

Main complications presented by patients diagnosed with COVID-19: integrative review*Complicaciones principales presentadas por pacientes diagnosticados con COVID-19: Revisión integradora**Principais complicações apresentadas por pacientes diagnosticados com COVID-19: revisão integrativa***Eva Natalina Ferreira Costa¹**

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Abstract

It was aimed to highlight and identify the main complications after infection by COVID-19 reported in the scientific literature. It is an integrative review of the literature. To achieve scientific production on the chosen theme, the Virtual Health Library (BVS) and the Databases: Medical Literature Analysis and Retrieval System Online (Medline), Latin American and Caribbean in the Caribbean in the search was used as a search. Health Sciences (Lilacs) and Pubmed. A total of 30 articles was obtained. After application of the inclusion and exclusion, reading and analysis criteria of the studies, 10 articles were reached for the construction of this review. Studies showed cardiovascular, renal, neurological, respiratory, liver, hematological, metabolic, functional and psychological complications. These include: ischemic injury of myocardial, pericarditis, renal failure, hematuria, proteinuria, stroke, yearsia, bronchopneumonia, bronchial mucosal edema, alterations in liver enzymes, venous thromboembolism, metabolic disorders, functional and psychological impairment. It is concluded that COVID-19 has high relevance during the appearance and development of its complications. We do not yet know how long these complications can reach patients if sequelae are temporary or definitive. Thus, the Unified Health System is prepared to continue watching these individuals.

Descriptors: COVID-19; Pathology; Health Conditions; Pandemic; Coronavirus.

Resumen

Tenía como objetivo resaltar e identificar las principales complicaciones después de la infección por COVID-19 informadas en la literatura científica. Es una revisión integradora de la literatura. Para lograr la producción científica sobre el tema elegido, la Biblioteca de Salud Virtual (BVS) y las bases de datos: Análisis de la literatura médica y sistema de recuperación en línea (Medline), Latinoamericano y Caribe en el Caribe en la búsqueda se utilizó como búsqueda. Ciencias de la salud (Lilas) y PubMed. Se obtuvieron un total de 30 artículos. Después de la aplicación de la inclusión y la exclusión de la exclusión, la lectura y el análisis de los estudios, se alcanzaron 10 artículos para la construcción de esta revisión. Los estudios mostraron complicaciones cardiovasculares, renales, neurológicas, respiratorias, hepáticas, hematológicas, metabólicas, funcionales y psicológicas. Estos incluyen: lesión isquémica de miocardio, pericarditis, insuficiencia renal, hematuria, proteinuria, accidente cerebrovascular, años, bronconeumonía, edema de la mucosa bronquial, alteraciones en enzimas hepáticas, tromboembolismo venoso, trastornos metabólicos, deterioro funcional y psicológico. Se concluye que Covid-19 tiene una gran relevancia durante la aparición y el desarrollo de sus complicaciones. Todavía no sabemos cuánto tiempo pueden llegar estas complicaciones a los pacientes si las secuelas son temporales o definitivas. Por lo tanto, el sistema de salud unificado está preparado para continuar observando a estas personas.

Descriptorios: COVID-19; Patología; Condiciones de Salud; Pandemias; Coronavirus.

Resumo

Objetivou-se evidenciar e identificar as principais complicações pós infecção pela COVID-19 relatadas na literatura científica. Trata-se de uma revisão Integrativa da literatura. Para alcançar a produção científica sobre a temática escolhida, utilizou-se como fonte de busca a Biblioteca Virtual em Saúde (BVS) e as bases de dados: Medical Literature Analysis and Retrieval System Online (MEDLINE), Literatura Latino-americana e do Caribe em Ciências da Saúde (LILACS) e PubMed. Obeve-se uma totalidade de 30 artigos. Após aplicação dos critérios de inclusão e exclusão, leitura e análise dos estudos, chegou-se ao número de 10 artigos para a construção da presente revisão. Os estudos evidenciaram complicações cardiovasculares, renais, neurológicas, respiratórias, hepáticas, hematológica, metabólicas, funcionais e psicológicas. Dentre elas, destacam-se: lesão isquêmica do miocárdio, pericardite, insuficiência renal, hematuria, proteinúria, acidente vascular cerebral, anosmia, broncopneumonia, edema de mucosa brônquica, alterações na enzimas hepáticas, tromboembolismo venoso, disfunções metabólicas, comprometimento funcional e psicológico. Conclui-se que a COVID-19 possui alta relevância durante o aparecimento e desenvolvimento de suas complicações. Ainda não sabemos após quanto tempo essas complicações podem atingir os pacientes, se as sequelas são temporárias ou definitivas. Assim, o Sistema Único de Saúde precisa está preparado para continuar assistindo estes indivíduos.

