

Impact of the mandatory confinement during the first wave of the SARS-CoV-2/COVID-19 pandemic in Portuguese patients with rheumatoid arthritis: results from the COVID in RA (COVIDRA) survey

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ABSTRACT

Objective. The aim of this study was to evaluate the self-reported impact of mandatory confinement occurring in the first wave of the SARS-CoV-2 pandemic in Portuguese patients with rheumatoid arthritis (RA), as a means to improve care during this and in future pandemics.

Material and methods. The web-based survey COVIDRA was developed to assess 5 domains including RA symptoms, attitudes towards medication, employment status, physical exercise and mental health. The questionnaire was sent to RA patients through e-mail and social media of the Portuguese Society of Rheumatology and two patient associations; and it was filled locally at two rheumatology centers in Lisbon. Recruitment took place during June and July 2020.

Results. We obtained 441 valid questionnaires. Most respondents were female (88.4%), caucasian (93.6%) with a mean age of 58 years. The majority had disease lasting >10 years and were treated with csDMARDs (63.2%) and/or bDMARDs/tsDMARDs (23.7%). Over 40% experienced symptom worsening during confinement, almost half considered moderate or severe. Mobility restriction and increased stress, anxiety or depression were responsible for this worsening. Only 2.5% reduced or withheld their immunosuppressive medication due to fear of becoming infected with SARS-CoV-2. After confinement, 16.2% of those previously employed were in a lay-off regime and 3% lost their jobs. Most employed RA patients practiced telework during confinement. The majority of patients decreased or did not practice any physical exercise (80.5%).

Symptoms of anxiety and depression developed or worsened in 67.3% and 51.9% respectively, approximately one third were considered moderate or severe.

Conclusions. Portuguese RA patients experienced significant symptom worsening, anxiety and depression during the first wave confinement. Only a minority changed their immunosuppressive treatment for fear of SARS-CoV-2 infection. Published literature on these matters shows results very similar to ours.

Keywords: Covid-19; Drug withdrawal; Rheumatoid arthritis

INTRODUCTION

The new coronavirus outbreak allegedly started in a wet market in Wuhan, China, and swiftly spread throughout the globe to infect dozens of millions. The World Health Organization stated in early March that COVID-19, the disease caused by SARS-CoV-2, should be considered a pandemic¹ and many governments adopted early containment strategies to avoid community transmission. These strategies were influenced by epidemiological status, regional healthcare resources and economic factors, but were otherwise similar between countries. In addition to case finding and widespread testing for SARS-CoV-2, social distancing, facial masks and partial or total confinement were used to mitigate virus spread and flatten the curve of new infections^{2,3}.

In Portugal, the first infection by the new SARS-CoV-2 was reported in the 2nd of March, 2020, and a national state-of-emergency was declared in the 18th of March lasting until the 3rd of May. During this period, confinement was mandatory and healthcare resources were allocated to fight the pandemic. Almost all scheduled

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clinical activity was withheld and chronic diseases were managed essentially through telemedicine.

The aim of this study was to evaluate the self-reported impact of the mandatory confinement in Portuguese patients with rheumatoid arthritis (RA), as a means to improve care during this and in future pandemics.

MATERIAL AND METHODS

SURVEY DEVELOPMENT AND PARTICIPANTS

The COVID in RA (COVIDRA) survey was developed using the online survey tool Google® Forms™. Aside from demographic characterization, the authors assessed 5 domains that were most likely affected during the mandatory confinement of RA patients, including: symptom variation (5 questions); attitudes towards medication (3 questions); employment status (3 questions); physical exercise (2 questions); and mental health (2 questions). Patients ≥ 18 years of age and with the diagnosis of RA made by a physician were invited to answer the questionnaire (available as Online Supplementary Data, in Portuguese).

SURVEY DIFFUSION

The survey was made available to RA patients either by e-mail or social media of the Portuguese Society of Rheumatology, the National Association of Patients with RA (ANDAR) and the Portuguese League Against Rheumatic Diseases. The questionnaire was also filled locally at two rheumatology centers in Lisbon, the Rheumatology and Osteoporosis Unit – Hospital de Sant’Ana, and the Rheumatology Department – Hospital de Egas Moniz, CHLO EPE. Responses were collected anonymously. Recruitment took place during June and July 2020.

