The effect of novel coronavirus disease-2019 (COVID-19) on fibromyalgia syndrome

F. Salaffi[1], V. Giorgi[2], S. Sirotti[2], S. Bongiovanni[2], S. Farah[1], L. Bazzichi[3], D. Marotto[4], F. Atzeni[5], M. Rizzi[6], A. Batticciotto[7], G. Lombardi[8], M. Galli[9], P. Sarzi-Puttini[2]

[1]Rheumatology Unit, Dept. of Clinical and Molecular Sciences, Università Politecnica delle Marche, Ancona; [2]Rheumatology Unit, ASST Fatebenefratelli-Luigi Sacco University Hospital, Milan; [3]Rheumatology Unit, Dept. of Clinical and Experimental Medicine, University of Pisa; [4]Rheumatology Unit, ATS Sardegna, P. Dettori Hospital, Tempio Pausania; [5]Rheumatology Unit, Dept. of Clinical and Experimental Medicine, University of Messina; [6]Respiratory Unit, L. Sacco University Hospital, ASST Fatebenefratelli-Sacco, Milan, Italy; [7]Rheumatology Unit, Dept. of Internal Medicine, ASST Settelaghi, Ospedale Di Circolo - Fondazione Macchi, Varese; [8]Laboratory of Experimental Biochemistry & Molecular Biology, IRCCS Istituto Ortopedico Galeazzi, Milan, Italy, and Dept. of Athletics, Strength and Conditioning, Poznań University of Physical Education, Poznań, Poland; [9]Dept. of Infectious Diseases, ASST-Fatebene-fratelli-Luigi Sacco University Hospital, Dept. of Biochemical and Clinical Sciences L. Sacco, University of Milan, Italy.

Fausto Salaffi, MD, PhD
Valeria Giorgi, MD
Silvia Sirotti, MD
Sara Bongiovanni, PhD
Sonia Farah, EngD
Laura Bazzichi, MD
Daniela Marotto, MD
Fabiola Atzeni, MD, PhD
Maurizio Rizzi, MD
Alberto Batticciotto, MD
Giovanni Lombardi, PhD
Massimo Galli, MD
Piercarlo Sarzi-Puttini, MD

Please address correspondence to:
Valeria Giorgi,
Rheumatology Unit,
ASST-Fatebenefratelli L. Sacco University Hospital,
Via G.B. Grassi 74,
20157 Milano, Italy.
E-mail: vale.gio@fastwebnet.it

Received on September 17, 2020; accepted in revised form on November 2, 2020.

Clin Exp Rheumatol 2021; 39 (Suppl. 130): S72-S77.

Key words: fibromyalgia, novel coronavirus disease 2019 (COVID-19), clinimetric scales, outcomes

Competing interests: none declared.

ABSTRACT

Objective. *Fibromyalgia syndrome (FM) is a complex disease that is mainly characterised by chronic widespread pain, fatigue and sleep disturbances and may be precipitated or worsened by many stressors. The aim of this study was to observe the behaviour of FM symptoms during the course of coronavirus disease 2019 (COVID-19).*

Methods. *Patients who had been diagnosed as having FM for ≥3 months were recruited between February and May 2020. The collected data were age, sex, educational level and marital status; height and weight; and the scores of the revised Fibromyalgia Impact Questionnaire (FIQR), the modified Fibromyalgia Assessment Status 2019 (FASmod), and the Polysymptomatic Distress Scale (PDS). The patients were divided into those with or without concomitant COVID-19 infection.*

Results. *Eight hundred and ninety-seven (93%) of the 965 patients (881 women [91.3%] and 84 men [8.7%]) were followed up on an outpatient basis because of FM and 68 (7.0%) were either followed up as out-patients or hospitalised because of COVID-19. There was no difference in the sociodemographic data of the two groups, but there were statistically significant between-group differences in the results of the clinimetric tests. The major differences between the score of the items (those with the greatest disease impact) were the following related symptoms: sleep quality (FIQR15), fatigue/energy (FIQR13), pain (FIQR12), stiffness (FIQR14).*

Conclusion. *The mean total and subdomain scores of all the tests were significantly higher in the patients with COVID-19, which suggests that global FM symptoms are more severe in patients with infection. Further studies of the post-COVID19 patients are being carried out in order to discover whether the worsened symptomatology continues because of their hypersensitised state.*

