# International Journal of Health Science

# POST-COVID 19 SYNDROME: LONG-TERM CONSEQUENCES

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Abstract: Introduction: Coronaviruses belong to a large family of viruses that have a single strand of single RNA. SARS-CoV-2 has high lethality and morbidity rates, which is the cause of one of the biggest pandemics in history, responsible for several acute and chronic symptoms, such as Post-Covid Syndrome (PCS). Objectives: To analyze the main sequelae resulting from the Covid-19 infection, as well as the impact on the quality of life and well-being of patients, evaluating the main forms of follow-up and/ or rehabilitation for the population affected by the post-covid-19 syndrome. Methods: The research carried out for the formulation of this work consists of a systematic review of a descriptive and exploratory nature about publications regarding the postcovid syndrome 19. The selection of articles was carried out through databases on the internet, being they: Scientific Electronic Library Online (SCIELO), Latin American and Caribbean Center on Health Science Google Information (LILACS), Scholar search engine and Pubmed. Results: During the search, 20 articles were found through the proposed databases, but after applying the exclusion and inclusion criteria, only 14 articles were selected that corresponded to the proposed objective. Conclusion: PCS is still something new and little understood, despite the number of articles already published. The propagation of its existence is necessary for a better understanding of the population about such comorbidity, thus being recognized and treated accordingly.

**Keywords:** Covid-19, Rehabilitation, Sequelae, Syndrome, SARS-CoV-2.

# INTRODUCTION

Since the end of 2019, humanity has been facing a reality that lasts until the present day, the Covid-19 pandemic, with a high rate of morbidity and lethality (CARVALHO et al., 2021). The persistence of debilitating and persistent physical and psychological signs and symptoms, for more than 4 weeks after the recovery phase of SARS-Cov-2 infection, has been termed Post-Covid Syndrome (PCS) or long Covid (ANAYA et al, 2021).

The coronavirus is a pathogen that mainly affects the upper respiratory tract, similar to a common cold, but which, over the course of the infection generated, can compromise the lower respiratory tract, causing severe acute respiratory syndrome (SARS). The risk of symptomatic infection increases with age, therefore, young individuals and children can be asymptomatic carriers of the infection. <sup>1</sup>

As for the pathogenesis, it is estimated that about 80% of those infected develop mild or asymptomatic symptoms, while the others have more severe symptoms, with the possibility and need for hospitalization. Of these, about 5% will require intensive care and mechanical ventilation (WHO, 2020b; WU; MCGOOGAN, 2020).<sup>2</sup>

The clinical presentation is comprehensive, with the most common symptoms being fever, cough, fatigue and myalgia, which may appear accompanied by other symptoms less frequently, such as: runny nose, headache, hemoptysis and diarrhea<sup>1</sup> The infection can cause serious complications, with the risk factors advanced age (over 60 years) and the presence of comorbidities (cardiovascular diseases, obesity, diabetes, hypertension, lung diseases, etc.) (KOLIFARHOOD et al., 2020).

According to the available literature and recently published studies, the effects of Covid-19 on the body affect, among others, the following systems: a) respiratory; b) cardiovascular; c) urinary; d) central nervous; e) sensory; f) digestive. <sup>2</sup>

The first directly affected system is the respiratory system, affected by inflammatory mechanisms and deregulation of the coagulation cascade. One of the reported possible consequences is pulmonary fibrosis, which impacts the quality of life due to the restriction of lung capacity, with less hematosis, fatigue and dyspnea on small efforts (GIANNIS; ZIOGAS; GIANNI, 2020; SERVICK; 2020; AM, 2020; YANG et al., 2020)<sup>2</sup>.

In the cardiac and vascular system, changes in laboratory parameters are observed, which may show a brief problem related to the combination of the systemic inflammatory response with inflammation at the vascular level and the presence of arterial plaques (CHEN et al., 2020). The elucidated complications include acute heart injury, heart failure, myocarditis, cardiac arrhythmias and vascular inflammation, which are capable of generating sequelae (CHEN et al., 2020).