DATA COLLECTION AND ANALYSIS

Descriptive statistics were generated by Google® Forms™, transported to Microsoft Office Excel v16.40 and evaluated using both Microsoft Office Excel v16.40 and IBM SPSS Statistics V.26 software.

ETHICAL CONSIDERATIONS

Since this study did not represent any deviation from normal clinical practice, did not require any intervention or interaction with any patient, and collected non-identifiable and non-traceable data, the study protocol was not submitted to an Ethics Committee.

RESULTS

RESPONDENTS’ CHARACTERISTICS AND DEMOGRAPHIC DATA

We obtained 447 questionnaires, 441 of which were considered valid (at least 1 question answered). Most respondents were female (88.4%), caucasian (93.6%) with a mean age of 58 (+/-13) years. The majority (57.6%) had longstanding disease (>10 years) and were treated with csDMARDs (63.2%) and/or bDMARDs/tsDMARDs (23.7%). All Portuguese districts were represented, except for Madeira island (respondents were more frequently from Lisbon, Setúbal and Oporto). Patients’ characteristics are summarized in Table I.

SYMPTOM VARIATION

Approximately 41% (N=178) of RA patients experienced symptom worsening during confinement, 17.8% (N=78) of which considered moderate or severe. Joint pain (47.2%, N=84) and impaired joint function (18.5%, N=33) were most frequently reported. Mobility restriction (34.0%, N=60) and increased stress, anxiety or depression (27.5%, N=49) were pointed out as the main causes for symptom worsening. Half of patients reported no symptom change and a minority (7%, N=33) felt better during confinement (Figure 1).

ATTITUDES TOWARDS MEDICATION

During the state-of-emergency mandatory confinement, only 14% (N=61) of patients discontinued or reduced the dosage or frequency of their RA treatment. Most did so according to indications by the attending physician (27.9%, N=17). Only 11 patients (18%) discontinued their immunosuppressive medication out of fear of becoming infected with SARS-CoV-2 (corresponding to 2.5% of total responders). Another 11 patients did so because they had no prescription, couldn’t go to the community/hospital pharmacy or couldn’t afford the medication (Figure 2).

EMPLOYMENT STATUS

Before confinement, most RA patients were either employed (45.2%, N= 198), retired (41.3%, N=181) or unemployed (7.1%, N=31). After confinement, 16,2% (N=32) of those previously employed were in a lay-off regime and 3% (N=6) lost their jobs. Most employed RA patients worked from home (55.4%, N=87), as opposed to onsite (27.4%, N=43).

TABLE I. CHARACTERISTICS OF RHEUMATOID ARTHRITIS PATIENTS RESPONDING TO THE COVIDRA SURVEY

Demographic characterization	
Age (mean±SD)	58±13
Female gender, n (%)	388 (88.4)
Caucasian, n (%)	410 (93.6)
Years from symptom onset, n (%)	
<1	4 (0.9)
1-5	101 (23.1)
6-10	79 (18.1)
11-20	112 (25.6)
>20	140 (32.0)
Does not know	2 (0.5)
RA treatments, n (%)	
No treatment	15 (3.5)
Glucocorticoids and/or NSAIDs only	40 (9.1)
csDMARDs	277 (63.2)
bDMARDs with or without csDMARDs	100 (22.8)
tsDMARDs with or without csDMARDs	4 (0.9)
Does not know	2 (0.5)
Employment status before the pandemic, n (%)	
Student	5 (1.1)
Employed	198 (45.2)
Unemployed	37 (7.1)
Temporary leave	2 (0.5)
Sick leave	16 (3.7)
Retired	181 (41.3)
Does not know	5 (1.1)

bDMARDs: biologic disease modifying antirheumatic drugs; csDMARDs: conventional synthetic disease modifying antirheumatic drugs; NSAIDs: non-steroidal anti-inflammatory drugs; RA: rheumatoid arthritis; tsDMARDs: targeted synthetic disease modifying antirheumatic drugs.

