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PERSPECTIVES IN RHEUMATOLOGY

Rheumatology and psychiatry: allies in times of COVID-19

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Abstract
The COVID-19 (coronavirus disease 2019) pandemic has had a significant global impact. Physical, emotional, and psychological health, particularly its specific mental health area, has been affected. Patients with rheumatic diseases are more likely to be concerned about COVID-19 than the public in general. Depression and anxiety are the symptoms most commonly reported by these patients. Therefore, now more than ever before, rheumatologists and psychiatrists should work together to improve the care of rheumatic disease patients, identifying the symptoms that uniquely reflect mental health problems, so the patients' quality of life can be substantially improved.

Keywords Coronavirus disease 2019 · COVID-19 · Mental health · Psychiatrists · Rheumatic diseases · Rheumatologists

The outbreak of coronavirus disease 2019 (COVID-19), caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), began in Wuhan, China, in the late 2019; since then, the disease has spread to practically all countries around the world, having been officially declared a global pandemic by the World Health Organization, on March 11, 2020 [1].

This pandemic has had a massive global impact, evident on the economic, political, and socio-cultural systems, and affecting the physical, emotional, and psychological health of the entire world society [2]. Social life is entirely disrupted: people are nearing their breaking points, standing on the verge of violating the constant isolation and quarantines imposed by local, national, and world health authorities. Health care systems, even in high-income countries, are overwhelmed, and the physical, emotional, and psychological health of people, directly or indirectly affected by COVID-19, has deteriorated significantly [3]. Political structures at the national and international levels are under substantial pressure. Globally, governments are making their best possible efforts to interrupt the virus' spread while at the same time minimizing its economic and social impacts on their countries and their inhabitants [4].

The current pandemic situation has also significantly disrupted the normal functioning of the regular health care systems and resources; the mental health departments have not been an exception. Treatment progress and outcomes are affected when patients are unable to interact with their mental health professionals like psychiatrists, psychologists, nurses, nurse practitioners, or physician assistants. The use of quarantine to maintain community health may not be comforting for psychiatric patients who are forced to renounce mental health care even as the need for it heightens [5, 6].

COVID-19 has caused those individuals either confirmed or suspected of having it, to experience fear of the consequences of an infection with a potentially fatal new virus, while those in quarantine might experience boredom, loneliness, frustration, and anger [7]. Moreover, in the early phase of the COVID-19 outbreak, a range of psychiatric morbidities, including persistent depression, anxiety, panic attacks,

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psychomotor excitement, psychotic symptoms, delirium, increased alcohol, and substance abuse [8], and even suicidality, were reported [9, 10].

Several studies have reported mental health problems among the general population during the COVID-19 pandemic; for example, Lei et al. in Chongqing, China, evaluated 1593 respondents and found the prevalence of anxiety and depression to be 8.3% and 14.6%, respectively [11]. Liang et al., also from China, found that 40.4% of 584 participants had psychological problems [12]. Another Chinese study by Zhou et al. reported the prevalence of depression, anxiety, and a combination of both to be 43.7%, 37.4%, and 31.3%, respectively in 8079 high school-age students [13]. Moreover, in the USA, the incidence of any psychiatric diagnosis in the 14 to 90 days after COVID-19 diagnosis in a group of 62,354 subjects was 18.1% (95% CI 17.6–18.6), including 5.8% (5.2–6.4) that were a first diagnosis. A psychiatric diagnosis in the previous year was associated with a higher incidence of COVID-19 diagnosis (relative risk 1.65, 95% CI 1.59–1.71; $p < 0.0001$) [14]. And in a cross-sectional study of 23,526 participants conducted in the general population of Peru, a third of the total showed depressive symptoms [15].

Pan et al. from the Netherlands reported that participants with underlying mental health disorders scored higher across validated scales for depressive symptoms, anxiety, worry, loneliness, and fear of COVID-19; these findings support the notion that people with psychiatric illnesses are more emotionally vulnerable during this crisis [16]. Also, the nature of the lockdowns imposed due to COVID-19, with non-emergent medical services being severely curtailed or altogether discontinued, has affected patients with rheumatic diseases like rheumatoid arthritis; these patients may feel increasingly isolated, unable to reach out to their physicians or support systems in a time of need; this situation results in greater stress with consequent worsening of existent mental health disorders, or the ensuing of new ones such as anxiety, posttraumatic stress disorder, or depression [17]. Furthermore, in a European study of 1800 patients with rheumatic diseases (ankylosing spondylitis/axial spondyloarthritis, fibromyalgia, gout, juvenile idiopathic arthritis, myositis, osteoarthritis, osteoporosis, peripheral spondyloarthritis, polymyalgia rheumatica, psoriatic arthritis, rheumatoid arthritis, synovitis, acne, pustulosis, hyperostosis and, osteitis, Sjögren's syndrome, systemic lupus erythematosus, systemic sclerosis, and vasculitis or arteritis), it was found that 57.3% had a high risk of anxiety whereas 45.9% had of depression, according to Hospital Anxiety and Depression Scale (HADS) [18]. Finally, an Egyptian case–control study of 360 participants that included 180 patients with rheumatic diseases and 180 healthy people showed a statistically significant difference ($p \leq 0.05$) between both groups regarding feeling angry/irritated, inferior, and insomniac; the 5-item Brief Symptom Rating Scale (BSRS-5) which was used to define a psychiatric case (according to the BSRS-5 scale) also differed significantly between patients and controls [19].