Introduction

Fibromyalgia syndrome (FM) is a complex disease that is characterised by a wide range of symptoms, particularly chronic widespread pain, fatigue and sleep disturbances (1, 2). It is quite common as its mean population prevalence is 2.2% in Italy (3) and 2.7% worldwide (4). Its complex symptomatology and the associated substantial disability not only lead to a poor health-related quality of life (5), but also a considerable economic burden for national health systems (6, 7). Its pathogenesis remains largely obscure, and no satisfactory medical treatment has yet been found (8, 9). The symptoms are rarely constant but usually fluctuate between a "FM" and a "non-FM" state (10), thus underlining the importance of aggravating and alleviating factors: for example, symptoms may be improved by moderate physical activity (11, 12), or worsened by physical or mental stressors such as, physical hyperactivity or physical trauma (13). Patients often associate stressors with the onset and exacerbations of the syndrome (14), which have also been found to be significantly associated with traumas and abuse (15-17). Furthermore, mainly on the basis of retrospective studies, it has been hypothesised that infections may precipitate the onset of FM (18).

The novel Coronavirus disease-2019 (COVID-19) pandemic is currently attracting the attention of most health authorities and the general public, and many FM patients are particularly worried about their health particularly because the clinical manifestations of COVID-19 include flu-like symptoms such as asthenia, myalgia, headache and diarrhoea that can mimic or aggravate FM (19).

The aim of this study was to evaluate the behaviour of FM symptoms in patients with a confirmed diagnosis of COVID-19 by means of disease-spe-

cific questionnaires. An observational study of this type may be of interest because of the high local burden of the disease (Italian Department of Civil Defence [*Dipartimento della Protezione Civile*], 2020) and the high level of morbidity associated with it.

Materials and methods

Patient recruitment

Patients who had been diagnosed as having FM for ≥3 months on the basis of the 1990 American College of Rheumatology (ACR) classification criteria (20) or the modified 2010/2011 ACR criteria (21) were enrolled as in- or out-patients at ASST Fatebenefratelli "L. Sacco" University Hospital, Milan, and C. Urbani Hospital, Jesi (Ancona) between February and May 2020. The patients with COVID-19 confirmed by means of a nasopharyngeal swab were recruited as in- or outpatients during a regular outpatient follow-up visit.

All procedures performed in this study were in accordance with the ethical standards of the Institutional Reviews Board of Ospedale C. Urbani and ASST Fatebenefratelli "Luigi Sacco" University Hospital and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Written informed consent was obtained from all individual participants included in the study.

Questionnaires

Every patient gave their written or verbal informed consent to the collection of data at the time of enrolment. The collected data were age, sex, educational level, and marital status; height and weight; and the results of the following clinimetric scales:

- The revised Fibromyalgia Impact Questionnaire (FIQR) is a disease-specific instrument consisting of 21 questions referring to the previous seven days (22). It is divided into three linked domains: 1) physical function (nine items); 2) the overall impact of FM on functioning and overall symptom severity (two items); and 3) symptoms (ten items), including memory, tenderness, balance, and environmental sensitivity to loud noises, bright lights, odours and cold temperatures. The total FIQR score is the sum of the three adjusted scores.
- The Widespread Pain Index (WPI) was used in the 2010/2011 ACR FM diagnostic criteria. It is based on the patient's perception of the painfulness of 19 body regions in the previous seven days (23).
- The Symptom Severity Scale (SSS) used in the 2010/2011 ACR FM diagnostic criteria is based on estimates of the severity of three symptoms (fatigue, unrefreshing sleep, and cognitive symptoms) in the previous seven days, plus the presence of three symptoms (headaches, pain/cramps in the lower abdomen, and depression) over the previous six months (final score 0-12) (24).
- The Polysymptomatic Distress Scale (PDS), also known as the FM symptom score, is the sum of the WPI and SSS (score 0-31) and measures the magnitude and severity of FM symptoms in patients satisfying and not satisfying the criteria (21).
- The modified Fibromyalgia Assessment Status 2019 (FASmod) combines the scores relating to fatigue and sleep quality with a count of painful body regions (similar to the WPI) in order to provide a single measure of disease activity. The modified version is an updated version of the original FAS questionnaire (final score 0-39) (25, 26).

Statistical analysis

The recorded data were entered into a database (Microsoft Office Excel 2011, version 11.4.1 Microsoft, Redmond, WA, USA), analysed using MedCalc®, version 19.0.1.0 (MedCalc Software, Mariakerke, Belgium). The continuous data are presented as mean values and standard deviations (SDs) or median values and interquartile ranges (IQRs) depending on their distribution, which was tested using the Kolmogorov–Smirnov test. The patients were divided into those with or without concomitant COVID-19 infection. The $\chi 2$ test was used to compare the categorical variables, and the Mann-Whitney U test was used to compare the continuous variables. Spydergrams were used to compare the FIQ-R and WPI subdomains (27). A p-value of <0.05 was considered statistically significant.

