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An integrative review of sequelae of COVID-19

Uma revisão integrativa das sequelas da COVID-19

Una revisión integradora de las secuelas del COVID-19

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ABSTRACT

Objective: To identify, in the literature available, the health sequelae developed by the population affected by COVID-19. **Methods:** This is an integrative review of publications retrieved from Medline via PubMed and the Regional Portal of the Virtual Health Library (Biblioteca Virtual em Saúde – BVS) in April 2021 that answered the research question: What are the main health sequelae developed by the population affected by COVID-19? The search strategy included the descriptors: Coronavirus Infections, COVID-19, SARS-COV-2, Complications, Disease, Adult, Long COVID. 348 publications were identified: 196 on BVS and 152 on PubMed. After analyzing the inclusion/exclusion criteria, 66 publications remained for full reading, with a final 27 articles included in the sample. **Results:** The selected evidence from the 27 articles allowed the identification of the main sequelae: neurological, mental health, cardiac, smell and taste, vascular, cutaneous, respiratory and gastrointestinal sequelae. The highest prevalence of neurological sequelae was found in women, whereas cardiac sequelae were found mostly in men; there was no difference in the prevalence of mental health symptoms between men and women. **Conclusion:** Based on these findings, the importance of long-term follow-up of people who had COVID-19 was highlighted since the symptoms developed as sequelae are not exclusive to this disease and can impact quality of life.

Descriptors: COVID-19; Post-COVID-19; long COVID-19; post-acute COVID-19; Sequelae.

RESUMO

Objetivo: *Identificar na literatura disponível as sequelas de saúde desenvolvidas pela população adoecida pela COVID-19.* ***Métodos:*** *Revisão integrativa com publicações recuperadas a partir do acesso ao Medline via PubMed e ao Portal Regional da Biblioteca Virtual em Saúde (BVS) em abril de 2021 que responderam à questão norteadora: Quais as principais sequelas de saúde desenvolvidas pela população adoecida pela COVID-19?. A estratégia de busca incluiu os descritores: Coronavirus Infections, COVID-19, SARS-COV-2, Complications, Disease, Adult, Long COVID. Identificaram-se 348 publicações, 196 da BVS e 152 no PubMed. Após análise dos critérios de inclusão/exclusão, permaneceram 66 publicações para leitura na íntegra, restando 27 artigos que compuseram a amostra.* ***Resultados:*** *As evidências selecionadas dos 27 artigos permitiram identificação*

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das principais sequelas: neurológicas, saúde mental, cardíacas, no olfato e paladar, vasculares, cutâneas, respiratórias e gastrointestinais. A maior prevalência de sequelas neurológicas ocorreu em mulheres, bem como as cardíacas nos homens; não havendo distinção da prevalência de sintomas de saúde mental entre homens e mulheres. ***Conclusão:*** *Com base nesses achados, evidenciou-se a importância do acompanhamento em longo prazo das pessoas que tiveram COVID-19, uma vez que os sintomas desenvolvidos como sequelas não são exclusivos dessa doença e podem impactar na qualidade de vida.*

Descritores: *COVID-19; Pós-COVID-19; COVID-19 longa; COVID-19 pós-agudo; Sequelas.*

RESUMEN

Objetivo: *Identificar en la literatura disponible las secuelas de salud desarrolladas por la población enfermada por COVID-19.* ***Métodos:*** *Revisión integradora con publicaciones recuperadas a partir del acceso al Medline por PubMed y al Portal Regional de la Biblioteca Virtual en Salud (BVS) en abril de 2021 que contestaron a la cuestión norteadora: ¿Cuáles las principales secuelas de salud desarrolladas por la población enfermada por COVID-19?. La estrategia de búsqueda incluyó los descriptores: Coronavirus Infections, COVID-19, SAR-COV-2, Complications, Desease, Adult, Long COVID. Fueron identificadas 348 publicaciones, 196 de la BVS Y 152 en PubMed. Después del análisis de los criterios de inclusión/exclusión, permanecieron 66 publicaciones para lectura completa, restando 27 artículos que compusieron la muestra.* ***Resultados:*** *Las evidencias seleccionadas de los 27 artículos permitieron la identificación de las principales secuelas: neurológicas, salud mental, cardíacas, en el olfato y paladar, vasculares, cutáneas, respiratorias y gastrointestinales. La mayor prevalencia de secuelas neurológicas ocurrió en mujeres, y las cardíacas en los hombres; no habiendo distinción de la prevalencia de síntomas de salud mental entre hombres y mujeres.* ***Conclusión:*** *Con base en estos hallazgos, se evidenció la importancia del acompañamiento a largo plazo de las personas que tuvieron COVID-19, ya que los síntomas desarrollados como secuelas no son exclusivos de esta enfermedad y pueden impactar en la calidad de vida.*

