

RHEUMATIC DISEASES AND COVID-19: A POSSIBLE ASSOCIATION

Marcos André Macedo do Vale Silva

<http://lattes.cnpq.br/0441854499145468>

Maria Vitória de Paiva Novaes

<https://lattes.cnpq.br/8693921284625232>

Clara Luísa Nunes Mota

<http://lattes.cnpq.br/4590569784146527>

Jéssika Mylleny Xavier dos Santos

<http://lattes.cnpq.br/4345840425063451>

Maria Clara Dias Coelho Menezes

<http://lattes.cnpq.br/2646237893795342>

Débora Martins Ramos

<https://lattes.cnpq.br/1663012760133102>

Gabriela Maria Souza Dias

<http://lattes.cnpq.br/0744973117908361>

Raysa Pereira de Sousa

<http://lattes.cnpq.br/0487726079659004>

Bruna Cardoso de Melo

<http://lattes.cnpq.br/7540412467401214>

Luiz Eduardo Gomes de Britto

<https://lattes.cnpq.br/6550399168403801>

João Lucas Soares Ferreira

<https://lattes.cnpq.br/1698779263889719>

Giovana Rocha Guida

<https://lattes.cnpq.br/4717694736416900>

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Abstract: Goal: To carry out the analysis and review of available articles on the relationship between Covid-19 and rheumatic diseases. **Bibliographic review:** The articles showed that there is a possible association between Covid-19 and the onset of rheumatic diseases. The association is associated with an exaggerated inflammatory response caused by viral replication. Furthermore, it was seen that evidence points to an increased risk of severe disease in rheumatopathies. However, the evidence is still scarce and there are few randomized clinical studies to prove the association. **Conclusion:** Although it is a possible association and with evidence and findings within the scientific literature, it is still not possible to say with certainty that there is an increase in the incidence of RD due to infection by the corona virus.

Keywords: Prostatic hyperplasia; inguinal hernia; association.

INTRODUCTION

In December 2019, a series of cases of severe pneumonia were reported in Wuhan City, capital of Hubei District, China. Soon after these notifications, investigations were initiated to identify the possible cause of this disease, identifying a new virus that was named “coronavirus disease 2019” or also called COVID-19 (AHN et al., 2020). Genetic analyzes have identified the new virus to be a close relative of another pathogen known as “severe acute respiratory syndrome virus” or SARS, an agent that caused outbreaks in Asia in 2002. This way, the new virus also became called “SARS CoV-2” (KADAM et al., 2021).

Some characteristics of this new virus made it a potential candidate for the outbreak of a new pandemic, which was later confirmed. Among these characteristics, it is mentioned the low virulence of the virus and the high capacity of transmission by the airways. In addition, the persistence of high viral loads for

long periods and the short interval between infection and the beginning of person-to-person transmission are factors potentiated by the large number of asymptomatic patients and the nonspecific symptoms associated with the disease, such as anosmia, fever and cough, which can be confused with other respiratory syndromes, such as colds (HU et al., 2021).

Since its first identification, SARS-CoV-2 has been the subject of great debate in the medical and scientific community, both because it is a new pathological entity, whose characteristics were not/are completely known, and because of the need to know its impact of disease in the human body. Over time, new complications, not necessarily associated with the respiratory system, were identified. Among these, there are cardiological, circulatory and even central nervous system complications (WHITE-DZURO et al., 2020).

One of the main complications associated with the new coronavirus was the possibility of triggering or exacerbating rheumatic diseases, due to possible dysfunctions of the immune system caused by the infection. Due to this, this review sought to elucidate the possible associations of COVID-19 and rheumatic diseases, evaluating the available scientific literature.

LITERATURE REVIEW

THE SARS-COV-2 VIRUS

The virus that causes Covid-19 is an enveloped, single-stranded RNA virus capable of infecting not only humans, but other animals, such as cats, dogs and bats, animals in which the virus is postulated to have developed. Its main consequence is a dysfunction in the respiratory system, however, gastrointestinal and neurological manifestations are common in the infection by the virus. Currently, dozens of strains are identified, which vary in pathogenicity, virulence and transmission capacity (WIERSINGA et al., 2020).