Table I. Educational level and marital status in FM patients with or without concomitant COVID-19 infection.

	FM	FM+COVID19	Total score
Education	n	n	n (%)
Primary school	61	5	66 (6.8)
Secondary school	237	13	250 (25,9)
High school	451	49	500 (51.8)
University	148	1	149 (15.4)
Marital status			
Single	153	12	165 (17.1)
Married	656	54	710 (73.6)
Divorced	75	2	77 (8.0)
Widow	13	0	13 (1.3)

Results

This cross-sectional study involved a total of 965 patients: 897 (93.0%) with FM alone and 68 (7.0%) with concomitant FM and COVID-19 (881 women [91.3%] and 84 men [8.7%] with a mean age of 51.6±10.6 years, a mean disease duration of 6.1±6.4 years, and a mean body mass index [BMI] of 25.9±3.7). Their educational level and marital status are shown in Table I. There was no difference in the BMI, age, gender, educational level, marital status or duration of FM between the two groups. Forty-nine of the 68 patients with COVID-19 were outpatients and 19 were in-patients, but there was no difference in the population characteristics of the two groups. Of the 68 patients, 20 were male and 48 were female. All patients were symptomatic with laboratory confirmation of COVID-19. The patients' ages ranged from 37 to 71 years with a mean of 53.9±17.6. Clinical presentations were fever, cough, expectora-

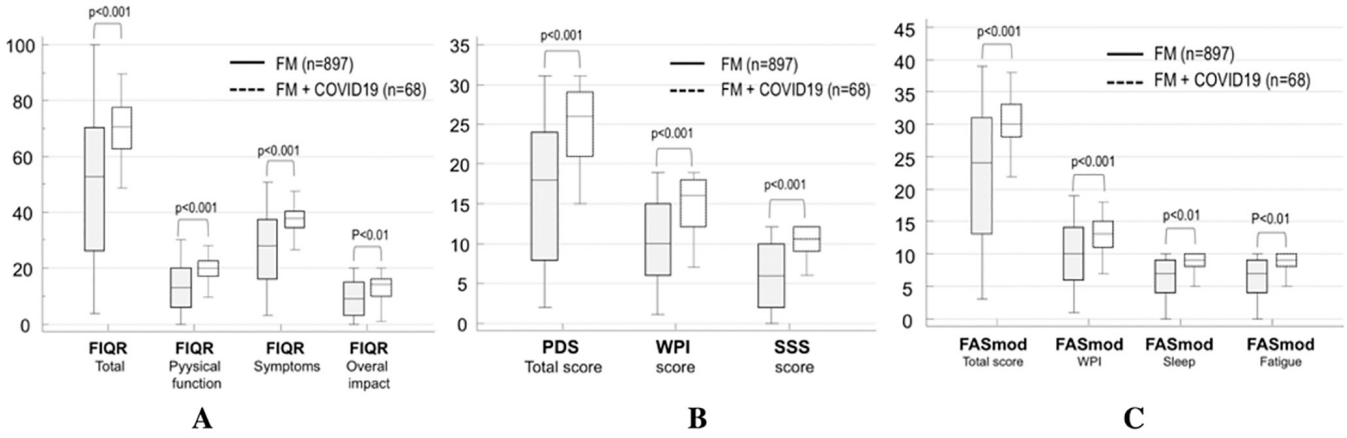

Fig. 1. Box and whisker plots of: (**A**) FIQR, (**B**) PDS and (**C**) FASmod values (y-axis) for total score and each subscale scores (x-axis) in FM patients with or without concomitant COVID-19 infection. The boxes represent the FIQR values from 25th to 75th percentiles. The middle lines inside boxes are the medians. The highest and lowest values are the maximum and the minimum data recorded. Mann-Whitney U test was used to compare FIQR scores.

Table II. FIQR, FASmod and PDS mean (SD) and median (25-75 percentiles) values for total score and each subscale scores.