Descriptores: *COVID-19; Post-COVID-19; COVID-19 de Larga Duración; COVID-19 Pos-agudo; Secuelas.*

INTRODUCTION

Since the first manifestations of the new coronavirus (SARS-CoV-2) in December 2019 in the city of Wuhan, China, the infection quickly spread to several countries due to its high rate of infectivity[1]. Since then, the disease caused by this agent was renamed Coronavirus Disease - 2019 (COVID-19) on March 11, 2020, and the numerous records of community transmissions led the World Health Organization (WHO) to declare the situation a pandemic[2].

Currently, the number of recorded cases of COVID-19 exceeds 529 million, with more than six million deaths worldwide. In Brazil, these numbers are around 31 million confirmed cases and 667 thousand deaths[3], with a large number of people who have had COVID-19 and who, despite being cured, may be affected with sequelae.

The clinical aspects of COVID-19 may vary from person to person; some may be asymptomatic, others develop mild symptoms and part of the population progresses to a severe form of the disease, presenting with Severe Acute Respiratory Syndrome (SARS) and thus requiring hospitalization and major interventions[4].

In moderate and severe cases, the disease can affect the body as a whole, causing acute damage in the medium or long term[5]. The impacts on the health of the infected patient can be diverse, which increases the concern of the health sectors and leads to higher care costs associated with this population group[6]. Another fundamental issue is monitoring the progress of these patients in order to offer rapid rehabilitation and improve quality of life and health promotion[6].

A study carried out in the United Kingdom with 1,077 patients revealed that in six months after infection by COVID-19, only 29% of the patients felt recovered, 20% persisted with some sequelae and about 19% had some alteration related to their occupational capacity, mostly among women[7]. A systematic review with meta-analysis carried out in 2021 showed that 80% of those infected with SARS-CoV-2 had at least one post-COVID-19 sequela[8].

However, the long-term post-COVID-19 sequelae are still poorly understood, and studies have sought to synthesize them according to the organic system[9-15]. However, the effects that COVID-19 can have after the period of the acute phase of the disease in the body and their duration are still under investigation[16].

Therefore, the reporting of these situations may contribute to the increase of chronic health conditions, which makes it necessary to have a persistent look at the reported issue for decision-making and the development of health promotion actions for the population[16]. Thus, in order to contribute to a synthesis of information on the subject, this study aimed to identify in the available literature the health sequelae developed by the population affected by COVID-19.

METHODS

This is an integrative review that aimed to gather and synthesize the best available evidence on acute or chronic sequelae resulting from COVID-19 in studies published between March 2020 and March 2021. The specific research question of this review was: What are the main health sequelae developed by the population affected by COVID-19?

The study was developed in five stages, which included: 1) Identification of the problem and definition of the research question; 2) Literature search and data collection; 3) Data evaluation according to inclusion and exclusion criteria; 4) Critical analysis of the data; 5) Presentation of results and integrative review[17].

Searches were carried out on the following databases: Medical Literature Analysis and Retrieval System Online (MEDLINE), via PubMed, and the Regional Portal of the Virtual Health Library (*Biblioteca Virtual em Saúde – BVS*), which includes the *Índice Bibliográfico Español en Ciencias de la Salud* (IBECS) and Latin American and the Caribbean Literature on Health Sciences (*Literatura Latino - Americana e do Caribe em Ciências da Saúde – LILACS*) databases. However, gray literature was not used in this review.

The search strategy included the following descriptors: coronavirus infections, COVID-19, SARS-COV-2, complications, disease, adult, long covid, combined using the Boolean operators AND and OR. The descriptors were selected at the time the work was prepared, a period in which the scientific literature on the subject was still scarce.

Inclusion criteria were: studies of any type written in Portuguese, Spanish or English addressing sequelae considered as signs and symptoms lasting more than 30 days. The exclusion criteria were: studies that were not fully available, letters, editorials from scientific journals and publications that did not answer the specific question of this review.