Infection occurs through contact with the viral particles with mucous membranes. This can be done through contact with viruses present in aerosols, droplets derived from sneezing and coughing or with those on surfaces. Studies have shown that the virus can be transmitted by an infected person over a space of up to 2 meters and greater distances, as well as wearing a mask dramatically decreases the chance of infection with the virus. Other forms of transmission, such as vertical transmission and blood transfusion, are less important and do not have a large space in the epidemiology of the disease (CHU et al., 2020).

IMMUNITY AGAINST CORONAVIRUS

Infection of host cells by the coronavirus is done in a way that is common to other viruses. Initially, the viral particles infect the cells of the nasal mucosa, bronchial epithelium and pneumocytes. The means of entry is through the binding of so-called spike proteins or S proteins, when in SARS-CoV-2 it has two subunits (S1 and S2), which the virus expresses on its surface and bind to specific receptors of these cells, leading to fusion of the viral envelope with the cell's plasma membrane and allowing the virus to enter the host. After the virus enters the cell, the protein machinery is hijacked and the viral replication cycle begins (SUNGNAK et al., 2020).

In the case of the coronavirus, the receptor used is the angiotensin 2 converting enzyme receptor, whose function is to regulate blood pressure within the Renin-Angiotensin System, being present in a wide variety of organs and systems, which, in part, it explains the wide variety of systems affected by the disease (KADAM et al., 2021).

After the initial phase, the virus starts to infect cells of the aveolar epithelium and the exacerbated replication provokes the immune

response characteristic of the virus infection. This immune response, mediated mainly by cells such as macrophages, neutrophils, and antibody-producing T cells, leads, through mediators of inflammation, such as interferons and tumor necrosis factors (TNF), to an exaggerated inflammatory response that effectively reduces the of viral replication, but causes intense cellular damage to the lung epithelium (HU et al., 2021).

Autopsy studies showed that patients who died due to the disease had intense alveolar necrosis, in addition to edema in the interstitium of the respiratory system. Other disorders are also seen, such as incorrect activation of the coagulation cascade in the endothelium, causing severe thrombotic events and diffuse intravascular coagulation. It is postulated that a large part of deaths are associated with an exacerbated and incorrect immune and cellular response, associated with secondary infections, whether bacterial or fungal (KLOK et al., 2020).

RHEUMATIC DISEASES

Rheumatic diseases are a heterogeneous group of diseases typically associated with musculoskeletal disorders with genetic, environmental or infectious origin. Regardless of the origin, these diseases are based on autoimmune disorders that cause damage to parts of the locomotor system, including joints, bones, cartilage, tendons and ligaments. However, other organs and systems such as eyes, lungs, kidneys and heart may be involved within these diseases (MARUOTTI; CORRADO; CANTATORE, 2014).

There are more than a hundred diseases identified, but the main ones are osteoarthritis, fibromyalgia, osteoporosis, gout, tendinitis, rheumatic fever, rheumatoid arthritis and other pathologies, such as spondylitis, which affect the spine. joint pain and swelling, difficulty moving, joint

stiffness when waking up and limitation of activities, and these diseases, according to the WHO, are one of the most impacting on the productive capacity of people in the world. The diagnosis can be made by a doctor generalist or rheumatologist. Unlike what is commonly said, these diseases do not affect only elderly people, but also people of all ages, however, being more common in women, due to a greater genetic predisposition in this sex (WEINER, 2019).

The treatment is varied and can be done either with anti-inflammatory drugs or with immunosuppressive drugs, generally associating both. Corticosteroids are first-line drugs and, when they do not have contraindications, are usually prescribed to patients who are still in the early stages of the disease. Other more specific drugs are used, such as TNF-alpha blockers, disease-modifying antirheumatic drugs (Dmards) and methotrexate (WEINER, 2019).

PRESENCE OF RHEUMATIC DISEASES IN PATIENTS WITH COVID-19

With the increase in the notification of coronavirus infections, it was seen that there was also an increase in the report of autoimmune diseases concomitant to the Covid-19 infection. Rheumatic diseases seem to be one of the most common manifestations associated with coronavirus infection, however, the presence of other pathologies associated with inflammatory mediators, such as systemic lupus erythematosus and psoriasis, is notorious.

