Relationship between SARS-CoV2 infection and the development of chronic non-communicable diseases

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ABSTRACT
COVID-19, a disease triggered by the SARS-CoV-2 coronavirus, emerged in Wahuan and became a global pandemic abruptly, causing great tensions around the world. The composition of the virus is based on a single-stranded RNA viral structure that uses the spike protein (S-spike) to bind to the ECA2 receptor in human cells. Symptoms can range from mild, moderate or severe symptoms and infection can lead to systemic complications and chronic sequelae. In addition, the disease can be classified into asymptomatic, acute, subacute, and post-covid syndrome when symptoms persist for more than 12 weeks. Sequelae can include heart, lung, neurological and renal problems, which can affect the quality of life of infected patients. The prognosis is motivated by the severity of the infection and the pre-existing health status. Preventive measures such as strict hygiene, social distancing, mask-wearing and vaccination are of utmost importance to mitigate the spread of the virus. However, long-term medical follow-up is necessary to monitor and treat complications arising from the infection.

Keywords: Sequelae, COVID-19, Inflammation, Exacerbated, Comorbidities, Chronic non-communicable diseases.

1 INTRODUCTION

COVID-19 is a disease caused by the SARS-CoV-2 coronavirus, which can lead to mild, moderate or severe symptoms. In addition, SARS-CoV-2 infection can lead to various sequelae, such as heart, lung, neurological and renal problems, which can affect the quality of life of infected patients (FORTUNATO et al., 2021).

The advance in the disease was alarming. The number of cases computed in Brazil, until 03/25/2023, was 37,258,663 cases with a number of deaths of 700,229 (BRASIL, 2023).

Individuals who have contracted the virus can present the disease in different forms such as mild, moderate and severe. The latter is related to sequelae of the disease. In addition, the disease can be classified into asymptomatic, acute, subacute, and post-covid syndrome when symptoms persist for more than 12 weeks. Patients have some more common symptoms such as cough, sore throat, pyrexia, rhinorrhea, anosmia, ageusia, nausea, vomiting, diarrhea, fatigue, hyporexia, dyspnea, among others (SOARES et al., 2021).

The pathophysiology of COVID-19 occurs mainly by two mechanisms: direct, which is the entry by the ECA-2 receptor that is present in many organs and systems such as blood, endothelium, eyes, kidneys, gastrointestinal system, vascular system, heart and airways, mainly of type II alveolar cells; and indirect by the systemic inflammation that activates the immune system leading to a "cytokine storm" (ALMEIDA et al., 2021).

According to the World Health Organization (WHO), there is still much to be discovered about COVID-19 and the best forms of prevention and treatment. The WHO states that ongoing research is needed to fully understand the disease and develop effective solutions. It is crucial that patients recovered from COVID-19 are monitored long-term by healthcare professionals in order to identify and treat any future complications. As stated by the WHO, COVID-19 is a new disease and we are still learning about the long-term effects of infection. Those who have recovered from COVID-19 should be closely monitored to assess possible long-term sequelae and provide appropriate treatment (WHO, 2021).

2 COVID-19 AND ITS AFTERMATH

2.1 THE HISTORY OF COVID-19

The year 2019 brought as a milestone a huge change to the lives of human beings. Since the start of the pandemic in Wuhan, China, with the pandemic signaling in March 2020, a new era of isolation and social distancing from family and friends began. In December 2020, the first vaccination campaigns began in some countries. However, social distancing and general hygiene measures continue to be used by some people to this day (MARINO *et al.,* 2021).

In February 2003, 305 cases of Severe Acute Respiratory Syndrome (SARS) were recorded. However, the first reports of the severe disease occurred in 2002 in southern China in Guangdong. The Chinese Ministry of Health came to the conclusion that it was an outbreak of unknown and atypical pneumonia that spread mainly among health personnel, who transmitted it in their homes. This syndrome has also affected other countries such as Canada, Vietnam, Hong Kong, and Singapore (XAVIER *et al.,* 2020).

Due to its spread, an international mobilization began to find the etiological agent of this infection. In 2003 in the United States of America (USA) and Hong Kong had already observed a new

virus, different from the other organisms of the group that causes diseases in humans. In April of that same year, the WHO proposed a global surveillance system to prevent international spread. The tests used in the identification of this new causal agent were: polymerase chain reaction (PCR) studies, cell culture and electron microscopy (XAVIER *et al.,* 2020).

In 2019, China reported the appearance of new cases of pneumonia of unknown etiology in the city of Wuhan in Hubei province. However, it was not until January 2020 that a new coronavirus was identified in China, which was later named SARS-CoV-2. Theories are that the first cases of COVID-19 appeared at a seafood market in Wuhan, where several people buying goods were infected. The infection is zoonotic, but the spread of cases was due to human interactions, and this transmission can occur even in asymptomatic individuals (XAVIER *et al.,* 2020; MARTIN *et al.,* 2020).

The novel coronavirus falls into the order Nidovirales, family Coronaviridae, subfamily Orthocoronavirinae. It received the designation of severe acute respiratory syndrome – coronavirus-2 (SARS-CoV-2) by the *International Committee on Taxonomy of Viruses* (ICTV), because it is very similar to another species of coronavirus that almost became a pandemic in 2002, SARS-CoV. It was declared as COVID-19 (coronavirus disease) in February 2020 by the World Health Organization (WHO) (XAVIER *et al.,* ., 2020).

In short, the first symptoms reported to WHO were in December 2019. In March 2020, a global pandemic state was decreed and until December 2020 vaccination and social isolation campaigns began. The disease has spread worldwide. In Brazil, reports of the first case of the disease were confirmed on February 26, 2020 and the first death occurred on March 16 of the same year (MARTIN *et al.,* 2020; Marino *et al.,* 2021). As of March 28, 2023, 13,331,975,343 vaccine doses have been administered (WHO, 2023).