PHYSICAL EXERCISE

More than half of responders (56.8%, N=247) did not practice any physical exercise during confinement, while 23.7% (N= 103) practiced less exercise than before. RA patients who reported practicing the same or more physical exercise were 12.4% (N=54) and 6.7% (N=29), respectively.

MENTAL HEALTH

Anxiety developed or worsened in 67.3% (N=297) of RA patients responding the survey. Symptoms were classified as moderate or severe in almost 30% of cases. Simi-

larly, more than half (51.9% N=228) reported development or worsening of symptoms of depression, moderate or severe in more than 20% of cases (Figure 3).

DISCUSSION

The uncontrolled dissemination of the SARS-CoV-2 infection forced health authorities worldwide to recommend mandatory confinement as a means to contain disease spread during the first wave. This confinement was not without consequences, and the COVIDRA survey disclosed that Portuguese RA patients developed significant symptom worsening, anxiety and depression during lock-down.

The worsening of symptoms following restrictions in mobility and physical exercise was somewhat expected due to the inflammatory nature of RA. Nonetheless, many responders attributed this worsening also to increased anxiety and depression, which emphasizes the importance of psychological factors in the modulation of pain and other RA symptoms⁴. In line with these results, Cleaton *et al.* assessed the impact of stringent social isolation during the COVID-19 pandemic on health-related quality of life of a large UK cohort of inflammatory arthritis patients (over 1600 responders), and found significantly worse physical component score of Short Form-12 (SF-12) compared to those not confined (-2.2; 95% CI -3.8, to 2.5; p<0.001)⁵.

In the early days of the pandemic, patients with inflammatory rheumatic diseases were considered at higher risk for SARS-CoV-2 infection due to their immune dysfunction, treatment with immunosuppressors and frequent comorbidities. This prompted scientific societies to issue recommendations urging patients not to discontinue immunosuppressive therapies, because this would result in disease activity flares and further increase the risk for infection⁶⁻⁸. We found that only 2.5% of responders discontinued or reduced the dosage or frequency of their RA treatment out of fear of becoming infected with SARS-CoV-2. Most international studies reported similar rates. Schmeiser *et al.* found 4% of discontinuation in a population of 656 German patients with inflammatory rheumatic diseases in the early days of the first wave⁹. Fragoulis *et al.* studied 500 inflammatory patients in Greece to find discontinuation rates of 2.2%¹⁰ and Pineda-Sic *et al.* did the same in 345 Mexican patients to find rates of 3.8%¹¹. Other studies show higher discontinuation numbers. For instance, more than 30% of 655 French

