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 [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, unrefreshed 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 diseases or when it coexisted with another disorder. Osteoarthritis, systemic lupus erythematicus and other diseases have often been and continue to be associated with fibromyalgia. Researchers focus on assessment of sleep, chronic pain, fatigue, stress, depression, anxiety, physical and mental health, disease activity and damage in FM [3].

Patients with FM report sleep disturbance, chronic pain, fatigue, stress, depression, anxiety, irrespective of SLE disease activity. It is sometimes difficult to distinguish between these symptoms and whether they are manifestations of SLE or secondary FM. Depression is a common disorder. One of five people has depression at some time in their life. Depression may worsen during the course of a chronic disease or a chronic disorder. It has been reported that physical impairments can increase during depression. Gonarthrosis, FM and rheumatoid arthritis are the disorders with the most significant impact4.

Aim

The aim of this clinical trial is to analyze the relationship of clinical manifestations and physical (PCS) and mental component summary (MCS) in patients with primary and secondary fibromyalgia (FM) compared with a control group of healthy volunteers.

Material/patients and methods

We present a prospective study in fibromyalgia patients conducted at the Clinic of Rheumatology of University Hospital “Sv. Ivan Rilski” and Medical center “Focus 5” in Sofia, between September 2013 and September 2017.
Mean age and gender distribution of patients from all groups and healthy individuals are:

- 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 ± 0.73 years;
- 23 patients, 22 women and 1 man with SLE and fibromyalgia, mean age 47.9 ± 8.6 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. Summarized data is presented in Table. 1.

**Research methods**

**Clinical methods**

1. Evaluation of the diagnosis of fibromyalgia according to the 2016 ACR criteria [2].
2. Assessment of anxiety and depression on the HADS scale for anxiety and depression. The HADS questionnaire has seven items each for depression and anxiety subscales. A total subscale score of > 8 points out of a possible 21 denotes considerable symptoms of anxiety or depression.
3. Assessment of Fibromyalgia Impact on Patients’ Life based on Fibromyalgia Impact Questionnaire (FIQ) [6]. Includes self-report questions and measures physical functioning, work status – missed days of work, job difficulty, depression, anxiety, pain, stiffness, fatigue, well-being over the past week. The developed questionnaire was an attempt to capture the total spectrum of problems related to the nature and management of fibromyalgia (FM). The 2009 version consists of 21 items across the following 3 domains: Function – 9 questions, Overall Impact – 2 questions, Other Symptoms – 10 questions [6].
4. Assessment of quality of life of patients with FM and healthy individuals based on SF-36. SF-36 is a survey to assess quality of life, physical functioning and mental health. The score ranges from 0 to 100%, where a score of 0% represents the worst possible health status and a score of 100% represents the best possible health status. In this case, the higher values on the scale represent a better quality of life [7].

SF-36 consists of 8 domains, measuring various aspects of life. By using this scale, the authors allow us to compare the scores of various domains with norm-based scores of the general population with a mean score of 50 and a standard deviation of 10. Results can also be transformed into 0-100 scale, where

<table>
<thead>
<tr>
<th>Patient group</th>
<th>Primary fibromyalgia</th>
<th>Fibromyalgia and osteoarthritis</th>
<th>Fibromyalgia and SLE</th>
<th>SLE</th>
<th>Healthy subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>83</td>
<td>39</td>
<td>23</td>
<td>27</td>
<td>36</td>
</tr>
<tr>
<td>Number/ % female</td>
<td>78 / 94%</td>
<td>39 / 100%</td>
<td>22 / 95.7%</td>
<td>25 / 92.6%</td>
<td>30 / 83.3%</td>
</tr>
<tr>
<td>Number/ % male</td>
<td>5 / 6%</td>
<td>0 / 0%</td>
<td>1 / 4.3%</td>
<td>2 / 7.4%</td>
<td>6 / 16.7%</td>
</tr>
<tr>
<td>Patient age (years), mean ± SD (range)</td>
<td>40.68 ± 11.15</td>
<td>50.77 ± 10.73</td>
<td>47.9 ± 8.86</td>
<td>46.96 ± 11.7</td>
<td>46.53 ± 9.9</td>
</tr>
<tr>
<td>Duration of FM</td>
<td>4.2 ± 3.2</td>
<td>7 ± 4.9</td>
<td>5.17 ± 3.38</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Mean age in beginning of FM (years) ± SD (range)</td>
<td>36.53 ± 10.32</td>
<td>43.2 ± 10.0</td>
<td>42.9 ± 7.58</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Reason for FM</td>
<td>Mentally reason</td>
<td>81.9</td>
<td>69.2</td>
<td>82.6</td>
<td>-</td>
</tr>
<tr>
<td>Physically reason</td>
<td>15.7</td>
<td>30.8</td>
<td>17.4</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Lack of work</td>
<td>2.4</td>
<td>0</td>
<td>0</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Summary</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Education</td>
<td>Elementary education</td>
<td>2</td>
<td>3</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Average education</td>
<td>36</td>
<td>15</td>
<td>10</td>
<td>14</td>
<td>15</td>
</tr>
<tr>
<td>Higher education</td>
<td>42</td>
<td>18</td>
<td>8</td>
<td>8</td>
<td>18</td>
</tr>
<tr>
<td>Professional education</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>0</td>
<td>1</td>
</tr>
</tbody>
</table>
a score closer to 100 represents better quality of life. Norm-Based Scores (NBS) have many advantages — simplified interpretation, an option to calculate two summary scores of physical and mental health, comparison of scores with other populations, etc. [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 ± 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. Global linear models analyze relationship of many factors, that give bigger weight in the model.