2.2 STRUCTURE AND VIRAL REPLICATION

Since the 60s, a recombination of coronavirus that only reached animals has resulted in outbreaks of infection in humans. It is known, so far, that there are 7 (seven) different strains known. All human coronaviruses are of animal origin, and this recombination probably occurred in bats (CARVALHO *et al.,* 2021).

According to Carvalho et al. (2021), SARS-CoV-2 has a much higher rate of spread than SARS-CoV and MERS-CoV, these three strains are the ones that cause most severe cases of the disease. Coronaviruses (CoVs) contain a positive-sense single-stranded RNA genome, with an extension that can reach 32 kilobases (Kb). They are enveloped viruses and can have pleomorphic capsids and have radial surface projections that look like a corona, hence the name coronavirus (ZHU *et al.,* 2020).

The viruses responsible for the diseases need the cellular machinery to produce their new viral particles. In this way, they need viral replication to survive. These viruses have developed proteins that make them capable of infecting other beings (MARTIN *et al.,* 2020).

The process of viral replication is summarized in the transcription and initial translation of genomic RNA, dependent on the RNA of the host, an enzyme replicasse viral follows completely transcribing a strand of negative simple RNA that will serve as a model for the transcription of subgenomic messenger RNA. The latter will be used to encode new proteins. COVID-19 is a pathology caused by the SARS-CoV-2 virus, which can have mild to moderate or severe symptoms and can affect the quality of life of infected individuals. Consequently, there are several sequelae that can occur (ALMEIDA *et al.,* 2020).

SARS-CoV-2 has unique characteristics that set it apart from its ancestors. These characteristics are in the most diverse post-replication nucleotypes. This is a specific feature of RNA viruses. With each replication, they have the chance to slightly modify its structure and virulence, arriving at the result and characteristic of this virus of having a unique and complex infection capacity (ALMEIDA *et al.,* 2020).

2.3 EPIDEMIOLOGY

The pandemic is a spread of a new disease, on an international scale, attacking almost all individuals from different regions, being related to geographical affect and not related to clinical severity (ÁVILA; 2020).

In just six months, 216 countries have been hit. The most affected was the United States, surpassing the numbers of infected and deaths. On 06/22/2020, there were 119,923 deaths and 2,275,645 contaminated. Worldwide, on the same date, there were 8,860,331 cases and 465,740 deaths (MARTIN *et al.,* 2020).

According to the World Health Organization (WHO, 2023), data as of March 29, 2023, record 761,402,282 confirmed cases of COVID-19 and 6,887,000 deaths reported to WHO. As of March 28, 2023, 13,331,975,343 doses of vaccine have been administered.

The computed number of cases in Brazil, until 03/25/2023, was 37,258,663 cases with a number of deaths of 700,229, reaching, at that moment, a mortality rate of 333.2 per 100 thousand inhabitants (BRASIL, 2023).

According to the study by Malta *et al.* (2021), during the pandemic there was a reduction in the practice of physical activity and the consumption of vegetables; increase in the time of use of television and computer/tablet; increased consumption of frozen, snacks and chocolate; people with at least one CNCD had a smaller increase in alcohol consumption compared to those who do not have NCDs.

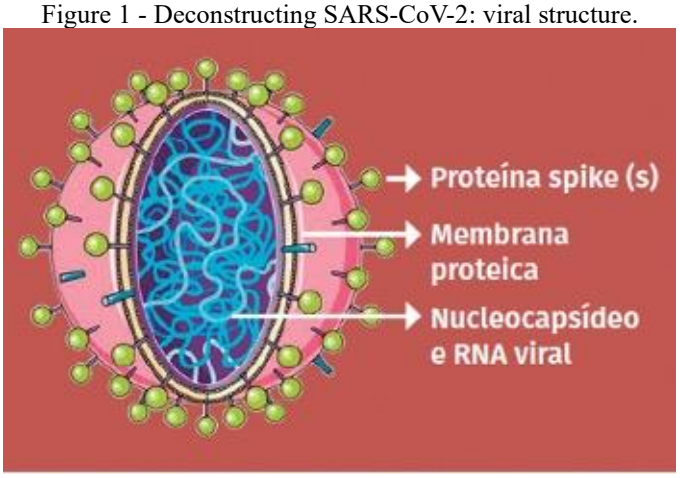
High mortality rates and the lower number of recovered individuals were associated with low schooling, black/brown class and residents of municipalities with lower MHDI (Human Development Index of the municipality) (BRASIL, 2023). However, mortality is also directly related to the clinical picture of the patient and the pathophysiological mechanism of the disease.

2.4 PATHOPHYSIOLOGY

SARS-CoV-2 infection in the host cell occurs through the spike protein (*S-spike*) as we can see in Figure 01, which has two subunits S1 and S2 present in the viral membrane, which binds to the angiotensin-converting enzyme II (ACE-2) being bound to the membrane of the target cell. Thus, its soluble portion in the blood is very low and is present in various tissues such as endothelium, eyes, kidneys, gastrointestinal system, vasculature, heart and airways, mainly of type II alveolar cells (CARVALHO *et al.,* 2021; CARNAÚBA, 2021).

The onset of this viral replication can be by two mechanisms: cleavage of the spike protein in the membrane or endocytosis. After this initial contact, viral replication begins in the infected cell. The pathogenesis of the coronavirus depends on which tissue will be affected by the virus (CARNAÚBA, 2021).