Descritores: COVID-19; Patologia; Condições de Saúde; Pandemias; Coronavírus.



the scientific literature. With this, it is intended that the combination of this knowledge can contribute to guide guidelines and to the development of new research.

Introduction

Coronavirus is a family of viruses that cause respiratory infections, known since the 1960s. A new coronavirus was discovered on December 31, 2019, after cases registered in Wuhan, China, named at the time SARS-CoV-2, infectious disease causing COVID-19¹.

The World Health Organization, on March 11, 2020, announced COVID-19 as a pandemic, due to its transmission rate worldwide. Brazil was the first country in Latin America to register a case, dated February 25, 2020².

By October 10, 2021, 2019 million cases and 4.55 million deaths were confirmed worldwide. In Brazil, on the same date, 21.6 million cases and 601,000 deaths were recorded. With the absence of a treatment recognized by the scientific community, restrictive measures such as social distancing and the use of masks were used during the pandemic as a way to reduce the number of infected people and as an aid to contain the disease. The researchers developed, in record time, vaccines against COVID-19 that were tested and approved by Organs competent bodies. The start of immunization took place at the end of 2020^{2,3}.

Researchers and front-line professionals are constantly challenged by the emergence of viral variants. The symptoms of COVID-19 such as fever, body aches, headache and dry cough resemble those of the flu. Its transmission occurs from person to person and can spread through small droplets and aerosols released through the nose and mouth of infected individuals².

Among the symptoms, it is noticed that the virus affects, in most cases, the respiratory system, causing one of its complications to be viral pneumonia with impairment of respiratory capacity, with dyspnea being one of the most frequent symptoms. There are records that it can also cause complications in other systems, such as cardiovascular, renal, neurological and hematological, associated with mild, moderate and severe symptoms, which can lead to death. It should be noted that COVID-19 caused panic in the world population due to the fear of contracting the disease, which can compromise the mental health of individuals in general⁴.

The etiologic agent of COVID-19, SARS-CoV-2, upon penetrating the body, associates with the angiotensin-converting enzyme 2 (ACE2) receptor, allowing it to enter the target cell, multiply and provoke an immune response in the patient, initiating the first signs and symptoms of the disease. Other organs that also have this receptor may manifest tropism such as the respiratory tract and lung tissue^{4,5}.

The justification for this research lies in factors related to the health situation faced worldwide caused by the new coronavirus and the little knowledge about its consequences and sequelae faced after infection with SARS-CoV-2, in view of the systemic impairment that the disease can cause. The motivation arose after observing in the hospital routine that people, even after some time after being infected by the COVID-19 disease, had systemic sequelae, causing long periods of hospitalization or monitoring of these complications.

Thus, the objective was to highlight and identify the main complications after infection by COVID-19 reported in

Methodology

This study is an Integrative Literature Review. To carry out this type of methodology, the process begins with: (1) delimitation of the theme and construction of the research's guiding question; (2) survey of publications in selected databases; (3) classification and analysis of the information found in each manuscript; (4) analysis of the chosen studies; (5) presentation of the results found and (6) critical analysis of the findings and synthesis of the literature review⁶.

To elaborate the guiding question of this study, the PICO strategy (P – Population, I- Intervention, Co – Context) was used, which in Portuguese means P population, I- intervention, Co- context. In this sense, the PICO strategy was designed as follows: P – general population, I – complications, Co – identify the main complications. It should be noted that the strategy ensures a rigorous search for scientific evidence related to the PICO object, as it establishes a direction⁷.

Therefore, the guiding question of this integrative literature review is: what are the main complications presented by individuals affected by COVID-19?