The first bulletins on Covid-19 from China do not mention the presence of rheumatic manifestations in patients (CHINA, 2020). Subsequent studies started to show the presence of small numbers of patients with both conditions, with a December 2019 study, which reported 2 cases of rheumatism in a cohort of 1099 patients (GUAN et al., 2020).

Another American study reported 21 patients admitted to intensive care centers. However, it was pointed out that 4 patients had rheumatopathies, however 3 were already using immunosuppressive therapy and one already had a preexisting rheumatic condition. Thus, it was hypothesized that a considerable number of diagnoses may be associated with rheumatological conditions not previously identified, in ineffective or non-optimized treatment (ARENTZ et al., 2020).

A Korean study looked at 24,117 newly diagnosed patients with rheumatoid arthritis. It was calculated that for every 1% increase in the number of patients infected with coronavirus, there is a 9.2% increase in the incidence of rheumatoid arthritis in the analyzed sample. However, the specific molecular mechanism, or whether there is any degree of immune cross-reaction between viral antigens and human cells, is not known, necessitating further investigations (JOO et al., 2019).

Other rheumatic syndromes, such as Kawasaki syndrome, have been reported to be associated with SARS-CoV-2 infection. In one report, 8 children were identified with a combination of rash, conjunctivitis, peripheral edema, pain in the extremities, and severe gastrointestinal symptoms, similar to a classic Kawasaki picture. It has been suggested that the association with the coronavirus may be due to the triggering of a severe hyperinflammatory reaction, however, the association is still diffuse and without direct evidence (RIPHAGEN et al., 2020).

RHEUMATIC SYNDROMES AND THE RISK OF SERIOUS ILLNESS

At the beginning of the pandemic by the new coronavirus, there was much debate about the possibility of patients with some type of disorder of the autoimmune system having a more severe infection or a course of

the disease less favorable to survival. Some of the factors associated with this statement is the presence of comorbidities in these patients together with the use of immunosuppressants to control the underlying disease. However, few conclusions can be drawn (STRADNER et al., 2020).

The increased risk has been evaluated by several studies. A study based on health service databases in England, with a sample of more than 17 million patients, found an increased risk of death in patients with rheumatic diseases, lupus and psoriasis. These findings were constant when considering age, sex and ethnicity. However, the impossibility of further clinical evaluation limits this statement, since due to the high heterogeneity of RD - mainly regarding severity and comorbidities - and not evaluation regarding the use of anti-rheumatic medications, are factors that reduce the impact of these findings (WILLIAMSON et al., 2020).

In contrast, a European study evaluated 1525 RD patients diagnosed with Covid-19. It was found, from the comparison of 117 cases and a control group, that there was no significant difference in the survival of both groups (FREDI et al., 2020). Another American study compared patients with some type of autoimmune disease, including RDs, with control patients without these diseases. Although laboratory tests had similar values, patients with RDs were more likely to need mechanical ventilation, which did not mean an increase in mortality in this group compared to the control group (D'SILVA et al., 2020).

A cohort carried out in the city of Wuhan, on the other hand, found a lower probability of mechanical ventilation in patients and mortality among patients affected by RD, pointing out that other factors may underlie the difference in evolution of the cases studied. Some authors have already raised

the possibility that other factors are involved in the difference in morbidity and disease course seen in these patients. The presence of comorbidity, the degree of disease activity and the use of drugs to control the syndromes are raised as factors as or more important than the presence of RD. Even the population discrepancy and the ability to meet the demands of health systems are possible variables to be taken into account (YE et al., 2020; ZHAO et al., 2021).

CONCLUSION

It is observed, according to the analyzed works, that the association of rheumatic diseases and Covid-19 is possible and has evidence within the scientific literature. However, despite this, evidence is scarce and without the possibility of confirmation, due to the absence of many randomized clinical trials associated with the topic. Furthermore, it was not possible to find any explanations leading to the pathophysiological nature of the association, speculating, however, the association of an inflammatory hyperreactivity and the triggering of the autoimmune process. It is also mentioned that rheumatoid diseases are only a part of the large group of autoimmune diseases and the non-association of SARS-CoV-2 with it does not exclude the possibility of other correlations.

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