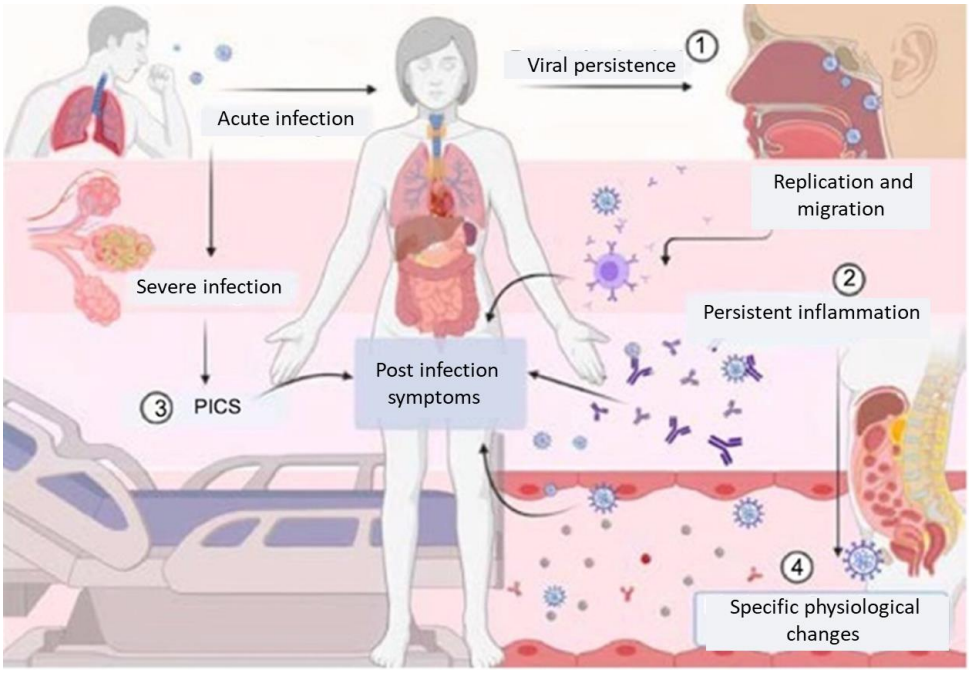
Figure 1 - Deconstructing SARS-CoV-2: viral structure.



Source: Bonjorno *et al.* (2020, p. 07)

The ECA-2 enzyme has many functions, being mainly related to the renin-angiotensin system (RAS), which is a hormonal mechanism, which converts angiotensin I to angiotensin II. The ACE-2, within this system, converts from angiotensin II, a vasoconstrictor peptide, to angiotensin, a vasodilator peptide, whose effect leads to antagonize angiotensin II. enzyme ECA-2, result of an increase in the effect of angiotensin II, thus occurs greater vasoconstriction, production of aldosterone, oxidative stress, inflammation, thrombogenesis and arteriogenesis (AGONDI; AUN; GIAVINA-BIANCHI, 2020; SALHA, 2022). As can be seen in Figure 02 the pathophysiology of COVID-19, which is directly related to the chronic consequences of the disease.

Figure 2 - Pathophysiological mechanisms for the development of post-COVID-19 symptoms. Pathophysiological mechanisms for the development of post-COVID symptoms. 1. The viral persistence found in PCR tests indicates viral replication, which can generate a persistent inflammatory response, promoting the development of symptoms. 2. High levels of inflammatory and angiogenic cytokines have been found, potentially causing post-COVID symptoms. 3. The pathophysiological changes caused by COVID-19 cause structural changes that can lead to system-specific post-COVID symptoms and persistence of the inflammatory response. 4. Severe COVID-19 as an initial disease implies the use of invasive supportive measures, which can lead to the development of PICS, with persistence of symptoms beyond critical illness.



Adapted: Gutiérrez *et al.* (2021, p. 425).

2.5 CLINICAL ASPECTS

COVID-19 has many signs and symptoms varying in infected individuals, and may be asymptomatic and transmit the disease, or have mild, moderate or severe symptoms. Most common symptoms are cough, sore throat, rhinorrhea, pyrexia, rhinorrhea, anosmia, ageusia, disorders, nausea, vomiting, diarrhea, fatigue, hyporexia, and dyspnea (SOARES *et al.,* 2021).

According to the Ministry of Health (2020), patients with severe disease usually have signs and symptoms of viral pneumonia and can progress to situations of Acute Respiratory Distress Syndrome (ARDS), acute heart failure, acute kidney injury, about infection, sepsis or shock.

According to Gutiérrez *et al.* (2021), infection can be classified by the persistence of signs and symptoms in acute: up to 4 weeks; subacute 4-12 weeks; and post-COVID-19 syndrome more than 12 weeks.

Treatment of post-COVID-19 syndrome is multifaceted and should address each patient's individual symptoms. Some treatments may include medications, occupational therapy, and physical therapy to help restore lung and cardiovascular function, as well as relieve symptoms of fatigue and pain. It is important for people who experience these symptoms after recovering from COVID-19 to consult a healthcare professional to get an accurate diagnosis and a proper treatment plan (SIVAN *et al.,* 2021).

According to Melo *et al.* (2019), we can cite five diseases as being the main NCDs: Cardiovascular Diseases (Such as Systemic Arterial Hypertension), Neurovascular Diseases, Chronic Lung Diseases, Diabetes Mellitus and Cancer.

2.6 PROGNOSIS

Lung damage and sequelae will depend on the severity of the disease. They present more frequently in the elderly, but the rate of young people has been increasing due to pneumonia associated with low immunity (LIMA *et al.,* 2021).

In the study by Franco *et al.* (2021), a digital survey was conducted in which 95 participants were counted. The sequelae recorded in this study were found mainly in patients with some comorbidity (61% of the sample).

Several authors have mentioned in their works cases of sequelae and morbidity and mortality after COVID-19 linked to patients who have some comorbidity (diabetes and hypertension, for example) or to cases of hospitalization and complications of the disease (BRAZÃO; NOBREGA, 2021; CARVALHO *et al.,* 2021; CASTRO *et al.,* 2021; ESTRELA *et al.,* 2021; LIMA *et al.,* 2021).

In Brazil, the prognosis remains disproportionate with a mortality rate of around 333.2 per 100,000 inhabitants. Higher mortality rates are observed in patients with low socioeconomic factors and low education (BRASIL, 2023).