Patients infected with Covid-19 may manifest accumulation of serum creatinine due to a decrease in the glomerular filtration rate. This results in renal failure for the urinary system, which after recovery is capable of generating a deficit in the exercise of renal function. Renal insult can result in severe acute tubular necrosis, with even greater decline in its function (DIAO et al., 2021; FAN et al., 2020a; YANG et al., 2020). Clinical events such as hematuria and proteinuria were also observed in a study in approximately 40% of patients and that, in a minority of cases, persisted in the post-Covid-19 period (Rabb, 2020).<sup>3</sup>

Due to the systemic inflammatory process generated, complaints and laboratory alterations related to the digestive system are frequent, especially when related to the polypharmacy treatment acquired by the patients, even after the end of the symptoms (FAN et al., 2020).

In studies, it was observed that the virus has tropism for neural cells, thus increasing its replication and direct infiltration in the central nervous system, triggering neuroinflammatory responses, such as dizziness, memory loss, headache and cognitive, motor and intellectual losses. In the literature, there were some records of the consequences of this neural invasion, such as cérebro vascular accidents (CVA), acute hemorrhages and meningitis (DA GAMA, 2020).

Dissertations demonstrate that an increasing number of patients are experiencing prolonged symptoms, especially patients who required admission to the ICU and/or ventilatory support in severe cases (MIRANDA et al., 2022).

According to FARO (2020), after the crisis experienced in the pandemic, society developed anxiety, depression, post-traumatic stress, abnormal behaviors, specific phobias and loss of social capacity, therefore, it is extremely necessary, still according to this author, to act of psychology for the treatment and follow-up of these affected individuals.

The prognosis of PCS is still unknown and probably varies according to the severity of the symptoms during the infection, previously existing comorbidities and the response to treatment (MIRANDA et al., 2022).

In clinical management, carried out in a multidisciplinary way, it is necessary to examine and treat decompensated comorbidities, such as diabetes and hypertension, evaluate general health care, adequate nutrition, prevention and treatment of smoking, alcohol use, quality of sleep and gradual increase in physical activity. (PARANÁ, Secretary of Health; 2021).

Therefore, PCS is increasingly present in our society, and the in-depth study of this condition is of paramount importance, in order to be able to provide better quality of life for affected patients, as well as, if possible, to prevent it from occurring.

# METHODOLOGY

The research carried out for the formulation

of this work consists of a systematic review of a descriptive and exploratory nature about publications that refer to the post-covid 19 syndrome. It was carried out through the following steps: search for articles through databases; definition of research objectives; establishment of inclusion and exclusion criteria; data collection from the selected articles and subsequent analysis and interpretation of the data obtained.

The selection of articles was carried out using databases on the internet, namely: Scientific Electronic Library Online (SCIELO), Latin American and Caribbean Center on Health Science Information (LILACS), Google Scholar search engine and pubmed. The searches took place from June to September 2022.

The terms used to search for data according to health science descriptors (DeCs), in Portuguese and English, were: "Síndrome", "Covid-19", "sequelae", "complications", "SARS- CoV-2" and "monitoring". The inclusion criteria for the study were: articles that had the chosen descriptors as titles and that presented the objectives of this research in the abstract. And as exclusion criteria are all those who deviated from the theme and objectives of the study.

The present work aims to analyze the main sequelae resulting from the Covid-19 infection, as well as the impact on the quality of life and well-being of patients and to evaluate the main forms of follow-up and/or rehabilitation for the population affected by PCS.

### RESULTS

During the search, 14 publications were defined to be used in this study. 20 articles were found, however 6 were eliminated for not meeting the criteria evaluated for the search. Among the 14 selected publications, 50% (07 articles) are from the year 2021; 28.57% (04 articles) are from the year 2022, 01 of which in English; 7.14% (01 article) from the year 2020 and 01 articles from the year 2019, which are equivalent to 21.42% of the total.