	FM				FM+COVID19				
	Mean	Median	SD	25 - 75 P	Mean	Median	SD	25 - 75 P	*p*
FIQR overall_impact	9.49	9.00	6.24	3.00-15.00	12.76	14.00	4.31	10.00-16.00	<0.01
FIQR physical_function	13.61	13.00	8.01	6.00-20.00	19.87	20.16	5.05	17.16-22.83	<0.001
FIQR symptoms	26.96	28.00	12.61	16.00-37.50	37.25	38.00	5.23	34.75-40.50	<0.001
FIQR total score	50.06	52.83	25.08	26.17-70.33	69.90	70.58	10.78	62.66-77.41	<0.001
SSS	6.25	6.00	4.09	2.00-10.00	10.38	12.00	2.32	9.00-12.00	<0.001
WPI	10.47	10.00	5.22	6.00-15.00	14.54	16.00	3.64	12.00-18.00	<0.001
PDS total score	16.73	18.00	8.43	8.00-24.00	24.92	26.00	4.76	21.00-29.00	<0.001
FAS WPI	10.03	10.00	4.77	6.00-14.00	12.941	13.000	3.0019	11.00-15.00	<0.001
FAS fatigue	6.19	7.000	3.14	4.00-9.00	8.60	9.00	1.64	8.00-10.00	<0.01
FAS sleep	6.15	7.00	3.16	4.00-9.00	8.69	9.00	1.36	8.00-10.00	<0.01
FAS total score	22.37	24.00	9.80	13.00-31.00	30.23	30.00	4.09	28.00-33.00	<0.001

tion, fatigue, headache, gastrointestinal discomfort, dyspnoea and muscle ache. The body temperature was below 37.3°C in eleven patients (16.1%), between 37.3°C and 38°C in 32 (47.1%) between 38°C and 39°C in 15 (22.1%), and over 39°C in 10 (14.7%). Cough was present in 40 (58.8%) patients, expectoration in 8 (11.8%), fatigue in 51 (75%), headache in 49 (72.1%), sore throat in 9 (13.2%), gastrointestinal discomfort in 49 (72.1%), and muscle ache in 66 (97.1%). More than half of patients (40 [58.8%] of 68) developed dyspnoea. The median duration from illness onset to dyspnoea was 7.0 days (IQR 5.0–12.0). Sixty-six percent of patients had at least one comorbidity. Hypertension was the most common comorbidity, affecting 20 (44.5%) of 45 patients. The second and third most common comorbidities were cardiovascular disease (13 patients, 28.9%) and hypercholesterolemia (10 patients, 22.2%). Only 2 patients (4.4%) had a history of chronic obstructive pulmonary disease. Twenty-eight patients reported depression (41.2%) as evaluated with a Numerical Rating Scale (NRS)≥ 5. Eleven patients (16.2%) of the 68 required hospitalisation.

Figure 1 a-b-c and Table II show the results of the FIQR, FASmod and PDS by means of box plots that include the median values, interquartile ranges, and minimum and maximum values of the total scores and each sub-scale score.

The results of each test were statistically different in the FM group and the FM+COVID-19 group (Table II). For all comparisons the difference was with *p*-values <0.01.

The spydergrams in Figures 2 and 3 show the mean values of the answers to each single item of the FIQR and WPI; once again, there were clear and significant differences between the two groups.

The major differences between the score of the items (those with the greatest disease impact) were the following symptoms related: sleep quality (FIQR15), fatigue/energy (FIQR13), pain (FIQR12), stiffness (FIQR14).

Discussion

The results of this cross-sectional study mirror the health status of FM patients affected by COVID-19. FM-associated symptoms (widespread pain, sleep disturbances, fatigue, functional symptoms) and the patients' quality of life were investigated by means of disease-specific questionnaires (PDS, FIQR, FASmod). The mean scores of all of the tests (overall and sub-domain scores) were significantly higher in the patients with COVID-19, which suggests that their FM symptoms greatly worsened during the course of COVID-19.

There two distinct but possibly co-existing mechanisms that may explain these

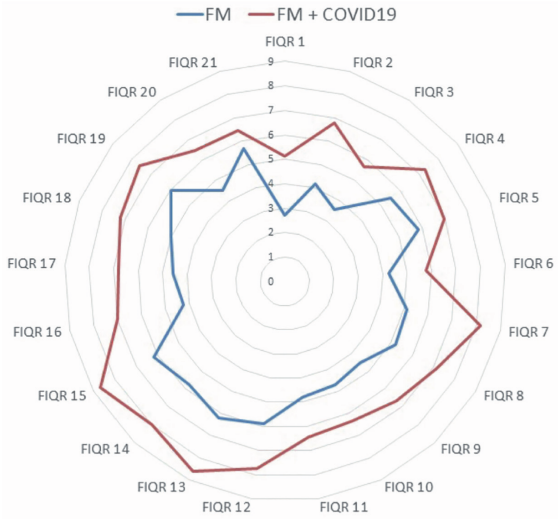

Fig. 2. Polar plot (spydergrams) of mean FIQR single item scores for FM patients with or without concomitant COVID-19 infection (all at p-value <0.01).
Note. The domain scores are plotted from 0 (best, at the center) to 10 (worst, at the outside).
FIQR: Fibromyalgia Impact Questionnaire Revised version.