2.7 PREVENTION

Contamination by the virus occurs through droplets breathed in close contact. It is very important to note that asymptomatic person is able to transmit the virus. To avoid contamination, some actions should be taken such as asepsis of the hands with soap or alcohol 70% frequently, avoid bringing the hands to the face, use of disposable and non-handmade masks, social isolation when sick. When sneezing or coughing, cover mouth and nose (SOARES *et al.,* 2021).

In addition, pandemic control measures, such as social distancing, can lead to a more sedentary lifestyle and a less healthy diet, which can further increase the risk of developing chronic non-communicable diseases (MORAIS *et al.,* 2022).

The risk depends on factors such as the severity of the infection, the age and previous health conditions of the individual. It is important that patients recovering from COVID-19 are regularly followed up by a healthcare professional to monitor and treat any possible long-term complications (GRAÇA *et al.,* 2020).

2.8 CHRONIC SEQUELAE OF COVID-19

2.8.1 COVID-19 and its relationship to nervous system damage

To better understand the sequelae of COVID-19, it is of fundamental importance to understand how SARS-CoV-2 causes neurological pathology and manifestations.

According to Costa and Silva-Pinto (2020), it is not yet known for sure the mechanism by which this virus reaches the central nervous system (CNS). Theories that stand out are that the virus is transmitted through hematogenous and transsynaptic pathways by infected neurons (olfactory bulb, for example).

Regarding the body's responses to COVID, Gomes, Medeiros Filho and Sousa (2020) state that "[...] In severe forms the resulting inflammatory response can lead to a 'cytokine storm', in which increased serum cytokine levels occur."

Regarding what the same authors expose, we arrive at one of the causes of central nervous system injury. Endothelial cells can be destroyed by inflammatory cytokines, and this can result in hypercoagulation and vascular problems in the brain. Meningitis, encephalitis, encephalopathy, and stroke are neurological diseases that have been linked to infection.

Neuroinflammation, due to inflammatory cytokines, can lead to several modifications in the central nervous system: activation of microglia (CNS immune cells that also release cytokines); changes in neuroplasticity; changes in neurotransmitter metabolism; dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis; and structural and functional changes in the brain. These effects may later lead to neurodegenerative diseases (ACCORSI *et al.,* 2020).

Neuronal pathogenicity is directly linked to the neuroinvasive properties of the virus. ECA-2 enzymes were found in the central nervous system. It is known that SARS-CoV-2 has the ability to bind to ACE-2, which shows us that the pathogenicity in this case is due to this binding in the CNS (GOMES; MEDEIROS FILHO; SOUSA, 2020).

The main neurological symptoms presented by patients affected by COVID-19 are headache, disturbances of consciousness, paresthesia, anosmia and dysgeusia (SILVA *et al.,* 2020). The manifestations found in the studies by Nunes *et al.* (2020) include dizziness, headache, myalgias, hypogeusia, hyposmia, and less common disorders including polyneuropathy, myositis, cerebrovascular diseases, and encephalitis.

Even though the neurological sequelae are still in the study phase, scientists point out that these problems stem from physical damage caused to the neurons themselves and from psychological damage brought on by social distancing and the pandemic. Changes in taste and smell, for example, may be irreversible and are related to the injury caused directly to the primary sensory neurons (LOPES; ABREU, 2021).

People reported feeling exhausted or fatigued, with concentration problems ("brain fog"), anosmia or ageusia, dizziness, tachycardia, palpitations, dyspnea, cough, mood disorders such as depression and/or anxiety, and other sequelae unrelated to the nervous system. What explains these sequelae would be the sum of aggravating factors in the affected patients. Studies report that this post-COVID-19 picture resembles immune system and autonomic nervous system dysregulation syndromes, in addition to aggravating factors found, such as malnutrition found in some post-COVID-19 patients (CASTRO et al., *2021).*

Also according to Castro *et al.* (2021)., the presence of dysregulation of beta-2 receptors and the acetylcholine M3 receptor was identified. This is due to autoantibodies against these receptors. This explains the reported mental fatigue and difficulty concentrating. May result from reduced cerebral blood flow due to excessive sympathetic vasoconstriction in the presence of dysfunctional beta-2 receptors.

2.8.2 COVID-19 and its relationship with damage to the Cardiac System

It is widely known that COVID-19 infection can cause changes in the cardiovascular system. The virus can directly affect myocardial cells and indirectly increase the inflammatory response, which can lead to activation of the immune system and elevated concentrations of lymphocytes and cytokines. These changes can result in significant impacts on the cardiovascular system (COSTA, 2020).

The enzyme ECA-2 is found in the cardiac system and plays a key role in regulating hormonal balance. According to Pecho-Silva *et al.* (2020), ACE-2 is involved in the renin angiotensin aldosterone system, which can lead to a hormonal imbalance. Normally, ACE-2 helps decrease the renin angiotensin aldosterone system by converting angiotensin II to angiotensin I, which is a vasodilator. However, when infected, this balance is affected, leading to increased angiotensin II and, consequently, vasoconstriction. This imbalance can also lead to decreased fibrinogen, increasing the chances of flat ruptures.

All this inflammation leads to a greater oxidative stress and increased metabolism, hindering the gas exchange of cells, having a difficulty pumping in the carotion (GUTIÉRREZ *et al.,* 2021).

Patients who have cardiovascular comorbidities, such as coronary vascular disease (CVD) and high blood pressure, have worse prognoses when infected with COVID-19, as these patients have higher levels of ACE-2. In addition, individuals belonging to other risk groups, such as those of advanced age, carriers of diabetes and cancer, also have worse prognoses when infected by the virus (MELO and MELO, 2023).

2.8.3 COVID-19 and its relationship to damage to the respiratory system

The main function of the respiratory system is the proper gas exchange of oxygen and carbon dioxide between the body and the external environment. When it comes into contact with SARS-CoV-2, an inflammatory process begins in the lung, which can reach other areas of the body, causing numerous problems and subsequent sequelae after infection (LIMA *et al.,* 2021).