In order to achieve scientific production on the chosen theme, the Virtual Health Library (VHL) and the databases contained therein were used as a search source: Medical Literature Analysis and Retrieval System Online (MEDLINE) via PubMed, Latin American Literature and the Caribbean in Health Sciences (LILACS). The survey of these documents to compose the results took place in August of the year 2021.

With the applicability of the previously established inclusion and exclusion criteria and the reading of the abstracts of these documents, the number of 10 articles was reached for the construction of the present review. All published in English. Among these, 6 were found in the MEDLINE database, 1 in LILACS and 3 in PubMed. Of these findings, 7 were published in 2020 and 3 in 2021. During the search, few scientific productions related to the topic were observed, probably because it is a new scenario and still in learning process.

During the search and selection of documents to compose the present study, the Health Sciences Descriptors (DeCS) were selected: "COVID-19", "Pathology", "Health Conditions", "Pandemic" and "Coronavirus". all associated with the Boolean operator AND, presented as follows: "COVID-19" AND "Pathology" AND "Health Conditions" AND "Pandemic" AND "Coronavirus".

As inclusion criteria for the documents, the following were included: articles published between the years 2020 and 2021, as this is an extremely current topic, that were written in Portuguese, English, Spanish and/or French and that answered the question previously chosen guide. As exclusion criteria, we mention: other reviews, dissertations, monographs, abstracts, theses, research and repetitive studies.



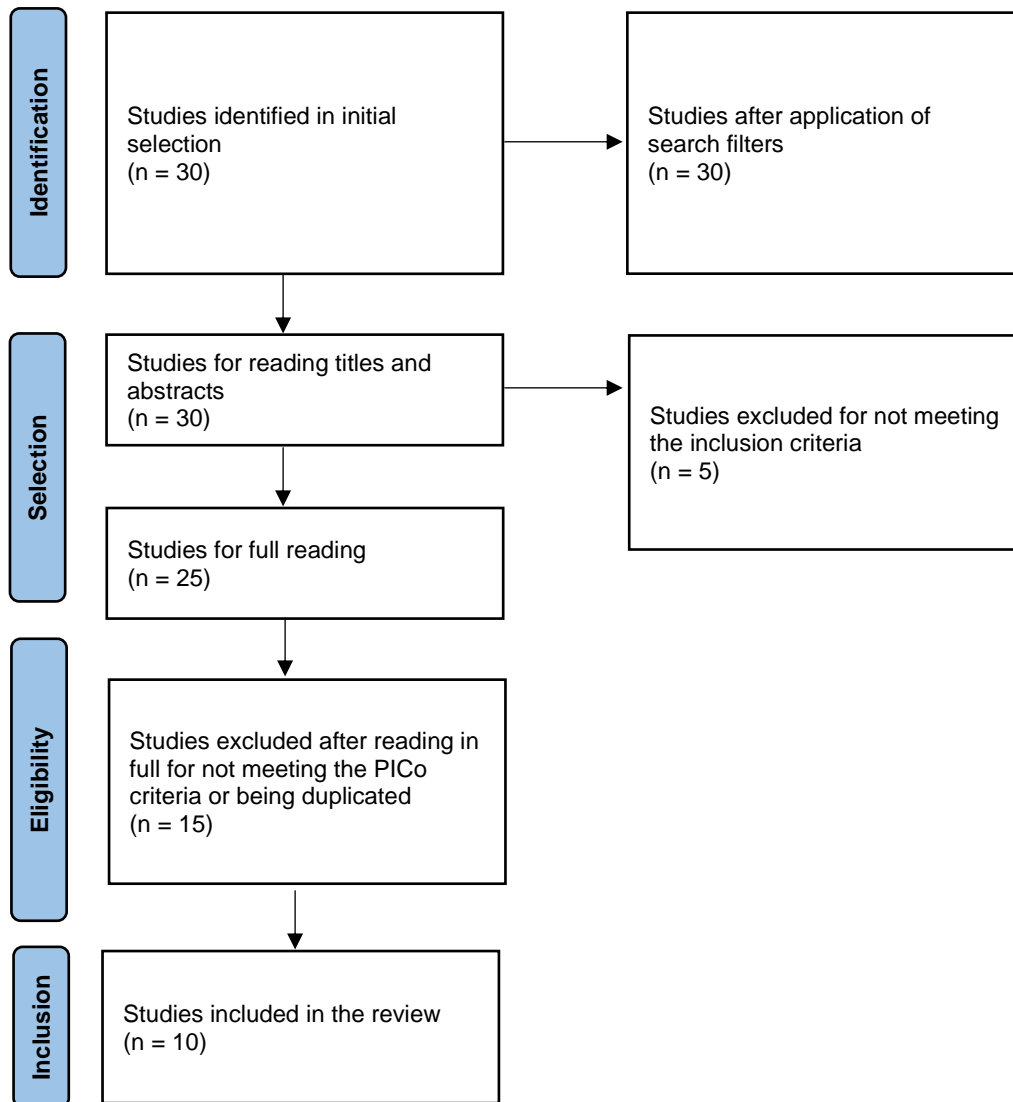
With regard to the ethical aspects of the research for the reviews, it is not necessary to submit it to the Ethics Committee, as the study was not carried out with human beings and the documents used for its writing have already gone through ethical appreciation and approval.