Item	Item Description	FM		FM+COVID19	
		Score	SD	Score	SD
FIQR-1	Brush or comb hair	2.69	3.17	5.13	2.73
FIQR-2	Walk continuously for 20 min.	4.19	3.49	6.77	2.44
FIQR-3	Prepare a homemade meal	3.56	3.17	5.70	2.39
FIQR-4	Vacuum, scrup, or sweep floors	5.49	3.25	7.32	1.89
FIQR-5	Lift and carry a bag full of groceries	5.83	3.44	6.95	2.35
FIQR-6	Climb one flight of stairs	4.26	3.21	5.76	2.59
FIQR-7	Change bed sheets	5.09	3.29	8.19	8.43
FIQR-8	Sit in a chair for 45 min	5.18	3.28	7.11	1.98
FIQR-9	Go shopping for groceries	4.53	3.41	6.66	1.98
FIQR-10	Cannot achieve goals	4.69	3.20	6.32	2.35
FIQR-11	Feel overwhelmed	4.81	3.31	6.44	2.51
FIQR-12	Pain rating	5.89	3.07	7.72	1.02
FIQR-13	Fatigue rating	6.19	3.15	8.60	1.64
FIQR-14	Stiffness rating	5.74	2.99	7.97	1.44
FIQR-15	Sleep quality	6.15	3.16	8.69	1.36
FIQR-16	Depression level	4.26	3.26	6.98	2.11
FIQR-17	Memory problems	4.57	3.10	6.79	1.94
FIQR-18	Anxiety level	4.98	3.15	7.20	2.45
FIQR-19	Tenderness level	5.94	3.11	7.59	1.55
FIQR-20	Balance problems	4.50	3.54	6.48	1.57
FIQR-21	Environmental sensitivity	5.68	3.22	6.47	2.23

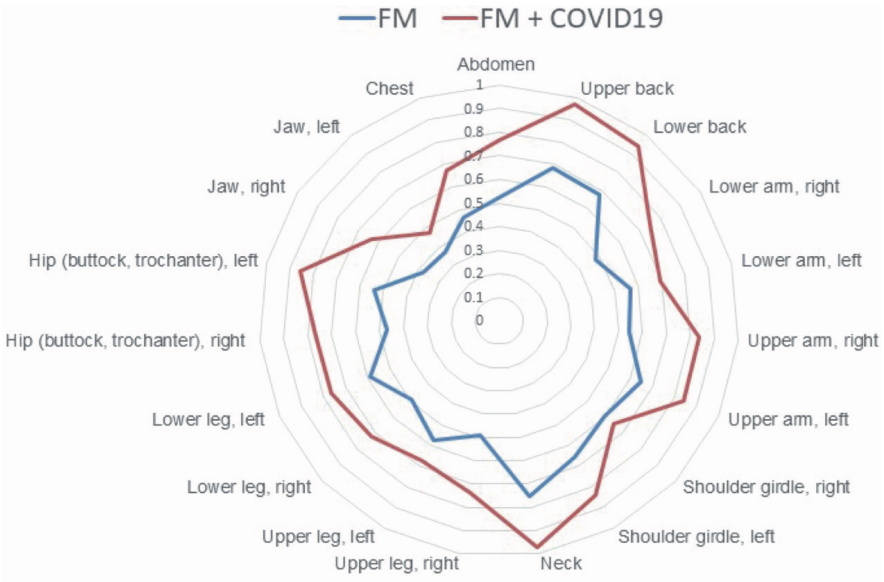

Fig. 3. Polar plot (spydergrams) of mean WPI single item scores for FM patients with or without concomitant COVID-19 infection. The scores are plotted from 0 (no pain, at the centre) to 1 (maximum pain, on the outside).

findings. Firstly, COVID-19 is associated with sensory disturbances (anosmia, ageusia, etc.) that suggest nervous system damage caused by the infection (28). Furthermore, the aetiology of FM itself may be related to autonomic nervous system (ANS) dysfunction (FM patients often suffer from ANS-related disturbances) (29, 30), which has both a symptomatic (such as, xerostomia or xerophthalmia) and pathological counterpart (the finding of frank small-fibre neuropathy in many FM patients) (30). Consequently, a possible worsening in ANS-related symptoms (reflected in the FIQ-R and PDS scores) may be related to the specific action of the virus. COVID-19 is also associated with typical flu-like syndrome, which may further exacerbate the widespread pain and myalgia of FM.