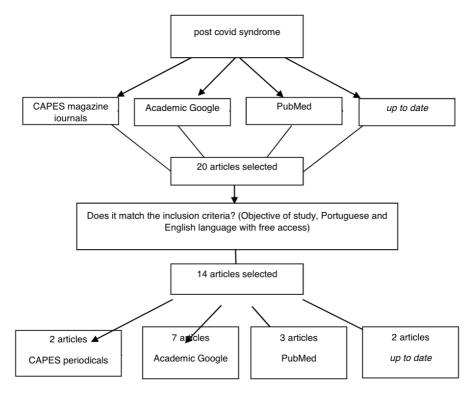


Figure 1- Study selection flowchart

Title	Author	Language/ Database	Kind of study	findings
Post-covid-19 syndrome: main conditions and impacts on society in focus	Viana Gal, et al. (2021)	Portuguese / GOOGLE	Systematic review	PCS generates respiratory, neurological and musculoskeletal sequelae. Dyspnea results from pulmonary fibrosis, anosmia is generated by inflammatory blockage of the olfactory clefts, musculoskeletal pain is due to tissue inflammation, social isolation, among other factors, causes loss of muscle mass, in addition to biopsychosocial impacts.
Quality of life and long-term outcomes after hospitalization for Covid-19: protocol for a prospective cohort study (Coalition VII)	Goulart RR, et al. (2021)	Portuguese / SCIELO	Prospective cohort study	After hospital discharge, patients may develop physical, cognitive and/or psychiatric disorders that will prolong the recovery time, in addition to generating dependence for activities of daily living, anxiety, depression, in some cases post-traumatic stress disorder (PTSD) and the need for greater health resources, resulting in the impairment of the quality of life of these individuals.
The impact on quality of life in individuals after COVID-19: What has changed?	Trindade CCM, et al. (2021)	Portuguese / GOOGLE	Observational cross-sectional study	During the pandemic with social isolation, there was a drastic change in routine, with little or no socialization with friends and family, being responsible for triggering and aggravating conditions of people already affected by mental illness, in addition to the change in the curriculum that created difficulty in performance of individuals, with stressful routines intensified or diminished by living conditions. Thus, the changes led to impacts on quality of life with greater demographic vulnerability.
Psychological impacts of post- covid syndrome	Melo PC, et al. (2020)	Portuguese / GOOGLE	Systematic review	PCS has manifested itself as a chronic disease, since the symptoms that persist do not improve spontaneously and possibly cannot be cured, thus forcing these patients to adapt to the new conditions of life. Several protocols are created with the aim of early intervention to the patient with a focus on biological care and aimed at mental health, taking into account the main morbidities generated, which include: anxiety, depression, post-traumatic stress, specific phobias and loss of social capacity.
Post-covid-19 syndrome: brief systematic review	Silva RCO, et al. (2022)	Portuguese / GOOGLE	Systematic review	The manifestations most present in the studies included respiratory failure, headache, mental health conditions and fatigue, which appeared after the acute phase of SARS-CoV-2 infection, an infection that provides a greater chance of developing multiple organ involvement. The approach and follow-up generated by the multidisciplinary team of patients recovered from COVID-19 were essential for the rehabilitation of the sequelae generated and for a better adaptation of the new conditions that will not progress to a cure.