To systematize the article selection process, the Preferred Reporting Items for Systematic Reviews and Meta-Analyses methodology was used (PRISMA)⁸. A search for references in the literature was carried out and Figure 1 graphically illustrates how this search and selection was carried out:

In the first stage, two independent authors carried out the search, reading and evaluation of the titles and abstracts of the articles selected in the databases, in accordance with the previously defined inclusion/exclusion criteria. Then, they elected the articles to be read in full.

The second step was the inclusion by these authors of the manuscripts according to the elements necessary to answer the guiding question of this study. There were no disagreements between the authors regarding inclusion. No tool was used to organize the references, being described in tables and charts according to the selection of articles.

Figure 1. Flowchart for selection of structured studies based on the PRISMA recommendation. Rio de Janeiro, RJ, Brazil, 2021



Results and Discussion

Of the 10 studies included in this review, the entire population consisted of adults and the main complications presented were related to the respiratory system (n=6), followed by the cardiological system (n=5), showing saturation lower than 80%, edema of bronchial mucosa and bronchopneumonia; the cardiac one showed acute myocardial infarction, pericarditis, myocarditis.

Other complications that also appeared in the data collection were neurological (n=2), metabolic (n=2)

hematological (n=1), renal (n=1), hepatic (n=1) psychological impairments (n=2) and functional (n=2).

In order to better present the results, two charts were prepared, Chart 1 with n=6 articles that address the complications related to the moment of the acute phase of the disease related to the compromised system, that is, referring to the patient's hospitalization period; and Chart 2 presents n=4 articles that address the post-infection syndrome due to the COVID-19 disease, that is, sequelae presented after the patient is discharged from the hospital.

Chart 1. Articles (N=6) that address complications related to the acute phase of the COVID-19 disease. Rio de Janeiro, RJ, Brazil, 2021

Commitments	Percentage	Number of articles	Complications
Cardiological	30%	(n=3)	- Acute myocardial infarction - Pericarditis - Myocarditis
Respiratory	20%	(n=2)	- Saturation less than 80% - Edema of the bronchial mucosa - Bronchopneumonia
Psychological	20%	(n=2)	- Feeling of loneliness
Neurological	20%	(n=2)	- Brain stroke - Encephalopathy/anosmia/ageusia - Neuromuscular disorders
Functional	10%	(n=1)	- Functional commitment - Imbalance of standing position - Inability to carry out daily activities
Metabolic	10%	(n=1)	- Dysfunction
Hematological	10%	(n=1)	- Venous thromboembolism
Hepatic	10%	(n=1)	- Liver enzyme changes
Renal	10%	(n=1)	- Renal tubular injury - Hematuria/proteinuria - Nephritis

Acute myocardial injury is the most commonly described cardiovascular (CV) complication in COVID-19 with 30% with one (n=3) articles found in the literature, being found both in patients in the acute phase of the disease and after being discharged from the hospital (n =2) Articles that mention, in addition to cardiac injuries, myocarditis and pericarditis are also presented.

