 7.04 (7.04 ± 3.68). HADS anxiety score in the healthy individuals was 7.08 (7.08 ± 4.75) (Fig. 4).

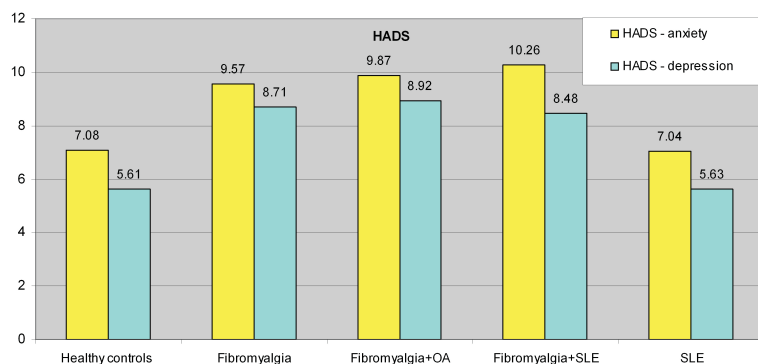


Fig. 4. HADS anxiety and depression – comparison between all groups of patients and the groups of healthy controls and SLE patients

Assessment of HADS depression results. The HADS depression score in patients with FM + OA was 8.92 (8.92 ± 4.46), followed by the FM group score of 8.71 (8.71 ± 4.17). The mean value of HADS depression scores in patients with FM + SLE was 8.40 (8.40 ± 2.9). SLE patients had HADS scores for depression of 5.63 (5.63 ± 4.06). The HADS depression score in the group of healthy individuals was 5.61 (5.61 ± 3.3) (Fig. 4).

A statistically significant difference of p for the HADS clinical parameter depression was found in the arithmetic mean values of the healthy individuals group, compared to the values between all FM groups of patients – with primary FM, FM + OA, FM + SLE; in the arithmetic mean values in patients with SLE, compared to the values of all FM groups and the group of patients with FM + OA. There was no significant difference in HADS depression scores between the three groups of fibromyalgia patients. There was no significant difference in terms of the clinical parameter of depression between the SLE and FM + SLE groups. Patients with SLE had similar rates of depression with those seen in healthy individuals.

Assessment of SLEDAI-2K results. There was no significant difference for SLEDAI-2K between the groups of patients with FM + SLE and patients with SLE.

Patients in both groups had low lupus disease activity, without a statistically significant difference between groups. Patients with SLE had mean SLEDAI-2K scores of 2.7. Patients with SLE + FM had mean SLEDAI-2K scores of 2.52 ($p < 0.05$).

Discussion. The clinical symptoms of FM develop as a result of complex mechanisms of central nervous and neuroendocrine regulation, which leads to a chronic musculoskeletal pain (psychogenic rheumatism, soft tissue rheumatism). The clinical presentation is complex as patients suffer from fatigue, sleep disorders, depression, anxiety and overload. The results of this clinical observation show a statistically significant difference in terms of arithmetic mean values of the number of areas with chronic widespread pain based on the 2010 criteria between the control group and the number of areas with chronic widespread pain in all FM groups of patients with primary FM, FM + OA, FM + SLE, including SLE. SLE is an autoimmune disease with multi-organ involvement and joints, skin, kidneys, lungs, heart, blood vessels and brain injuries. The prevalence of the disease is between 14 and 50 patients per 100 000 population. SLE is associated with higher mortality compared to inflammatory joint diseases. An important and objective tool for assessment of disease activity is the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI), which rates the manifestations of damaged organs and systems with a certain number of points [8]. The presence of concomitant FM in patients with SLE has been studied by various authors and was found in 20% of patients with SLE. The frequency of FM in patients with SLE is higher than in the general population. A study of SLE patients in Brazil provides information on chronic pain and its relationship to SLE disease activity. In patients with SLE-only, disease activity had more serious impact than in the other two groups. Our results prove this data in terms of number of tender points, number of painful areas, chronic fatigue.