Post Covid-19 syndrome: case study	Nogueira VCR, et al. (2022)	Portuguese / GOOGLE	Case report	The post-covid-19 syndrome is considered a diffuse and multisystem inflammatory condition that generates persistence of symptoms for weeks or months after infection and that are associated with changes in the central nervous system and musculoskeletal system as sequelae. Social isolation intensified chronic musculoskeletal pain, emotional and sleep changes. People with associated pathologies are more vulnerable to sequelae generated post-covid-19.
Complications/ Sequels after SARS- CoV-2 Infection: Literature Review	Maria da Luz Brazão et al.	English/ PUBMED	REVIEW ARTICLES	The most common findings in hospitalized patients with COVID-19 are cough, dyspnea, respiratory failure, and changes on computed tomography (CT) that appear as ground-glass opacities and/or consolidations. The virus can affect the lungs in three ways: causing acute respiratory distress syndrome, with diffuse alveolar damage; triggering a diffuse thrombotic alveolar microvascular occlusion, and causing inflammation of the airways associated with inflammatory mediators.
In addition to SARS-CoV-2, the implications of Post-COVID-19 Syndrome: what are we producing?	Audrey Moura Mota Gerônimo et al. (2021)	Portuguese GOOGLE	Review article	The post-COVID-19 syndrome represents a clinical picture composed of a set of nonspecific symptoms. Being something recent, not much is known about it, but what is clear is that it does not only affect people who developed the severe form of COVID-19 and who were admitted to the UTI for a long period.
Aspects of post- COVID-19 syndrome manifestations: a narrative review	Mércia Alexandra Amorim Silveira et al (2021)	Portuguese GOOGLE	Review article	Post-covid syndrome is a term used in the literature to designate debilitating and persistent physical and psychological signs and symptoms, beyond the usual time, presented by patients who are already in the recovery phase of SARS-CoV-2 infection. Some risk factors for this syndrome are: advanced age, presence of comorbidities, female gender and hospitalization. Among the clinical manifestations of long-term COVID-19, which is the other name used for PCS, we can mention: fatigue, dyspnea, chest pain and neuropsychiatric symptoms. Furthermore, complications resulting from PCS, such as pulmonary fibrosis, bronchiectasis and thromboembolic events, have also been reported.
Post-Covid-19 Syndrome - Literature Review: Precautions after improvement of Covid-19 symptoms	Mariana Wu. (2021)	Portuguese Bioscience Magazine CAPES	Literature review	This article aims to compile data on the main consequences left by the SARS-CoV-2 virus. In this research, it was concluded that, even after the improvement of Covid-19, some people have persistent symptoms, such as fatigue, headache, attention disorder, hair loss, dyspnea, among others. In short, it is indicated that there are long-term sequelae, even after the "cure".

Post covid-19: the consequences left by Sars-Cov-2 and the impact on the lives of affected people	Thalia Lima Nogueira et al. (2021)	Portuguese pubmed	Literature review	Upon analysis of the material found, conditions related to the pulmonary system are the most evident because they represent the target organ of the virus, commonly triggering symptoms such as dyspnea, fatigue and, in more severe clinical conditions, pulmonary fibrosis. Cardiovascular involvement results in acute cardiac injury, myocarditis, vascular inflammation and cardiac arrhythmias, while olfactory and gustatory dysfunctions pertaining to the neurological system are widely reported. Musculoskeletal sequelae involve weakness caused by sarcopenia and loss of muscle strength in response to viral infaction, immobility, and poor nutrition. The psychological and emotional shock arises as a result of the process of social isolation, in addition to fear of the potential risk of death, deteriorating the mental health of these individuals due to anxiety,
Pulmonary rehabilitation in patients with post- covid syndrome	Marques SCCB, et al. (2019)	Portuguese / Scielo	Systematic review	Covid 19 mainly affects the respiratory system, after recovery, persistence of symptoms occurs in most patients who required hospitalization, there are no specific rehabilitation guidelines. Rehabilitation begins six to eight weeks after the infection. The Brazilian Association of Cardiorespiratory Physiotherapy and Physiotherapy in Intensive Therapy (Assobrafir) suggested methods to assess the reduction in exercise tolerance, muscle strength, respiratory dysfunctions, loss of balance and changes in mobility, as well as the use of questionnaires and scales that assess symptoms of dyspnea and fatigue, disabilities and quality of life and sleep.
COVID-19: Questions and answers		English/ up to date	Article	
COVID-19: Evaluation and management of adults with persistent symptoms following acute illness ("Long COVID")	MIKKELSEN et al. (2022).	English/ up to date	Article	The coronavirus disease 2019 (COVID-19) pandemic has resulted in a growing population of individuals recovering from severe acute respiratory syndrome coronavirus 2 (SARS- CoV-2) infection. Accumulating observational data suggest that these patients may experience a wide range of symptoms after recovery from acute illness, referred to by several terms including "long COVID," "post-COVID conditions," and "postacute sequelae of SARS- CoV-2 infection (PASC).

Table 1-Publications selected for data analysis according to author, title, year of publication, journal and main research findings.