It was also observed that in one (n=2) article in the acute phase of the disease, it was possible to identify edema of the bronchial mucosa and bronchopneumonia, these being part of the symptoms identified in a hospital in Wuhan, which motivated the search for more information about the new disease that affected the population at the time.

Psychological impairment was addressed in n=2 mentioned in Chart 1. According to the scale used in the study, the feeling of loneliness was the most mentioned.

The complication of the neurological system was found in n=2 articles, one of these studies being carried out in a reference hospital for the treatment of COVID-19 in the state of São Paulo. The main symptoms presented were:

stroke, hemorrhage, encephalopathy, anosmia, ageusia, and neuromuscular disorders.

With regard to functional impairments, n = 2 studies highlight that in the acute phase of the disease, the most prevalent impairments were imbalance in the orthostatic position and inability to carry out daily activities.

The fragility of the psychological system was addressed in n=2 articles, which address the use of scales to measure the degree of commitment to psychological, social and economic variables, with spirituality, emotional loneliness and social loneliness being psychological. The economic and social ones were hours of communication on social media, neighborhood safety, job security and income. Among them, the ones that most prevailed according to the study were social and emotional loneliness.

The alterations in one of n=1 article of the metabolic, hematological, hepatic and renal system the symptoms presented more prevalent in the acute phase are mentioned pancreatic dysfunctions, venous thromboembolism, alterations in the hepatic enzymes, renal tubular injuries, hematuria, proteinuria and nephritis.

Quadro 2. Artigos (N=4) que relataram Síndrome pós-infecção pela doença COVID-19. Rio de Janeiro, RJ, Brasil 2021

Commitments	Percentage	Number of articles	Complications
Respiratory	40%	(n=4)	- Dyspnoea - Fibrosis
Cardiological	20%	(n=2)	- Acute myocardial infarction - Myocarditis - Arrhythmia
Locomotor	10%	(n=1)	- Functional commitment - Inability to carry out daily activities
Metabolic	10%	(n=1)	- Dysfunction

When evaluating the data regarding the complications presented by patients after infection with COVID-19, we have the respiratory system with (n=4) articles, showing that the lungs are constantly physiologically impaired. Ground-glass opacity is frequently reported in studies. Persistent respiratory disorders occur, the severity of the infection and previous health status are

the main determinants of long-term radiological and functional impairment.

When compared to cardiological complications in the acute phase and post-COVID-19 infection, we have acute myocardial infarction and myocarditis that appear in both phases. Being demonstrated in one (n=2) articles; arrhythmia is present only after infection by the virus⁹⁻¹¹.

The functional impairment presented after infection is cited related to the inability to perform daily activities, being mentioned in one (n=1) article, as shown in Chart 2.

Functional impairment appeared in one (n=1) article in the initial phase of the disease, which caused disabilities, such as: imbalance in the orthostatic position, due to the patient presenting myalgia and arthralgia. In individuals after hospital discharge, the most commonly reported damage was the inability to perform daily activities. The instrument used to assess these impairments was the Short Physical Performance Battery Scale (SPPB), which has the following parameters to be evaluated: walking speed of

4 meters, lifting a chair with 5 repetitions. A score greater than 10 is the expected value for healthy individuals.

Extrapulmonary complications have been frequently identified in the studies evaluated for writing this review, including the metabolic, hematological, hepatic and renal systems. The effect of COVID-19 is seen to extend far beyond the lungs.

After separating the data from the articles in the two tables presented above, the findings of these studies were organized as follows in Table 3, which presents the authors, year of publication, objective, conclusion and journals. And then the data were discussed approaching the evidence related to each complication.