Secondly, the physical and psychological stress these patients are subject to during the course of COVID-19 and/or hospitalisation (severe inflammation, mental and physical distress, and the disease-related anxiety) may be important factors in worsening FM. A viral infection may itself be an important stressor that FM patients or genetically predisposed subjects may have difficulty in dealing with, without losing their bodily homeostasis. This is mirrored by the fact that the prevalence of FM is significantly higher in populations infected by hepatitis B virus, hepatitis C virus, human immunodeficiency virus (HIV), and mycoplasma (31-34), although the studies are not always consistent (35), and greater seropositivity for some infectious agents has been detected among FM patients (36). Furthermore, it has been shown that people with FM have difficulties in dealing with stress and significantly reduced resilience levels and effective coping strategies (37). This altered resilience is mirrored by the interesting hypothesis that the sympathetic ANS is hyperactive but also hypo-reactive in FM, blunting the response to stressors (37). A low level of resilience is inversely associated with the probability of developing post-traumatic stress disorder (38), which is quite prevalent among

FM patients, also in its subthreshold forms (39), and is significantly able to influence FM clinical course: indeed, it was found that lifetime post-traumatic stress symptoms negatively influence the quality of life and severity of FM symptoms (40). Therefore, it is probable that traumatic or very stressful life events are not the actual cause of FM, but in genetically predisposed individuals may contribute to the dysmodulation of brain circuitries involved in pain and emotional processing (41), constituting the link between significant psychological factors and FM symptoms (42).

In summary, not only the disease itself, but also the high levels of mental stress associated with COVID-19 and the stigma of having been infected may all be important factors (43).

Although the evaluation of depression and psycho-affective aspects in general requires complex tools and questionnaires (44), our data obtained with a simple numerical scale of 0-10 shows that the group of patients with FS affected by COVID-19 report significantly higher levels of depression (6.98 ± 2.11 *vs*. 4.26 ± 3.26, $p<0.01$) compared to the control group affected by FM.

The major limitations of the present study were the number of COVID-19 patients (which is much lower than that of the patients with FM alone), that they come from both out- and in-patient settings, and the fact that many relevant factors (*e.g*. depression, anxiety, catastrophising) are not considered or reported. In addition, the cross-sectional design limits the interpretation of causality and longevity.

In conclusion, the mental and physical stress associated with COVID-19 can greatly worsen FM symptoms and intensify the patients' suffering. However, as the findings of this cross-sectional study may return to normal after the patients have recovered from COVID-19, further studies are being carried out in order to discover whether the worsened symptoms of the post-COVID-19 patients continues because of their hypersensitised state.

Acknowledgements

We thank all rheumatologists and clinical staff of the Rheumatology Departments for the collaboration in data collection. We are very grateful to all FM patients who kindly completed the questionnaires.