# DISCUSSION

From the reviewed studies on PCS, nonspecific symptoms are verified, which extend for months after the recovery of the infected person, affecting individuals at random, not being dependent on other factors such as the presence of previous comorbidities, gender, age or even level severity of the disease, which is the reason for the most discussion among specialists (PERES, 2020).

The incidence of PCS in patients treated on an outpatient basis varies between 10 and 35%, while in hospitalized individuals it reaches almost 80%.<sup>1</sup>

Common sequelae among those affected by PCS are: complete absence of taste (ageusia) and smell (anosmia), misinterpretation of smells and flavors, which become unbearable odors (parosmia), and distorted detection of smells that are not present in the body. environment (phantosmia) (SANIASIAYA, 2021).

Mechanism explained by the affinity and ease of the virus to replicate in neural cells, a fact that also causes dizziness, cognitive loss, headache and memory loss (DA GAMA, 2020). These conditions, in addition to causing great discomfort to the victim, also prevent the carrier from eating in the necessary and correct way, with the main consequence of eating disorders, which in turn brutally impact social relationships and routine, and may cause psychological demands (SANIASIAYA, 2021).

There were records that this brain infection caused by Covid-19 also resulted in cerebrovascular accidents (CVA), acute bleeding and meningitis, identified in infected patients, young and without any comorbidity or early symptoms. The neural manifestation of the disease also affects and compromises the nervous system in patients who develop the most severe form of the disease, causing loss of motor and intellectual capacity (DA

## GAMA, 2020).

Neuropsychological rehabilitation must be used above all in patients with cognitive disorders caused by hypoxic encephalopathy or alterations of vascular origin in the postcovid period. Furthermore, occupational therapy must be prescribed for elderly people who have lost their independence and are restricted in their daily tasks. In addition, psychological follow-up is also important for patients who have acquired depressive disorders, post-traumatic stress and anxiety (BRAZÃO MA and NÓBREGA SO, 2021).

The generated neuropsychiatric sequelae must be followed up in a unique and strategic way, in addition to the multidisciplinary team and family involvement to influence adherence to the follow-up and rehabilitation of the assisted person (Santana, Fontana & Pitta, 2021).

It is worth considering that the presence of prolonged symptoms of fatigue and dyspnea is indicative of the need for cardiopulmonary rehabilitation, focusing on reducing the limitations presented in the systems involved. For cases of persistent anosmia, the most efficient recovery identified is olfactory training, which seeks to promote the regeneration of neurons that were affected by the viral infection, since pharmacological interventions have not yet been developed (DANIEL, et al.; 2020).

In addition, complications arising from the pulmonary involvement of Covid-19 are also reported, such as fibrotic and non-fibrotic interstitial changes, organizing pneumonia, bronchiectasis, pulmonary embolism, and others such as acute cardioembolic ischemia of the limbs, arthritis, systemic lupus erythematosus, Guillain-Barré, myocarditis, acute kidney injury, liver injury and Graves' disease, and there may be others not yet reported (KOROMPOKI E, et al., 2021).

Satterfield BA, et al. (2021) reported an

increase in cases of systolic dysfunction and heart failure due to myocardial injury by SARS-CoV-2, in addition to the association with acute coronary syndrome, myocarditis, ventricular dysfunction, arrhythmias, deep vein thrombosis, pulmonary thromboembolism and pericarditis, resulting excessively aggressive immune response and hypercoagulable state.

A common symptom in PCS patients is a persistent cough. Even though there is no scientific evidence for the specific condition, the use of honey and central antitussives (opioids) has been reported. There is also the use of other drugs such as antimuscarinic, anti-inflammatory and neuromodulators to alleviate this symptom (SONG WJ, et al., 2021).

Another post-Covid involvement is acute kidney injury, especially in those patients who contracted the severe form of the disease and required admission to the ICU. As stated by Fajgenbaum D and June C (2020), one of the causes is the reaction of the immune system itself in the fight against SARS-CoV-2, generating an intense response capable of causing kidney damage. In these cases, there is a need for follow-up with nephrology (MEIER P, et al., 2011 apud NALBANDIAN A, et al., 2021). Despite the frequent renal involvement, the number of studies on the possibility of worsening the acute renal failure (ARF) to a possible chronic kidney disease (CKD) is still scarce.