**RESULTS**

Results for multivariate relationship of clinical manifestations and physical component summary (PCS) in FM

Fig. 1 presents the relationship between some clinical manifestations in FM – physical self-maintenance, impact of FM on daily functioning, Von Zerssen depression score and physical component summary (PCS). Each clinical sign was found to contribute to the physical component summary and the three clinical features selected based on statistical significance (p < 0.05) contributed to a small extent to the modelling of physical health.

The coefficient adjusted R² = 0.182 shows the proportion of PCS that can be explained by the developed model. Here, this coefficient is very low, i.e., the modelling is not powerful enough to use only the clinical manifestations of physical self-maintenance, impact of FM on daily functioning and Von Zerssen depression score to determine the physical component summary (Fig. 2).

2. Results for multivariate relationship of clinical manifestations and mental component summary (MCS) in FM. Fig. 3 presents the relationship between some clinical manifestations in FM – depression/anxiety, impact of FM on daily functioning – social functioning, HADS score for depression and mental component summary (MCS).

Fig. 1. Multivariate relationship of clinical manifestations and physical component summary (PCS) in FM

Fig. 2. Multivariate relationship of clinical manifestations and PCS in FM

Fig. 3. Multivariate relationship of clinical manifestations and mental component summary (MCS) in FM
Each clinical sign was found to contribute to the mental component summary and the three clinical features selected based on statistical significance \((p < 0.05)\) contributed to a small extent to the modeling of mental health.

The coefficient adjusted \(R^2 = 0.275\) shows the proportion of MCS that can be explained by the developed model. Here this coefficient is very low, i.e., the modelling is not powerful enough to use only the clinical manifestations of depression/anxiety, impact of FM on daily functioning – social functioning and HADS score for depression to determine the mental component summary (Fig. 4).

According to our results, patients with SLE + FM have moderate positive correlation with a significant correlation coefficient between depressive episodes assessed using the three depression scales – HADS, ZUNG and Von Zerssen \((p < 0.001)\). The total of all criteria for FM – fatigue, unrefreshing rest, cognitive changes and other symptoms has a slight positive correlation and insignificant correlation coefficient between the number of tender points and the number of areas of diffuse pain in patients with SLE + FM, with depression on the three scales of depression \((p < 0.001)\).
Daily stress leads to changes in sleep – poor sleep quality, broken sleep or lack of sleep. These changes have negative impact on general condition of patients with osteoarthritis. Obesity also has negative impact on pain and general condition of patients with osteoarthritis, and leads to deterioration of articular cartilage. This leads to changes in the pathophysiology of pain in osteoarthritis, affecting physical and mental health, which are related to the quality of sleep. In osteoarthritis, patient’s condition affects sleep, fatigue, capacity to work, physical activity [9]. These facts lead to emotional and physical stress. Depression and immobilization lead to obesity and they are the main factors for poor sleep quality. Depression is as twice as common in women as in men. The higher level of depression in women requires medical attention. Patients with osteoarthritis compared to those with fibromyalgia have chronic sleep problems that correlate with chronic pain and secondary inflammation due to osteoarthritis, subsequent depression, stress, cognitive dysfunction. By identifying various factors that lead to stress and sleep changes in patients with osteoarthritis, the extent of these symptoms can be reduced through add-on therapy, rehabilitation, cognitive therapy [9].

Symptoms associated with widespread pain were assessed using the Fibromyalgia Impact Questionnaire (FIQ) and 36-Item Short Form Health Survey questionnaire (SF-36). In patients with a mean number of 15 tender points, the negative impact on daily activities and mental health was found to be more frequent than in patients with a mean number of 6 tender points [3].

Clinical studies usually use FIQ which is a comprehensive questionnaire to assess fatigue, physical activity, anxiety and depressive changes. It is a combined questionnaire with an average of 2-3 questions for each clinical symptom. Fatigue questionnaires have been used in patients with systemic lupus erythematosus (SLE) and have been found to provide high informative value for this disease10. These facts have led to the selection of these questionnaires in FM.

The obtained results prove that development of pain in FM is not an isolated process, but rather related to development of concomitant clinical symptoms. Therefore, this is a confirmation of the comprehensive clinical presentations in fibromyalgia personality [8]. The coefficient adjusted $R^2 = 0.182$ shows the proportion of PCS that can be explained by the developed model. Here this coefficient is very low, i.e. the modelling is not powerful enough to use only the clinical manifestations of physical self-maintenance, impact of FM on daily functioning and Von Zerssen depression score to determine the physical component summary. The coefficient adjusted $R^2 = 0.275$ shows the proportion of MCS that can be explained by the developed model. Here this coefficient is very low, i.e. the modelling is not powerful enough to use only the clinical manifestations of depression/anxiety, impact of FM on daily functioning – social functioning and HADS score for depression to determine the mental component summary.

An individual approach for patient management and education is required in order to improve other symptoms in FM. Therefore, primary care in the family is important for treatment success. Future clinical follow-up must focus to find the most effective treatment for the patient with FM, considering his/her clinical characteristics, and the selection of the most efficient combination therapy for the symptoms. Comprehensive treatment of patients with FM aims to achieve clinical improvement and better quality of life.

**Conclusions**

1. Patients with primary fibromyalgia, osteoarthritis and FM, systemic lupus erythematosus and FM, have comparable pain intensity and comparable impact of fibromyalgia on daily activities.

2. The obtained results prove that development of pain in FM defines the development of concomitant clinical symptoms.

4. Impact of FM on daily functioning is associated with the presence of Von Zerssen depression score to determine the physical component summary.

5. Impact of FM on daily functioning – social functioning, is associated with the HADS score for depression to determine the mental component summary.

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