References

1. ARNOLD LM, BENNETT RM, CROFFORD LJ *et al*.: AAPT Diagnostic Criteria for Fibromyalgia. *J Pain* 2019; 20: 611-28.
2. CLAUW DJ: Fibromyalgia: A clinical review. *JAMA* 2014; 311: 1547-55.
3. SALAFFI F, DE ANGELIS R, GRASSI W *et al*.: Prevalence of musculoskeletal conditions in an Italian population sample: Results of a regional community-based study. I. The MAPPING study. *Clin Exp Rheumatol* 2005; 23: 819-28.
4. QUEIROZ LP: Worldwide epidemiology of fibromyalgia. *Curr Pain Headache Rep* 2013; 17: 356.
5. SALAFFI F, SARZI-PUTTINI P, GIROLIMETTI R, ATZENI F, GASPARINI S, GRASSI W: Health-related quality of life in fibromyalgia patients: a comparison with rheumatoid arthritis patients and the general population using the SF-36 health survey. *Clin Exp Rheumatol* 2009; 27 (Suppl. 56): S67-74.
6. KNIGHT T, SCHAEFER C, CHANDRAN A, ZLATEVA G, WINKELMANN A, PERROT S: Health-resource use and costs associated with fibromyalgia in France, Germany, and the United States. *Clinicoecon Outcomes Res* 2013; 5: 171-80.
7. SPAETH M: Epidemiology, costs, and the economic burden of fibromyalgia. *Arthritis Res Ther* 2009; 11: 117.
8. CALANDRE EP, RICO-VILLADEMOROS F, SLIM M: An update on pharmacotherapy for the treatment of fibromyalgia. *Expert Opin Pharmacother* 2015; 16: 1347-68.
9. MACFARLANE GJ, KRONISCH C, DEAN LE *et al*.: EULAR revised recommendations for the management of fibromyalgia. *Ann Rheum Dis* 2017; 76: 318-28.
10. WOLFE F: Fibromyalgianess. *Arthritis Care Res* 2009; 61: 715-6.
11. STAUD R, ROBINSON ME, WEYL EE, PRICE DD: Pain variability in fibromyalgia is related to activity and rest: Role of peripheral tissue impulse input. *J Pain* 2010; 11: 1376-83.
12. CAZZOLA M, ATZENI F, SALAFFI F, STISI S, CASSISI G, SARZI-PUTTINI P: What kind of exercise is best in fibromyalgia therapeutic programmes? A practical review. *Clin Exp Rheumatol* 2010; 28 (Suppl. 63): S117-24.
13. MCLEAN SA, WILLIAMS DA, CLAUW DJ: Fibromyalgia after motor vehicle collision: evidence and implications. *Traffic Inj Prev* 2005; 6: 97-104.
14. BENNETT RM, JONES J, TURK DC, RUSSELL IJ, MATALLANA L: An internet survey of 2,596 people with fibromyalgia. *BMC Musculoskelet Disord* 2007;8: 27.
15. HÄUSER W, KOSSEVA M, ÜCEYLER N, KLOSE P, SOMMER C: Emotional, physical, and sexual abuse in fibromyalgia syndrome: A systematic review with meta-analysis. *Arthritis Care Res* (Hoboken) 2011; 63: 808-20.
16. HÄUSER W, HOFFMANN EM, WOLFE F *et al*.: Self-reported childhood maltreatment, lifelong traumatic events and mental disorders in fibromyalgia syndrome: a comparison of US and German outpatients. *Clin Exp Rheumatol* 2015; 33 (Suppl. 88): S86-92.
17. PARAS ML, MURAD MH, CHEN LP *et al*.: Sexual Abuse and Lifetime Diagnosis of Somatic Disorders. *JAMA* 2009; 302: 550-61.
18. JIAO J, VINCENT A, CHA SS, LUEDTKE CA, KIM CH, OH TH: Physical Trauma and Infection as Precipitating Factors in Patients with Fibromyalgia. *Am J Phys Med Rehabil* 2015; 94: 1075-82.
19. HÄUSER W, SARZI-PUTTINI P, FITZCHARLES MA: Fibromyalgia syndrome: under-, over- and misdiagnosis. *Clin Exp Rheumatol* 2019; 37 (Suppl. 116): S90-7.
20. WOLFE F, SMYTHE HA, YUNUS MB *et al*.: The American College of Rheumatology 1990 Criteria for the Classification of Fibromyalgia. Report of the Multicenter Criteria Committee. *Arthritis Rheum* 1990; 33: 160-72.
21. WOLFE F, CLAUW DJ, FITZCHARLES MA *et al*.: 2016 Revisions to the 2010/2011 fibromyalgia diagnostic criteria. *Semin Arthritis Rheum* 2016; 46: 319-29.
22. SALAFFI F, FRANCHIGNONI F, GIORDANO A, CIAPETTI A, SARZI-PUTTINI P, OTTONELLO M: Psychometric characteristics of the Italian version of the revised Fibromyalgia Impact Questionnaire using classical test theory and Rasch analysis. *Clin Exp Rheumatol* 2013; 31 (Suppl. 79): S41-9.
23. WOLFE F, CLAUW DJ, FITZCHARLES MA *et al*.: The American College of Rheumatology preliminary diagnostic criteria for fibromyalgia and measurement of symptom severity. *Arthritis Care Res* 2010; 62: 600-10.
24. WOLFE F, CLAUW DJ, FITZCHARLES MA *et al*.: Fibromyalgia criteria and severity scales for clinical and epidemiological studies: A modification of the ACR preliminary diagnostic criteria for fibromyalgia. *J Rheumatol* 2011; 38: 1113-22.
25. SALAFFI F, SARZI-PUTTINI P, GIROLIMETTI R, GASPARINI S, ATZENI F, GRASSI W: Development and validation of the self-administered Fibromyalgia Assessment Status: a disease-specific composite measure for evaluating treatment effect. *Arthritis Res Ther* 2009;11: R125.
26. SALAFFI F, DI CARLO M, FARAH S *et al*.: Diagnosis of fibromyalgia: comparison of the 2011/2016 ACR and AAPT criteria and validation of the modified Fibromyalgia Assessment Status. *Rheumatology* (Oxford) 2020; 59: 3042-9.
27. STRAND V, CRAWFORD B, SINGH J, CHOY E, SMOLEN JS, KHANNA D: Use of "spydergrams" to present and interpret SF-36 health-related quality of life data across rheumatic diseases. *Ann Rheum Dis* 2009; 68: 1800-4.
28. WU Y, XU X, CHEN Z *et al*.: Nervous system involvement after infection with COVID-19 and other coronaviruses. *Brain Behav Immun* 2020; 87: 18-22.
29. VINCENT A, MCALLISTER SJ, SINGER W *et al*.: A report of the autonomic symptom profile in patients with fibromyalgia. *J Clin Rheumatol* 2014; 20: 106-8.
30. DI CARLO M, VENTURA C, CESARONI P, CAROTTI M, GIOVAGNONI A, SALAFFI F: Sural nerve size in fibromyalgia syndrome:

study on variables associated with cross-sectional area. *Front Med* 2020; 7: 360.
31. CASSISI G, SARZI-PUTTINI P, CAZZOLA M: Chronic widespread pain and fibromyalgia: could there be some relationships with infections and vaccinations? *Clin Exp Rheumatol* 2011; 29 (Suppl. 69): S118-26.
32. MARQUEZ J, RESTREPO CS, CANDIA L, BERMAN A, ESPINOZA LR: Human Immunodeficiency Virus-Associated Rheumatic Disorders in the HAART Era. *J Rheumatol* 2004; 31: 741-6.
33. MOHAMMAD A, CAREY JJ, STORAN E, SCARRY M, COUGHLAN RJ, LEE JM: Prevalence of fibromyalgia among patients with chronic Hepatitis C Infection: Relationship to viral characteristics and quality of life. *J Clin Gastroenterol* 2012; 46: 407-12.
34. OZSAHIN M, GONEN I, ERMIS F *et al*.: The prevalence of fibromyalgia among patients with hepatitis B virus infection. *Int J Clin Exp Med* 2013; 6: 804-8.
35. NARVÁEZ J, NOLLA JM, VALVERDE-GARCÍA J: Lack of association of fibromyalgia with hepatitis C virus infection. *J Rheumatol* 2005; 32: 1118-21.
36. AKKAYA N, AKKAYA S, POLAT Y *et al*.: Helicobacter pylori seropositivity in fibromyalgia syndrome. *Clin Rheumatol* 2011; 30: 43-9.
37. CASALE R, SARZI-PUTTINI P, BOTTO R *et al*.: Fibromyalgia and the concept of resilience. *Clin Exp Rheumatol* 2019; 37 (Suppl. 116): S105-13.
38. SALAFFI F, ATZENI F, TALOTTA R, DI CARLO M, SARZI-PUTTINI P: Earthquake Vulnerability of Fibromyalgia Patients: Six-Month Follow-Up After the Catastrophic Disasters in Central Italy. *Clin Exp Rheumatol* 2017; 35 (Suppl. 105): S93-9.
39. CONVERSANO C, CARMASSI C, BERTELLONI CA *et al*.: Potentially traumatic events, post-traumatic stress disorder and post-traumatic stress spectrum in patients with fibromyalgia. *Clin Exp Rheumatol* 2019; 37 (Suppl. 116): S39-43.
40. DELL'OSSO L, CARMASSI C, CONSOLI G *et al*.: Lifetime posttraumatic stress symptoms are related to the health-related quality of life and severity of pain/fatigue in patients with fibromyalgia. *Clin Exp Rheumatol* 2011; 29 (Suppl. 69): S73-8.
41. SARZI-PUTTINI P, GIORGI V, MAROTTO D, ATZENI F: Fibromyalgia: an update on clinical characteristics, aetiopathogenesis and treatment. *Nature Rev Rheum* 2020; 16: 645-60.
42. MALIN K, LITTLEJOHN GO: Psychological factors mediate key symptoms of fibromyalgia through their influence on stress. *Clin Rheum* 2016; 35: 2353-7.
43. BAZZICHI L, GIACOMELLI C, CONSENSI A *et al*.: One year in review 2020: fibromyalgia. *Clin Exp Rheumatol* 2020; 38 (Suppl. 123): S3-8.
44. VELTRI A, SCARPELLINI P, PICCINNI A *et al*.: Methodological approach to depressive symptoms in fibromyalgia patients. *Clin Exp Rheumatol* 2012; 30 (Suppl. 74): S136-42.