One of the main complaints after facing SARS-CoV-2 infection is the musculoskeletal limitation related to loss of muscle strength and sarcopenia (inflammatory response to the virus, insufficient nutrition and immobility associated with hospitalization). Affecting at least 25% of people who have experienced Covid-19, such sequelae compromise the quality of life of these people, from a physical-functional point of view (PAZ, et al., 2021).

Mandatory components of some cardiopulmonary rehabilitation programs include resistance and strength activities, in addition to exercising the inspiratory muscles. In addition, educational approaches, an important point in the development of treatment, must include techniques for re-educating breathing, techniques for eliminating secretions, benefits of practicing physical activities, techniques for conserving energy during activities of daily living, healthy eating and leisure (CACAU L, et al., 2020).

As portrayed, patients who have experienced covid-19, especially with severe cases of the disease, will eventually present a reduction in physical and functional conditioning after their recovery. Thus, they will sometimes need outpatient or home physiotherapeutic care, thus aiming at a bodily and functional rehabilitation of the individual (AVILA PE, et al., 2020).

Rehabilitation in order to promote the recovery of people who have gone through the infection, whether from physical, functional or even mental deficits, must be accompanied by a multidisciplinary team. The focus must be on health promotion, aiming at maximizing the independence and capacity of each individual, always considering the subjective needs they may have (SILVA CC, et al., 2021).

Physiotherapeutic treatment in post-covid 19 is based on the appropriate prescription of individualized physical exercises, combined or not with strategies related to the character of the patient's sequelae. In addition, they must be started approximately 72 hours after episodes of fever or use of antipyretics (AVILA PE, et al., 2020).

The therapy of post-Covid patients consists of a global multidisciplinary analysis that assesses the functionality, nutritional, cognitive and psychic dysfunctions capable of interfering with the rehabilitational development after hospital treatment. After the evaluation, a rehabilitation scheme is drawn up with the aim of promoting posthospital care, thus aiming at the social and functional return of the individual to their pre-hospital situation within the shortest possible time, always respecting the clinical circumstances related to their expectations (MATOS L, et al., 2020).

After weaning from mechanical ventilation and oxygen therapy, physical, motor and cognitive reconditioning treatment is recommended to correct the worsening effects of prolonged ICU stay. In this sense, lowintensity physical activities are highlighted and, whenever possible, the execution of the 6-minute walk test, to evaluate the saturation response during exercise and functional capacity during the test (HERRERA LC, 2020).

The post-Covid multi-component physical exercise interventions scheme combined resistance training with about 1-2 sets of 8-19 repetitions. Resistance training was performed with aerobic exercises of up to 15 minutes, with cycle ergometer, walking or steps. There was also balance training with walking over obstacles or on unstable surfaces. Treatment was individualized for each individual's physical circumstances (UDINA C, et al., 2021).

According to the "Universidade Estadual do Rio de Janeiro" (UERJ), medical negligence was one of the variants of great impact on PCS, since most of the patients who required prolonged hospitalization were discharged early as soon as they stopped transmitting the virus, due to the overload generated in the health system. As for those patients who had a mild form of the disease, most did not seek medical help. In both cases, multidisciplinary follow-up aimed at identifying and recovering from Covid-19 sequelae is rarely carried out.

The long-term follow-up of the individual infected with Covid-19 serves as a triage

for possible carriers of PCS, making it appropriate, when present, for their inclusion in rehabilitation services, so that they can resume their quality of life, since some of the symptoms, if not are resolved beforehand, they can be prolonged.

# FINAL CONSIDERATIONS

Despite the large number of published studies, post-covid syndrome is still poorly understood. Thus, it becomes extremely important to spread diagnostic knowledge, aiming at facilitating early recognition, in order to carry out rehabilitation adequately, with the best scientific evidence, aiming at improving the quality of life of affected individuals.

According to Taribagil, et al. (2021), the presence of a multidisciplinary team for the development of preventive measures, rehabilitation techniques and clinical management strategies aimed at addressing the care of patients identified with long-term Covid-19 is crucial for coronavirus studies.

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