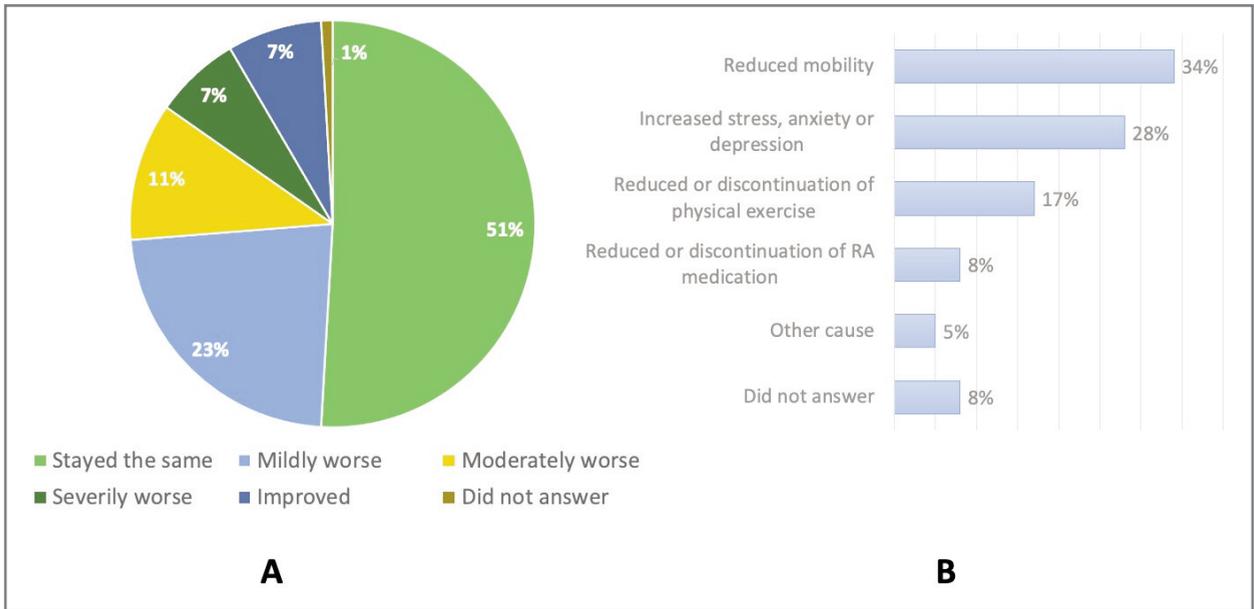


FIGURE 1. Rheumatoid arthritis symptom variation during mandatory confinement of the first wave of the SARS-CoV-2/COVID-19 pandemic (A) and reasons pointed by those reporting symptom worsening (B). RA: Rheumatoid arthritis

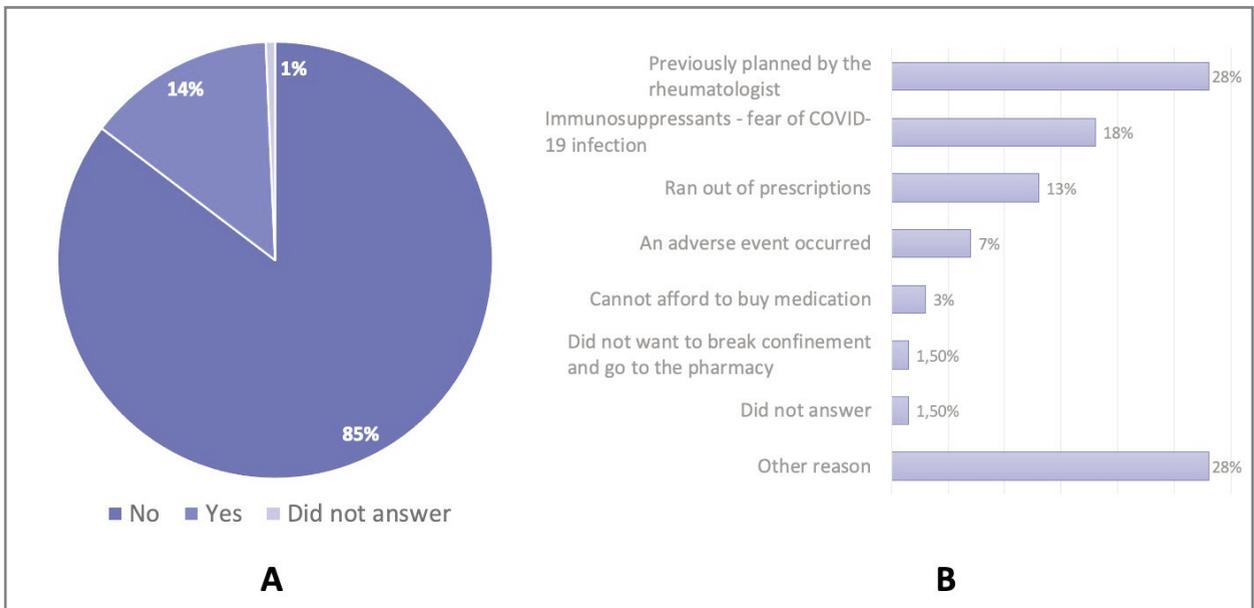


FIGURE 2. Attitudes towards medication during mandatory confinement of the first wave of the SARS-CoV-2/COVID-19 pandemic. A) Percentage of patients discontinuing or changing the dosage or frequency of their medication; B) Reasons for doing so.

patients with inflammatory conditions suspended or decreased the dosage of their treatment during lockdown, but this population also included patients who tested positive for COVID-19 and we must bear in mind that France was one the European countries that was hit the hardest during the first wave¹².