Chart 3. Selected studies, separated by author, year, main findings and journals. Rio de Janeiro, RJ, Brazil, 2021

No.	Authors and Year	Main findings	Journal
01	Ayoubkhan, d.; et al., 2021.	Analyzed dysfunctions in patients after discharge from COVID and who returned for new hospitalizations, respiratory disease, cardiovascular disease and diabetes are observed.	The BMJ
02	Bellan, m.; et al., 2021.	As a post-COVID-19 outcome, it includes severe impairment of lung function saturation less than 80%, post-traumatic stress and functional impairment.	JAMA Network Open
03	Buja, l. m.; et al., 2020.	Analysis of autopsy reports in patients who died as a result of COVID-19 was performed and chronic inflammation and edema in the bronchial mucosa, ischemic myocardial injury, acute bronchopneumonia, pulmonary pathology and pericarditis were verified.	Elsevier – Cardiovascular Pathology
04	Fraser, e., 2021.	Venous thromboembolism was present in about a quarter of adult individuals admitted to intensive care units. In addition to complications related to the respiratory system, extrapulmonary ones are included, such as: diabetes, adverse cardiovascular events, liver and kidney dysfunctions.	The BMJ
05	Pan, Yan, j. lu, w.; Shan, m., 2021.	In this study, 17,078 questionnaires were delivered with 16,820 actual questionnaires collected, and 10,715 subjects (63.7%) were found to have moderate SHS. The subscale with physiological complications obtained the highest score, followed by the psychological and social subscales [The World Health Organization (WHO) defines SHS without organic pathological changes, but with functional changes].	Journal of Korean Academy of Nursing
06	Stuart-Neto a.; et al., 2020.	Among the neurological area, the most prevalent in a reference hospital for COVID-19 were: Encephalopathy, Stroke, Neuromuscular disorders and mild neurological symptoms.	Arquivos de Neuro-Psiquiatria
07	Tuason, t.; Güss, c. d.; Boyd, l 2021	The psychological issue is addressed, including the feeling of loneliness, especially emotional and social.	Plos One
08	Wadhwa, r. k.; et al., 2021.	It was noticed that in the pandemic there was a disproportionate increase in mortality due to heart and cerebrovascular problems, so it may lead to believe that it is a post-COVID consequence.	Circulation
09	Wu, x.; et al., 2021.	This study carried out an analysis of patients who had COVID-19, during the interval of 3, 6, 9 and 12 months after discharge, these individuals had no antecedent comorbidities. However, a subgroup had persistent pulmonary physiologic and radiographic abnormalities.	The Lancet – Respiratory Medicine
10	Yekedüz, E.; et al., 2020.	The study analyzed the finding of a patient during the acute process of the disease, observing areas of mild ground-glass opacity in the lung parenchyma. The patient was discharged after improvement of the condition, but died after 10 days due to cardiac complications.	Journal of Oncology Pharmacy Practice

The main complications reported in the literature resulting from the coronavirus were: respiratory, cardiovascular, functional impairment, psychological, neurological, metabolic, renal, hepatic and hematological system complications. One of the surveys highlights that, on average, of the 47,000 patients admitted for the new coronavirus, more than 14,000 were readmitted to the hospital due to some complication¹².

With regard to pulmonary complications, a study carried out in northern Italy showed that during the hospitalization of 66 patients, 27.7% did not require the use of oxygen. However, in 102 patients, 42.9% needed oxygen

through the nasal cannula or Venturi mask. 21 patients, that is, only 8.8% needed invasive mechanical ventilation and intensive care beds, as they had severe respiratory failure⁹.

Within the organs associated with dysfunction due to the disease COVID-19, we can mention that in 2021 individuals considered at low risk admitted to a hospital in the United Kingdom with the pathology, 33% had lung impairment, 32% heart, 12% kidneys and 10% liver. The author reports that these rates were higher than expected for the study¹².

An association was observed between the new coronavirus and the increased likelihood of acute kidney



injury, hemodialysis, insulin use, stroke, pulmonary embolism, myocarditis, arrhythmia and increased serum troponin values in veterans admitted to a hospital in the United States United with SARS-CoV 2, when compared to a control group of patients with seasonal influenza. The research also shows that of the patients who were readmitted, about 12% died¹².

Regarding cardiovascular complications, the process of diagnosis and treatment of a patient with COVID-19 is described. In the study, it is possible to see that the patient was discharged, but later died of heart problems. However, it should be considered that the patient already had underlying cardiovascular diseases, hypertension and diabetes¹¹.

Furthermore, there was a high incidence of cases with multifocal acute lesion of cardiac myocytes. In addition to these, some complications are included with less prevalence, but still present, such as: lymphocytic myocarditis, lymphocytic pericarditis, depletion of the splenic white pulp, among others¹³.