Lung injury is the result of the inflammatory process (which begins in the lung). This inflammatory process leads to lung destruction and results in pulmonary remodeling with fibrosis. Fibrosis is a chronic and aggressive process (SILVA, 2021).

What should happen is a recovery of this lung infected by pneumocyte type 2 (PNC2) cells. These cells are the ones that give rise to type 1 pneumocytes (PNC1), which produce surfactant and prevent lung collapse. What happens is that these PNC2 have a higher amount of ACE-2, and are then attacked in greater numbers (LIMA *et al.,* 2021).

It is common for several of the pulmonary symptoms to linger for weeks. This is due to severe hypoxemia, lung injury and respiratory muscle dysfunction as a consequence of cardiopulmonary dysfunctions. Thus, decreasing the tolerance of patients to perform their activities of daily living (SILVA *et al.,* 2022).

2.8.4 COVID-19 and its relationship with damage to the gastrointestinal and hepatobiliary systems

The virus has the ability to infect the gut microbiota. There are receptors of ACE-2 in intestinal epithelial cells and lymphocytes, that is, the virus infiltrates and generates intestinal dysbiosis, which can generate some of the symptoms, anorexia, nausea, dyspepsia, abdominal pain and diarrhea (GUTIÉRREZ *et al.,* 2021).

The gut microbiota is strongly linked to the immune system, generating an immune response by releasing high amounts of inflammatory factors, triggering injury to the gastrointestinal system. Patients with COVID-19 may present hypoxia, resulting in an imbalance in oxygen supply, thus occurring an alteration of intestinal homeostasis, causing loss of integrity of the intestinal epithelium barrier (MORAIS *et al.,* 2021).

There is a gut-lung axis, the virus attacks the pulmonary ECA-2 receptors being then released and through the mucociliary movement goes to the gastrointestinal system, there changes the absorption of some essential amino acids such as tryptophan generating an intestinal dysbiosis (OLIVEIRA *et al.,* 2022).

Another important point to be addressed is that during the infection in most patients was used antibiotics and steroids indiscriminately as a consequence occurs an alteration of the intestinal microbiota (NECOCHEA, 2022).

The hepatic system has high expression of ACE-2, occurring the entry of SARS-CoV-2 in the cells, but the lesion of the hepatic system has not yet been very well elucidated, believed to be multifactorial, such as use of medications, cytokine storm and the entry of the virus into the cells, occurring a metabolic increase and damaging the system (LIMA, 2020).

2.8.5 COVID-19 and its relationship with Rheumatic Diseases

COVID-19 infection generates a large systemic inflammation activating the immune system. The first line of defense is the innate immune system, which generates the so-called cytokine storm, which helps fight the antigen/virus. The main cytokines and chemokines involved are IL-1β, IL-2, IL-6, IL-7, IL-10, TNF and interferon gamma. This high amount of immune response can cause damage to the body's cells. In this sense, the activation of the complement system occurs, mediating dendritic cells, neutrophils and monocytes until there is the collaboration of the adaptive immune system (BONJORNO *et al.,* 2020; FIGUEIREDO *et al.,* 2021).

When activated, adaptive immunity triggers the production of B lymphocytes, which in turn give rise to plasma cells, cells responsible for producing specific antibodies against antigens. However, in some situations, this response can be misdirected, leading to the emergence of autoimmune diseases (CICHELERO and FRAPORTI, 2022).

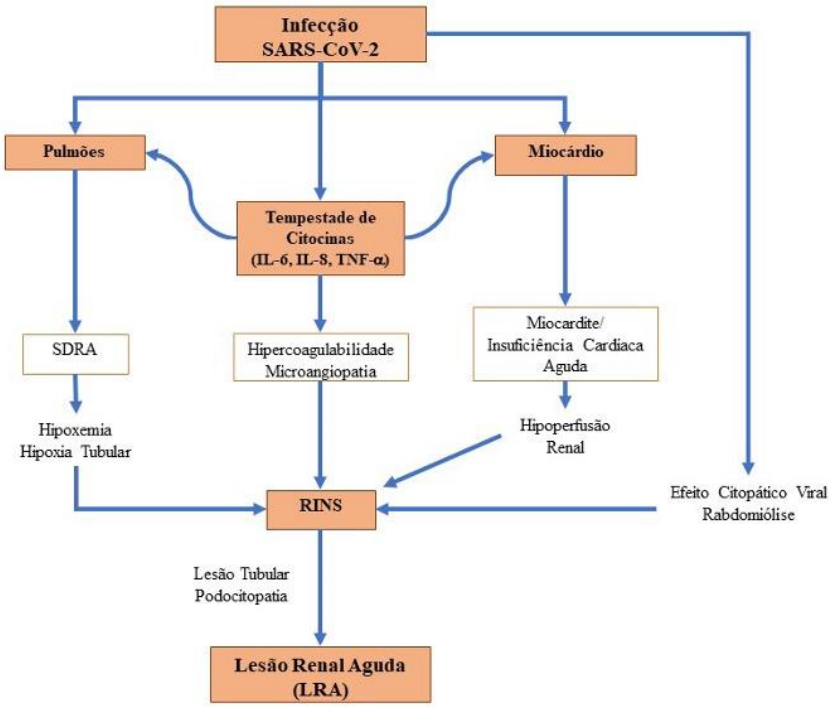
According to Benites, Bagio and Filho (2023), the following diseases were found in descending order: reactive arthritis, Systemic Lupus Erythematosus (SLE), Rheumatoid Arthritis (RA), Adult Still's Disease (ASD), dermatomyositis, large cell arteritis, microscopic polyangiitis, systemic sclerosis and acute gout crisis.

2.8.6 COVID-19 and its relationship with damage to the Renal System

According to a study by Hirsch et al. (2020), patients with COVID-19 are at a high risk of developing kidney complications, including acute kidney injury and proteinuria, even in the absence of pre-existing kidney disease.