Several studies assessed the psychological impact of confinement, either in healthy individuals¹³⁻¹⁶ or patients with chronic diseases¹⁷⁻¹⁹. Pirro *et al.* found 18% and 12% of abnormal anxiety and depression scores, respectively, using the Hospital Anxiety and Depression Scale (HADS) in a cohort of 226 Italian patients

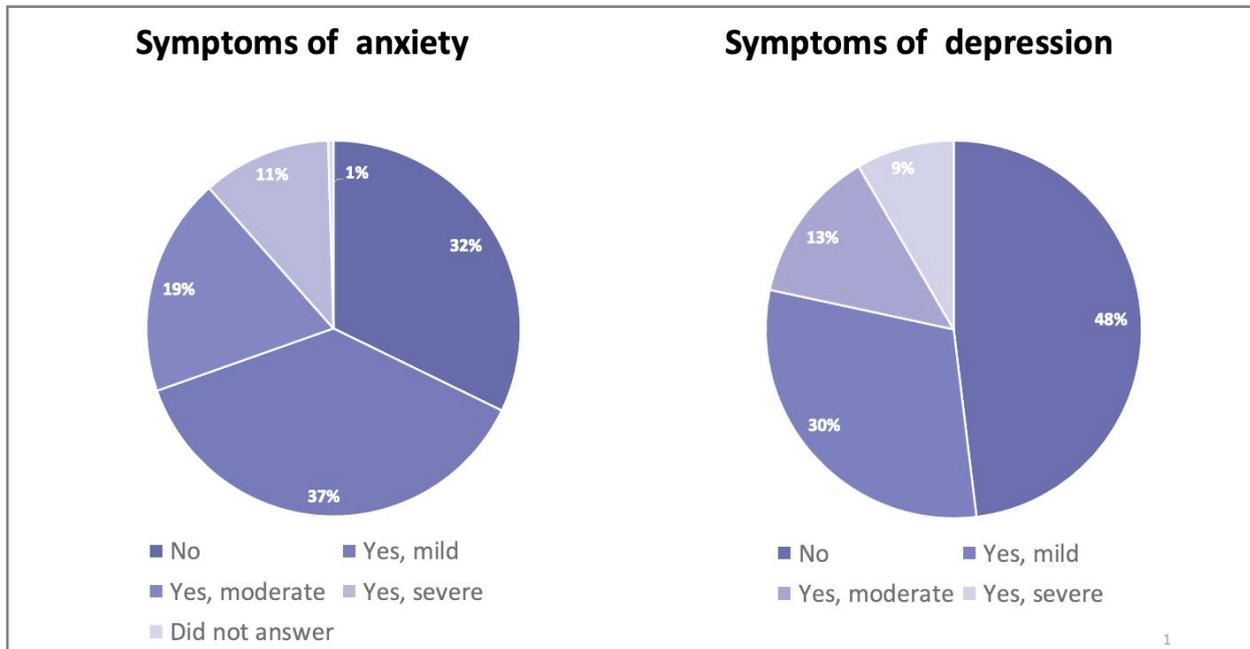


FIGURE 3. Proportion of patients developing or worsening symptoms of anxiety or depression during confinement of the first wave of the SARS-CoV-2/COVID-19 pandemic, and classification of the intensity of symptoms.

with psoriasis treated with biological therapies during lockdown²⁰. Ciaffi *et al.* did not find significant differences in the prevalence of depression between patients with inflammatory arthritis and healthy controls using the Beck's Depression Inventory II, however the same was not true when HADS was used (32% vs 18%, $p = 0.008$, for depression; 40% vs 28%, $p = 0.032$, for anxiety)²¹. In the previously mentioned study by Cleaton *et al.*, the rigorously confined group also had significantly lower mental component score of SF-12 (-2.1; 95% CI -2.9, to 1.4, $p < 0.001$) compared to those not confined⁵.