In respiratory complications, in order to understand and monitor the development and persistence of injuries, the main actions to be considered are radiological and functional impairment¹⁴. This same information about the radiological part was also observed in another similar study, justifying the importance of attention and continued care for these patients¹⁵.

All participants in this study were hospitalized in the acute phase of the disease at a reference hospital for the treatment of the new coronavirus, at a University Hospital in the State of São Paulo; consultation with a neurologist was requested for 89 of the 1,209 patients hospitalized within 30 days. The most common comorbidities among them are type II diabetes mellitus and systemic arterial hypertension. The main signs presented were encephalopathy, stroke, neuromuscular disorders and mild neurological symptoms¹⁶.

It is observed that the post-COVID-19 infection syndrome has caused concern to researchers. An association between the disease and increased chances of a stroke, myocarditis, arrhythmia, increased troponin, acute kidney injury requiring hemodialysis, pulmonary embolism, insulin use. These occurrences were found in patients infected with SARS-CoV-2, being compared with a group of patients with seasonal flu. Compared to the general population, this study found that individuals who were discharged after acute post-COVID-19 syndrome have increased rates of multiple organ dysfunction with a higher prevalence of respiratory and cardio-metabolic system impairment¹²⁻¹⁵.

In this pandemic period, a study carried out in the United States showed a significant increase in the number of deaths from cardiovascular and cerebrovascular complications compared to the previous year. 339,076 cardiac and 76,767 cerebrovascular deaths from March to August 2020 compared to 321,218 and 72,190 deaths during the same months in 2019. For both cardiac and cerebrovascular deaths, Black, Asian and Hispanic populations showed a relatively greater increase compared with the white and non-Hispanic population¹⁷. Regarding functional impairment, it is noteworthy that more than 50%

of patients had low performance in the functional part. This test was carried out with the intention of predicting future impacts on the performance of basic activities of daily living. It is also important to mention the information that more than 17% reported signs and symptoms related to post-traumatic stress during the tests of psychological symptoms⁹.

Following the same line, another research confirms the presence of psychological symptoms, focusing on understanding well-being, it was noticed that the coronavirus triggered and/or worsened the situations of social loneliness. This loneliness is directly related to the COVID-19 pandemic, as one of the main strategies used against the virus was social isolation, causing unimaginable impacts on the mental health of the entire population¹⁰.

However, the data presented in the second study showed factors that contributed to the population having this psychological aggravation, such as: lack of information and effective treatment for the disease, rapid dissemination by droplets/aerosols when in close contact, lack of prevention materials in the early stage of pathology. These conditions generated a certain panic and anxiety causing an emotional imbalance resulting in a fragile psychological health condition¹⁸. For patients hospitalized and infected by COVID-19, the psychological therapy carried out was in the context of emotional strengthening and information from their family members via telephone¹⁹⁻²¹.

Health care must be present in all sectors and departments, not just in health departments, especially during the current moment of the pandemic. It is essential to carry out a greater panorama for the population that has a high risk of contracting SARS-CoV-2 and/or that is more likely to develop complications^{18,20,21}.

Finally, the results made it possible to identify gaps in knowledge, especially in relation to studies that demonstrate the prevention of such complications and sequelae left after treatment of the disease, that is, after hospital discharge. Most of the articles found highlight complications presented during the manifestation of the disease in the acute phase.

Conclusion

It is concluded that COVID-19 is highly relevant for the appearance and development of complications, mainly cardiovascular, respiratory, renal, neurological and psychological. We still do not know how long these complications can affect patients, and whether the sequelae will be temporary or permanent. In this sense, we understand that the Unified Health System needs to be prepared to continue assisting these individuals in the different levels of health care, and that for comprehensive and effective care, multidisciplinary follow-up will be necessary.

It is worth noting that special attention must be taken into account, psychological factors, as the pandemic has drastically affected the mental health of the entire population, from users of health services, even professionals who are working on the front line.



As recommendations for future work, we mention conducting research to monitor the post-COVID-19 syndrome, as the careful follow-up of these patients will allow a more detailed definition of the real complications

and their duration. The assent of the study limitation was the scarce publication of the theme, as it is a new infectious disease.

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