SARS-CoV-2 infection can result in acute kidney injury as shown in Figure 03, affecting podocytes, proximal tubular cells, and endothelial cells. This lesion can occur by direct mechanisms in the renal cells, as well as by deposits of immune complexes, as well as indirect mechanisms, such as the cytokine storm generated by the immune system, which can lead to renal hypoperfusion. Additionally, pharmacological neurotoxicity may also contribute to the development of kidney injury in patients with COVID-19. Therefore, it is possible to perceive that kidney injury in patients with COVID-19 is multifactorial and complex, involving several pathophysiological mechanisms, as can be seen in Figure 03 (PECLY et al., 2020).

Figure 3 - Pathophysiology of acute kidney injury in SARS-CoV-2 infection. Brief schematization and summary of the main aspects related to the pathophysiology of AKI in patients with COVID-19.



Source: Pecly et al. (2021, p. 558).

2.8.7 COVID-19 and its relationship to endocrine damage

Several factors may be involved in the complications of the endocrine system, such as direct damage to the beta cells of the pancreas due to the expression of ACE-2, resulting in diabetes mellitus, or the possibility of bone demineralization in individuals who have made prolonged use of corticosteroids (BRAZÃO; NOBREGA, 2021; SERNA et al., 2023).

Subacute thyroiditis with thyrotoxicosis, bone demineralization and the onset of diabetes mellitus have been reported as endocrinological consequences. Systemic inflammation, prolonged immobilization, corticosteroid exposure, or vitamin D deficiency may lead to bone demineralization (BREASON; NOBREGA, 2021).

According to D'caminha *et al.* (2022), COVID-19 has directly impacted the decrease in hospitalizations for NCDs in all Brazilian states and in other countries. This was a result of the overload of the Unified Health System in Brazil due to hospitalizations for infected people and social isolation itself. So those pandemic years have been bad for public health control of chronic diseases.

REFERENCES

ACCORSI, Daniela Xavier *et al.* COVID-19 e o Sistema Nervoso Central. Ulakes Journal Of Medicine, São José do Rio Preto, Sp, Brasil, v. 1, p. 81-87, 2020.

AGONDI, Rosana C.; AUN Vivolo, Marcelo; GIAVINA-BIANCHI Pedro. COVID-19, enzima conversora da angiotensina 2 e hidroxicloroquina. Arq Asma Alerg Imunol. 2020;4(1):138-140. Recuperado de: http://aaai-asbai.org.br/detalhe_artigo.asp?id=1075

ALMEIDA, Aline de Souza *et al,* A Fisiopatologia da COVID-19 e o Papel da Fisioterapia Respiratória: Revisão Sistemática. Revista da Faculdade de Ciências Médicas de Sorocaba, v. 23, n. 3, p. 129-138, 2021.

ALMEIDA, Juliana O. de *et al.* COVID-19: fisiopatologia e alvos para intervenção terapêutica. Revista Virtual de Quimica, Rio de Janeiro, v. 12, n. 6, set. 2020.

ÁVILA DE TOMÁS, José. Francisco. CORONAVIRUS COVID-19; PATOGENIA, PREVENCIÓN Y TRATAMIENTO. Disponível em: <https://ebevidencia.com/wp-content/uploads/2020/03/CORONAVIRUS-COVID-19-4%C3%82%C2%AA-Ed-18.03.2020.pdf>.

BENITES Gabriel Monteiro; BAGIO Tony Maronesi; FILHO José Marques. Manifestações reumatológicas na Síndrome Pós-COVID-19. REAS [Internet]. 10jan.2023 [citado 11abr.2023];23(1): e11723. Disponível: https://acervomais.com.br/index.php/saude/article/view/11723

BONJORNO Letícia Pastorelli *et al.* Imunopatologia induzida por COVID-19: avaliação da resposta imune inata e adaptativa. Rev Paul Reumatol. 2020 jul-set;19(3):6-11. DOI: https://doi.org/10.46833/reumatologiasp.2020.19.3.6-11

BRASIL. Ministério da Saúde. Secretarias Estaduais de Saúde (comp.). COVID-19 NO BRASIL. 2023. Disponível em: https://infoms.saude.gov.br/extensions/COVID-19_html/COVID-19_html.html. Acesso em: 31 mar. 2023.

BRASIL. Protocolo de manejo clínico da Covid-19 na Atenção Especializada [recurso eletrônico] / Ministério da Saúde, Secretaria de Atenção Especializada à Saúde, Departamento de Atenção Hospitalar, Domiciliar e de Urgência. – 1. ed. rev. – Brasília, Ministério da Saúde, 2020.

BRAZÃO Maria da Luz, NÓBREGA Sofia. Complicações/sequelas pós-infeção por sars-cov-2: revisão da literatura. Rpmi [internet]. 18 de junho de 2021 [citado 11 de abril de 2023];28(2):184-9. Disponível em: https://revista.spmi.pt/index.php/rpmi/article/view/65

CARNAÚBA, *Valquíria*. Eca2 + spike = covid-19. Revista entreteses, edição 14, nº 14, pag 96 – 99, novembro 2021. Recuperado de: https://www.unifesp.br/reitoria/dci/publicacoes/entreteses/item/5505-edicao-14-entreteses

CARVALHO, Fábio Ramos de Souza *et al.* FISIOPATOLOGIA DA COVID-19: repercussões sistêmicas. Unesc em Revista, Espírito Santo, v. 2, n. 4, p. 170-184, 2021. Recuperado de http://200.166.138.167/ojs/index.php/revistaunesc/article/view/245.

CASTRO, Anita Perpetua Carvalho Rocha de *et al.* Dor no Paciente com Síndrome Pós-COVID-19. Revista Científica Hospital Santa Izabel, Salvador, Bahia, Brasil, v. 5, n. 2, p. 56-62, 9 ago. 2021. Revista Cientifica Hospital Santa Izabel. http://dx.doi.org/10.35753/rchsi.v5i2.204.