Pandemics will remain in the agenda of modern societies both on the short-term and the long-term. Although worldwide vaccination is ongoing, it is likely that new waves of the infection strike before herd immunity is achieved, and it is uncertain whether vaccines will maintain efficacy after new SARS-CoV-2 variants emerge²². Furthermore, rapid population growth, urbanization and climate change will probably contribute to the increase of pandemics in the future²³. This puts additional stress to healthcare systems because they need to provide for chronic patients as well. The impact reported on this study by Portuguese RA patients reveals an unprepared system and warrants reflections for the future.

Patients with inflammatory conditions should main-

tain their regular follow-up visits and access to the attending rheumatologist should be assured. Approximately 41% of COVIDRA respondents reported no contact with their rheumatologist during confinement (data not shown). When the risk of contagion is too high or when confinements are in place, digital resources should be used. This is of the utmost importance to manage disease activity, keep symptoms under control and renew drug prescriptions. Rheumatologists also play a central role in educating their patients about the characteristics of the infection, prevention of transmission and risks associated with the inherent immune dysfunction and immunosuppressive treatment. Although the reported impact on employment was apparently mild during the first wave, an increase in unemployment and a profound economical and social crisis are expected in the following months. This will probably result in lower access to medical care, diagnostic exams and treatments, and rheumatologists will have yet another challenge to face in the management of disease activity. The restriction of individual liberties in effect since early March 2020, which have included total and partial confinement, combined with social isolation and uncertainty about the pandemic, have taken its toll on the mental health of RA patients. Once again, the rheumatologist should be aware of any symptoms of anxiety or depression and discuss with the pa-

tient the need for psychological counseling, psychiatric evaluation or other available resources (like self-help groups or mental health hotlines). The main explanation for the worsening of symptoms during lockdown was mobility restriction. Home-based physical exercise (using information from social media, websites of patient associations and physical therapy, for instance) and outdoor exercise (when confinement is not mandatory and using all measures to avoid contagion) should be suggested.

Despite its merits, our study has limitations. First, the cross sectional design gives us a limited perspective of the first wave of the pandemic, and we hypothesize that the impact in disease activity, treatment discontinuation, unemployment and mental health is far greater after the following waves. Secondly, some of the answers may have been influenced by recall bias as the questionnaire was filled some weeks after the mandatory confinement was lifted. Lastly, no validated measurement scales were used to assess some of the outcomes (for instance, HADS for mental health).

CONCLUSION

Portuguese patients with RA experienced significant symptom worsening, anxiety and depression during the first wave of the SARS-CoV-2/COVID-19 pandemic. Only a minority changed their immunosuppressive treatment for fear of SARS-CoV-2 infection. Most patients reduced or did not practice any physical exercise during confinement. Although literature on patient-reported impact of the SARS-CoV-2 pandemic in rheumatic conditions is scarce, other authors report similar results about treatment discontinuation due to fear of being infected, worsening of health-related quality of life, anxiety and depression.

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ONLINE SUPPLEMENTARY DATA

IMPACTO DO CONFINAMENTO DEVIDO A PANDEMIA A SARS-COV-2/COVID-19 NOS DOENTES PORTUGUESES COM ARTRITE REUMATÓIDE

1. DADOS GERAIS

Idade
 Género
 Raça
 Distrito de residência

2. ARTRITE REUMATÓIDE

Há quantos anos se iniciaram os sintomas de artrite reumatóide? (<1 ano, 2-5 anos, 6-10 anos, 11-20 anos, >20 anos)

Desde o início do confinamento devido à pandemia a SARS-CoV-2/Covid-19, os sintomas da sua artrite reumatóide: (mantiveram-se iguais; melhoraram; pioraram ligeiramente; pioraram significativamente; não sabe/não responde).