An incidence rate of 20 to 30% has been reported for FM in patients with various rheumatic conditions. In a North American databank cohort of over 6000 patients, FM was identified in 21% with rheumatoid arthritis (RA), 37% with

systemic lupus erythematosus, and 17% with osteoarthritis (OA). Ten percent of 238 people with osteoarthritis (OA) were reported with comorbid FM [9, 10].

People with OA localized pain exhibit hyperalgesia even at sites distant from the OA site, indicating widespread multimodality changes in the nociceptive system [10].

According to de Araujo [3], 12% of SLE patients have FM and the mean age of SLE patients is 40 years, for FM patients it is 44 years, and 43.5 years for those with both SLE and FM. There is no significant difference in the SS score between the two groups.

According to Di Franco [4], 8.2% of SLE patients in India develop FM, 9.5% in Mexico, 10% in Spain, and 25% in Turkey. SLE is characterized by inflammatory, peripheral and central neuropathic pain. Chronic widespread pain is found in 65–80% of SLE patients. 50 to 80% of SLE patients suffer from fatigue.

According to CHANDRAN et al. [9], 9.5% of patients in the group with mild FM, 53.1% in the group with moderate to severe FM, and 43.6% in the patients with severe FM suffered from chronic fatigue. In a 2012 observational study, patients with FM were divided into categories of, mild, moderate and severe FM, based on the severity of chronic widespread pain, assessed by VAS and results of the specific questionnaires. According to YACIZI et al. [8] after pain, fatigue is the second most debilitating symptom that worsens the quality of life of FM patients.

The results of our study show that patients with SLE + FM, OA + FM and primary FM have the same degree of fatigue, but it differs statistically from those seen in healthy individuals and patients with SLE. Patients with SLE without FM have similar levels of chronic fatigue with healthy individuals and similar statistically significant low-grade fatigue with the group of FM + SLE patients. Increasing stress and workload among the general population and all risk factors for the development of fibromyalgia cause concomitant fatigue. We used two questionnaires (FSS and MFIS) to assess the fatigue in our study. Fatigue questionnaires have been used in systemic lupus erythematosus patients and appear highly informative for this disease [5, 11]. This information guided the choice of the mentioned questionnaires in primary and secondary FM.

In some studies, it has been noted that the quality of life, associated with pain and other clinical symptoms is extremely low in patients with FM. Based on the results of an observational study, a Canadian team of physicians concluded that the combination of FM with SLE is associated with deterioration in the quality of life, overall condition and mental health compared to patients with SLE-only [12]. In the study of Italian rheumatologists, 33% of patients with SLE had FM. There is a close relationship between chronic pain and fatigue, but there is no relationship between the degree of disease activity of SLE and FM [14]. Patients need to be informed about their FM and trained how to communicate and maintain a good quality of life. It is associated with an increase in the pain threshold based on pharmacological and non-pharmacological treatment. An individual pro-

gramme for treatment and education is needed for patients to address all other FM symptoms. Therefore, primary care in the family is important for the success of treatment. Receiving adequate care from the employer and primary healthcare centres, socialisation of these patients are essential for the success of treatment [13,14]. While taking care of FM patients physicians need to be more persistent in monitoring and treating these patients, have these patients examined or contacted by phone at least once every month, and communicate more with these patients.

A one-hour visit to the rheumatologist has a strong impact on these patients both to train patients how to overcome triggers and as a psychotherapy session. It is important that the physician can take a detailed medical history and reach the deeper problems of the patient. This is essential for both the trust between patient and doctor, and for the treatment effect. The complex treatment of FM patients aims at clinical improvement and higher quality of life for patients.

Conclusions.

1. Patients with primary fibromyalgia, osteoarthritis and FM, systemic lupus erythematosus and FM have comparable features in terms of pain intensity, fatigue, anxiety and depression.

2. Patients with SLE without fibromyalgia have fewer areas with chronic widespread pain and a lower degree of depression, anxiety and fatigue, comparable to these symptoms in patients with SLE + FM and healthy individuals.