CICHELERO, Eduarda Barcarolo; FRAPORTI Liziara. OCORRÊNCIA DE DOENÇAS AUTOIMUNES EM PACIENTES PÓS (COVID- 19), Revista do Centro Universitário FAI – UCEFF, Itapiranga –SC, 2022, pag 19-21.

COSTA, Andreia; SILVA-PINTO, André. Manifestações Neurológicas e COVID-19. Acta Médica Portuguesa, Porto, Portugal, v. 33, n. 12, p. 787-788, 2020.

COSTA Isabela Bispo Santos da Silva Costa *et al.,* O Coração e a COVID-19: O que o Cardiologista Precisa Saber. Arq Bras Cardiol [Internet]. 2020May;114(Arq. Bras. Cardiol., 2020 114(5)):805–16. Available from: https://doi.org/10.36660/abc.20200279

D'CAMINHA, Maria Katarina de Morais *et al.* DOENÇAS CRÔNICAS NÃO TRANSMISSÍVEIS: panorama de incidência e internações hospitalares antes e pós-pandemia de COVID-19 no estado do tocantins. Jnt- Facit Business And Technology Journal., [S. L.], v. 1, n. 38, p. 166-174, jul. 2022. QUALIS B1. FLUXO CONTÍNUO. SN: 2526-4281 http://revistas.faculdadefacit.edu.br. E-mail: jnt@faculdadefacit.edu.br.

ESTRELA, Maria Cristina Araújo, *et al.* COVID-19: sequelas fisiopatológicas e psicológicas nos pacientes e na equipe profissional multidisciplinar/ COVID-19. Brazilian Journal Of Development, Curitiba, v. 7, n. 6, p. 59138-59152, 16 jun. 2021. South Florida Publishing LLC. http://dx.doi.org/10.34117/bjdv7n6-349.

FIGUEIREDO Bárbara Queiroz de, et al. Cytokine storm and development of autoimmune diseases as a sequel of COVID-19. RSD [Internet]. 2021Aug.22 [cited 2023Apr.10];10(11): e38101119385. Available from: https://rsdjournal.org/index.php/rsd/article/view/19385

FORTUNATO, R. S. *et al.* COVID-19: perspectivas, diagnóstico e tratamento. Revista de Medicina, São Paulo, v. 100, n. 2, p. 100-108, 2021.

FRANCO, Jady Moraes *et al.* SEQUELAS PÓS-COVID-19. ANAIS CONGREGA MIC - ISBN 978-65-86471-05-2, v. 17, p. 329–335, 2021.

GOMES, Andressa de Souza; MEDEIROS FILHO, Osman Batista de; SOUSA, Milena Nunes Alves de. ASSOCIAÇÃO ENTRE O COVID-19 E MANIFESTAÇÕES NEUROLÓGICAS / ASSOCIATION BETWEEN COVID-19 AND NEUROLOGICAL MANIFESTATIONS. Brazilian Journal Of Development, Patos-PB, v. 6, n. 11, p. 88950-88961, 2020. Brazilian Journal of Development. http://dx.doi.org/10.34117/bjdv6n11-350.

GRAÇA Nadja Polisseni *et al.* COVID-19: Seguimento após a alta hospitalar. Publicação Oficial da Sociedade de Pneumologia e Tisiologia do Estado do Rio de Janeiro PulmãoRJ - Volume 29 - Número 1 – pag 32-36, Ano 2020.

GUTIÉRREZ Bautista Deyanira *et al.* Efectos a largo plazo de la COVID-19: una revisión de la literatura. Acta Med. 2021;19(3):421-428. doi:10.35366/101741.

HIRSCH Jamie S, et al. Acute kidney injury in patients hospitalized with COVID-19. Kidney Int. 2020;98(1):209-18.

LIMA, Brenda Caroline Marchetti *et al.* Fisioterapia pulmonar: reabilitação pulmonar e muscular pós-COVID-19 / pulmonary physiotherapy. Brazilian Journal Of Development, Coacal, RO, v. 7, n. 11, p. 107710-107722, 23 nov. 2021. South Florida Publishing LLC. http://dx.doi.org/10.34117/bjdv7n11-413.

LIMA, Fábio Santos de. Etiologia das lesões hepáticas em pacientes com COVID-19: uma revisão da literatura / Fábio Santos de Lima. - 2020. 36f.: il.

LOPES, Daniela Oliveira; ABREU, Fabiano de. Eletroterapia ivl no tratamento de covid-19 e sequelas no sistema nervoso central / ivl electrotherapy in the treatment of covid-19 and central nervous system sequelae. Brazilian Journal Of Development, São Paulo, v. 7, n. 4, p. 42332-42340, 2021. Brazilian Journal of Development. http://dx.doi.org/10.34117/bjdv7n4-615.

MALTA, Deborah Carvalho *et al.* Doenças crônicas não transmissíveis e mudanças nos estilos de vida durante a pandemia de COVID-19 no Brasil. Revista Brasileira de Epidemiologia, São Paulo, v. 24, 2021. FapUNIFESP (SciELO). http://dx.doi.org/10.1590/1980-549720210009.

MARINO, Ian Kisil *et al.* Como contar a história da COVID-19? Reflexões a partir dos arquivos digitais no Brasil. Esboços: histórias em contextos globais, Florianópolis, v. 28, n. 48, p. 558-583, 12 ago. 2021. Universidade Federal de Santa Catarina (UFSC). http://dx.doi.org/10.5007/2175-7976.2021.e80966.

MARTIN, Pollyanna da Silva *et al.* História e Epidemiologia da COVID-19. Ulakes Journal Of Medicine, São Paulo, p. 1-12, 20 jul. 2020.

MELO, Silvia Pereira da Silva de Carvalho *et al.* Doenças crônicas não transmissíveis e fatores associados em adultos numa área urbana de pobreza do nordeste brasileiro. Ciência & Saúde Coletiva, [s. l], v. 24, n. 8, p. 3159-3168, 2019.