Se na pergunta anterior respondeu que os sintomas pioraram, indique o que mais o(a) perturbou: (mais dor nas articulações; mais rigidez nas articulações; mais inchaço nas articulações; mais dificuldade de desempenhar as tarefas diárias; não sabe/não responde).

Se nas perguntas anteriores respondeu que os sintomas pioraram, qual considera ser a causa dessa pioria? (menor mobilidade devido ao confinamento; suspensão da prática regular de exercício físico; suspensão ou redução da medicação para a artrite reumatóide; maior stress, ansiedade ou sintomas depressivos; outra causa; não sabe/não responde).

Durante o período de confinamento devido à pandemia a SARS-CoV-2/Covid-19, teve contacto com o seu reumatologista assistente? (Não; sim, por via telefónica; sim, por e-mail; sim, consulta presencial; não sabe/não responde).

3. MEDICAÇÃO

Faz medicação regular para a sua artrite reumatóide? (não; sim, apenas corticóides e/ou anti-inflamatórios; sim, imunossuppressores convencionais (metotrexato [Ledertrexato], leflunomida [Arava], sulfassalazina [Salazopirina], hidroxicloroquina [Plaquinol]); sim, medicamentos biológicos (influximab, etanercept, adalimumab, golimumab, certolizumab-pegol, tocilizumab, abatacept, rituximab, anakinra) associados ou não a imunossupressão convencional; sim, inibidores da JAK cinase (tofacitinib [Xeljanz], baricitinib [Olumiant]); não sabe/não responde).

Durante o período de confinamento, suspendeu ou alterou a dose ou frequência da toma dos medicamentos para a artrite reumatóide? (sim; não; não sabe/não responde).

Se respondeu sim à questão anterior, qual o motivo? (Suspensão ou alteração da dose planeada pelo médico assistente; por serem imunossuppressores e aumentarem o risco de contrair infecção por SARS-CoV-2/Covid-19; por ter ocorrido um efeito adverso; por terem acabado as caixas de medicação e não ter novas receitas; para evitar deslocar-me à farmácia da comunidade/do hospital; por não ter dinheiro suficiente para comprar medicação; outro motivo; não sabe/não responde).

4. EMPREGO

Qual a sua situação laboral antes do confinamento devido à pandemia a SARS-CoV-2/Covid-19? (Estudante; Empregado; Desempregado; Reformado; De baixa; De Licença; não sabe/não responde)

Se respondeu “Empregado” na pergunta anterior, qual a sua situação laboral após o confinamento obrigatório decretado pelo Estado de Emergência? (Mantenho-me empregado; em regime de *lay-off*; desempregado; reformado; não sabe/não responde).

Se respondeu “Empregado” nas perguntas anteriores, qual o regime de trabalho que praticou durante o confinamento? (Presencial; Teletrabalho; Presencial alternando com teletrabalho; regime de assistência a filhos menores).

5. EXERCÍCIO FÍSICO

Antes do confinamento devido à pandemia a SARS-CoV-2/Covid-19, praticava exercício físico regular (pelo menos duas vezes por semana)? (Sim; não; não sabe/não responde).

Como caracteriza a sua prática de exercício físico durante o confinamento devido à pandemia a SARS-CoV-2/Covid-19? (Não pratiquei exercício físico; Reduzi a prática de exercício físico; Mantive a prática de exercício físico; Aumentei a prática de exercício físico; não sabe/não responde).

6. SAÚDE MENTAL

Durante o período de confinamento devido à pandemia a SARS-CoV-2/Covid-19, desenvolveu ou agravou sintomas de ansiedade (como tensão, sensação de medo, apreensão, inquietude, insónia ou sensação de ansiedade)? (Não; sim, ligeiros; sim, moderados; sim, intensos; não sabe/não responde).

Durante o período de confinamento devido à pandemia a SARS-CoV-2/Covid-19, desenvolveu ou agravou sintomas de depressão (ausência de prazer, tristeza, desânimo, choro frequente, lentificação do raciocínio, desinteresse no auto-cuidado e aspecto físico)? (Não; sim, ligeiros; sim, moderados; sim, intensos; não sabe/não responde).