The COVID-19 pandemic has brought up major changes in rheumatology practice, especially in terms of treatment; for example, guidelines have proposed that clinicians should consider switching intravenous biologic DMARDs to subcutaneous forms to minimize face-to-face patient contact at the hospital or the infusion center [20]. Additionally, treatment adherence in patients with rheumatic diseases has been affected; fear of immunosuppression, lack of resources, and drug shortages have been recognized as some of the reasons behind these patients' poor adherence [21]. In this study, 2.2% of 500 patients discontinued autoimmune inflammatory treatment because of fear while 3.8% did it because of lack of resources or drug shortages [21].

Of great importance is the fact that rheumatic diseases are known to have a high association with psychiatric conditions such as depression and anxiety. In fact, high rates of these disorders have been reported in patients with various rheumatological conditions such as systemic lupus erythematosus (SLE) [22–24], rheumatoid arthritis (RA) [25], ankylosing spondylitis (AS) [26], and psoriatic arthritis (PsoA) [27]. O'Malley et al. [28], for example, studied 185 patients who had been referred to two hospital-based rheumatology clinics and a general medicine clinic in a US hospital and found that 40% of them had a psychiatric disorder as determined by the Primary Care Evaluation of Mental Disorders questionnaire. During this pandemic, Adnine et al. [29] have reported a high frequency of undiagnosed depression, anxiety, and insomnia symptoms in rheumatic disease patients being cared for in Morocco. Moreover, in a study conducted in Turkey, which included 771 patients with different rheumatic diseases, Seyahi et al. found that the majority of them were unwilling to keep their outpatient visits, and one-fifth skipped or stopped their immunosuppressive agents altogether [30].

Mental health disorders and rheumatic diseases share in common the production of pro-inflammatory cytokines such as TNF-a and IL-6 [31] so their co-occurrence has some pathophysiological basis. The neuropsychiatric manifestations/complications of COVID-19 are gradually being recognized but the full picture is yet to emerge. An association between viral infections and neuropsychiatric symptoms has been recognized in past pandemics, although causality and etiopathogenic mechanisms have not been clarified to date [32, 33]. Currently, various theories have emerged trying to explain the mechanism by which, for example, psychotic symptoms may appear in patients affected by COVID-19: whether these symptoms are the result of the direct invasion of the central nervous system by the virus, the systemic

immune response to the virus, or adverse reactions to drugs used against COVID-19, among others, have been postulated but not clearly established [34].

Evidence is emerging that the multi-organ injury observed in COVID-19 is a consequence of cytokine-induced endothelial dysfunction, or endotheliitis [35]. IL-6 causes endothelial activation and neutrophil infiltration, which results in nitric oxide-mediated changes to vascular permeability and loss of vascular tone [36]. This is reflected clinically by an increased neutrophil to T-cell lymphocyte ratio and the development of septic shock [37]. Endotheliitis could cause damage anywhere in the brain and in multiple brain locations simultaneously as well as in other organs [38–40]. Cytokines like IL-1 and IL-6 have been reported to be increased in patients with chronic psychotic disorders such as schizophrenia [41]; in one case of psychosis, IL-6 was found to be elevated in the cerebrospinal fluid (CSF) [42]. Given the relationship between elevated levels of cytokines in COVID-19 as well as in psychiatric and rheumatological disorders, immune/inflammatory pathways can be considered as one of the mechanisms involved in the mental health problems that occur during the course of this infection [41].

Moreover, it seems that patients with rheumatic diseases are more likely to be concerned about COVID-19 than other patients or the general population, despite their low risk of having a severe disease compared to patients with other diseases and/or predisposing factors. Data to this effect come from a study conducted in England, using the platform OpenSAFELY to explore factors associated with COVID-19-related death; it was found that autoimmune diseases like RA, SLE, and psoriasis were associated with a low risk of death (hazard ratio (HR) 1.30 (95% confidence interval (CI) 1.21–1.38)), compared to individuals aged 80 or older (HR 20.60 (95% CI 18.70–22.68)) [43]. Nevertheless, the number of patients with rheumatic diseases reporting suspected depression has increased significantly after the COVID-19 pandemic began, and these patients are also more likely to experience anxiety symptoms as well [44]. Factors like female gender, comorbidities, not working, having a lower educational level, using biological treatments, and poor quality of life have been found to be associated with both anxiety and self-isolation in a study conducted in Denmark [45]. In contrast, rheumatic disease diagnosis and disease-related variables had no effect on children's psychological status; furthermore, there were no differences in the hospital anxiety and depression scale and the state-trait anxiety inventory for children scale according to the rheumatic disease diagnosis and the type of physician in charge of treatment [46]. The resilience of these patients with a chronic disease could be an asset in adapting to this pandemic.

Rheumatologists do need psychiatrists' help to sharpen their skills in the detection and diagnosis of mental illnesses and to properly manage or refer patients who are suffering from complex mood and anxiety disorders [47]. Rheumatologists and psychiatrists should be readily available to collaborate with each other, to learn from each other, and to appropriately regulate the use of techniques (psychopharmacological and psychotherapeutic) from both specialties [47].

Rheumatologists and psychiatrists must work together to improve the patients' quality of life, especially during this pandemic which will certainly linger for many more months across the world. Therefore, it is recommended that physicians from both specialties should receive basic trained in both fields, so that rheumatologists can confidently identify the presence of anxiety and depression, treat them appropriately, and refer them when necessary. Both specialties should adopt a unifying sensory, emotional, and cognitive model for an adequate and well-integrated management of these patients.

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Declarations

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