3. Patients with SLE and fibromyalgia have additional symptoms of moderate pain, depression, anxiety and fatigue that are not related to SLE and require treatment for FM, regardless of their current SLE treatment.

REFERENCES

- [1] RESHKOVA V. (2020) Clinical characteristics and neuroendocrine changes in primary and secondary fibromyalgia, DSc Dissertation, Medical University of Sofia, Bulgaria.
- [2] WOLFE F., D. J. CLAUW, M. A. FITZCHARLES et al. (2016) 2016 Revisions to the 2010/2011 fibromyalgia diagnostic criteria, *Semin. Arthritis Rheum.*, **46**(3), 319–329.
- [3] DE ARAUJO A. L., I. C. PALIARES, M. I. DE ARAUJO et al. (2015) The association of fibromyalgia and systemic lupus erythematosus change the presentation and severity of both diseases, *Rev. Bras. Rheumatol.*, **55**(1), 37–42.
- [4] DI FRANCO M., M. P. GUZZO, F. R. SPINELLI et al. (2014) Pain and systemic lupus erythematosus, *Reumatismo*, **66**(1), 33–38.
- [5] MARCHIONE V. (2016) Fibromyalgia pain and osteoarthritis linked in how brain experiences chronic pain, *Arthritis Research Facility*, **5**.
- [6] GLADMAN D. D., M. B. UROWITZ, A. KAGAL, D. HALLETT (2000) Accurately describing changes in disease activity in systemic lupus erythematosus, *J. Rheumatol.*, **27**(2), 377–379.

- [7] POLACHEK A., D. D. GLADMAN, J. SU, M. B. UROWITZ (2017) Defining low disease activity in systemic lupus erythematosus, *Arthritis Care Res. (Hoboken)*, **69**(7), 997–1003.
- [8] YACIZI K., S. TOT, A. BIÇER et al. (2003) Anxiety, depression and quality of life in patients with lowback and neck pain, *Turkish J. Clin. Psy.*, **6**(2), 95–101.
- [9] CHANDRAN A., C. SCHAEFER, K. RYAN et al. (2012) The comparative economic burden of mild, moderate and severe fibromyalgia: results from a retrospective chart review and cross-sectional survey of working-age US Adults, *J. Manag. Care Pharm.*, **18**(6), 415–426.
- [10] MOSS P., E. KNIGHT, A. WRIGHT (2016) Subjects with knee osteoarthritis exhibit widespread hyperalgesia to pressure and cold, *PLoS ONE*, **11**, e0147526.
- [11] WOLFE F., M. PETRI, G. ALARCON et al. (2009) Fibromyalgia, systemic lupus erythematosus (SLE) and evaluation of SLE activity, *J. Rheumatol.*, **36**, 82–88.
- [12] MIDDLETON G. D., J. E. MCFARLIN, P. E. LIPSKY (1994) The prevalence and clinical impact of fibromyalgia in systemic lupus erythematosus, *Arthritis Rheum.*, **37**(8), 1181–1188.
- [13] HALILOGLU S., A. CARLIOGLU, D. AKDENIZ et al. (2014) Fibromyalgia in patients with other rheumatic diseases: Prevalence and relationship with disease activity, *Rheumatol. Int.*, **34**, 1275–1280.
- [14] KNUPP L. B., N. G. LA ROCCA, L. C. SCHEINBERG (1989) The fatigue severity scale, Application to patients with multiple sclerosis and systemic lupus erythematosus, *Arch. Neurol.*, **46**, 1121–1123.

¹“St. Ivan Rilski” Multiprofile University Hospital for Active Treatment,
 Medical University – Sofia, Rheumatology Clinic, 13 Urvich St, 1612 Sofia, Bulgaria
 e-mail: v_reshkova@abv.bg, proff_rashkov@yahoo.com

²“St. Naum” Multiprofile Hospital for Active Treatment in Neurology and Psychiatry,
 1 Dr. Lyuben Rousev St, 1113 Sofia, Bulgaria
 e-mail: milanovivan54@gmail.com