MELO Flávio Henrique de, MELO Lucas Henrique Ladeira. Complicações cardiovasculares pós-COVID-19. REAMed [Internet]. 1fev.2023 [citado 10abr.2023];23(1): e11726. Disponível em: https://acervomais.com.br/index.php/medico/article/view/11726

MORAIS Léticia Rezende *et al.* COVID-19 e o trato gastrointestinal: fisiopatologia e evolução clínica dos pacientes / COVID-19 and tomse gastrointestinal tract: pathophysiology and clinical evolution of patients. Braz. J. Hea. Rev. [Internet]. 2021 Mar. 4 [cited 2023 Apr. 10];4(2):4556-69. Disponível em: https://ojs.brazilianjournals.com.br/ojs/index.php/BJHR/article/view/25659

NECOCHEA Cacho Isaac A. Manifestaciones gastrointestinales en el sindrome post covid agudo: Revisión de la literatura y su impacto en la actualidad. Interciencia méd. [nternet]. 20 de diciembre de 2022 [citado 9 de abril de 2023];12(4):41-7. Disponivel em: https://intercienciamedica.com/intercienciamedica/article/view/117

NUNES, Maria Jussara Medeiros *et al.* Alterações Neurológicas Na COVID-19: uma revisão sistemática. Revista Neurociências, Mossoró-Rn, Brasil, v. 28, p. 1-22, 2 dez. 2020. Universidade Federal de Sao Paulo. http://dx.doi.org/10.34024/rnc.2020.v28.10949.

OLIVEIRA, Daiane.Santos. *et al.* Alterações gastrointestinais causadas pela infecção do Sars-Cov-2, Arquivos de Ciências da Saúde da UNIPAR. Umuarama. v. 26, n. 3, p. 1427-1436, set./dez. 2022.
OMS- ORGANIZAÇÃO MUNDIAL DE SAÚDE. 2023. Painel do Coronavírus da OMS (COVID-19). Disponível em: https://covid19.who.int/. Acesso em: 01 abr. 2023.

OMS- Organização Mundial da Saúde. (2021). Long-term effects of COVID-19. https://www.who.int/emergencies/long-term-effects-of-COVID-19.

PECLY Inah Maria D. *et al.* A review of COVID-19 and acute kidney injury: from pathophysiology to clinical results. Braz J Nephrol [Internet]. 2021Oct;43(Braz. J. Nephrol., 2021 43(4)):551–71. Disponível em:: https://doi.org/10.1590/2175-8239-JBN-2020-0204

PECHO-SILVA, Samuel *et al.,* Complicaciones extrapulmonares de la enfermedad por COVID-19, Revista Peruana de Investigación en Salud, vol. 4, núm. 4, 2020, Octubre-, pp. 183-189 Universidad Nacional Hermilio Valdizán, Perú.

SALHA, Daniel Pla. COVID-19: Fisiopatología e infectividad. La proteína ACE2 como vía de entrada del virus y posible diana terapéutica. UNIVERSITAS Miguel Hermádez, Sant Joan d'Alacant, pag 4 - 11, fevereiro 2022. Recuperado de: http://dspace.umh.es/bitstream/11000/28988/1/Salha%20Pla%2C%20Daniel%20tfg.pdf

SERNA-TREJOS Juan S *et al.* Principales alteraciones endócrinas generadas en el síndrome Post-COVID-19. Rev. Peru. Investig. Salud. [Internet]; 2023; 7(1): 41-43. https://doi.org/10.35839/repis.7.1.1597

SILVA, Aurijonison Souza da. FUNÇÃO PULMONAR EM INDIVÍDUOS PÓS-COVID-19: uma revisão de escopo. 2021. 26 f. TCC (Graduação) - Curso de Bacharelado em Fisioterapia, Instituto de Saúde e Biotecnologia, Universidade Federal do Amazonas, Coari, Am, 2021.

SILVA, Maria Eduarda da *et al.* MANIFESTAÇÕES NEUROLÓGICAS PROVOCADAS POR COVID-19: uma revisão integrativa da literatura. Brazilian Journal Of Development, Vitória de Santo Antão-Pe, v. 6, n. 7, p. 52155-52163, 2020. Brazilian Journal of Development. http://dx.doi.org/10.34117/bjdv6n7-750.

SILVA, Caio Cruz. Da, *et al.* Sequelas da covid-19 sobre a função cardiorrespiratória e os impactos de um treinamento muscular inspiratório (tmi) na melhora na função pulmonar. Revista científica da faculdade de educação e meio ambiente, *[s. L.]*, v. 13, n. Edespjmcpc, 2022. Disponível em: https://revista.unifaema.edu.br/index.php/revista-faema/article/view/1201. Acesso em: 13 abr. 2023.

SIVAN, Manoj., Taylor, Sharon., & NICE guideline committee. (2021). NICE guideline on long covid. The Lancet Respiratory Medicine, 9(12), 1293-1295. https://doi.org/10.1016/S2213-2600(21)00463-1 SOARES Karla Hellen Dias *et al.* Medidas de prevenção e controle da COVID-19: revisão integrativa. REAS [Internet]. 5fev.2021 [citado12abr.2023];13(2):e6071. Available from: https://acervomais.com.br/index.php/saude/article/view/6071

XAVIER, Analucia R. *et al.* COVID-19: clinical and laboratory manifestations in novel coronavirus infection. Jornal Brasileiro de Patologia e Medicina Laboratorial, Rio de Janeiro, p. 1-9, 09 jun. 2020. GN1 Genesis Network. http://dx.doi.org/10.5935/1676-2444.20200049.

ZHU, Wei *et al.* RNA-Dependent RNA Polymerase as a Target for COVID-19 Drug Discovery. Slas Discovery, Bethesda, USA, v. 25, n. 10, p. 1141-1151, dez. 2020. Elsevier BV. http://dx.doi.org/10.1177/2472555220942123.