Thus, the search initially identified 348 publications, 196 of which were retrieved from BVS and 152 from PubMed. After analyzing the inclusion/exclusion criteria and the screening phase (reading of title and abstracts), only 66 of the publications remained for full reading. After full reading, 27 articles were included in the final sample of this review and had their data extracted. The search steps are described in Figure 1.

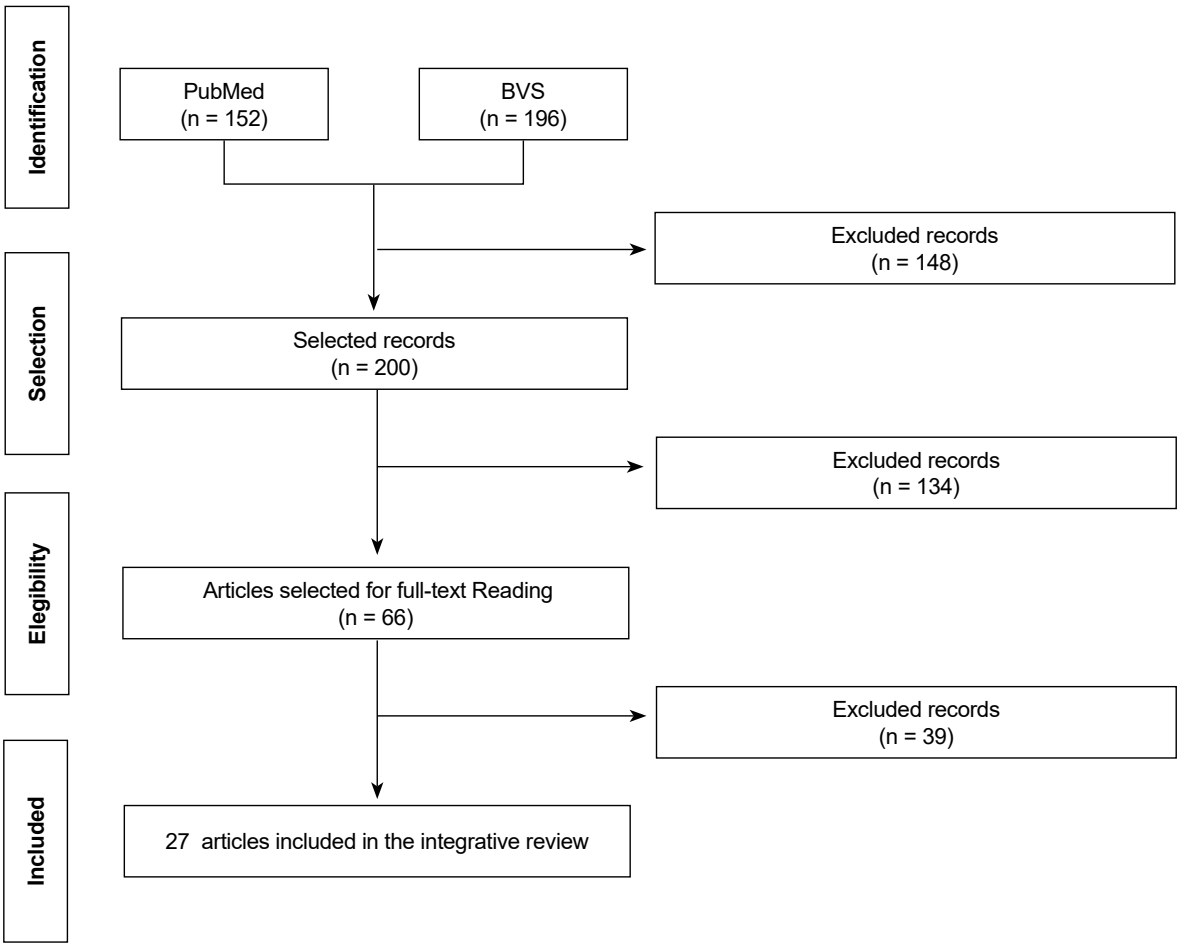

Figure 1 - Flowchart of articles included in the review.
Source: Own elaboration.

RESULTS

Of the 27 studies included in this review, 40.74% (n=11) are observational studies[7,18-27], 33.33% (n=9) are systematic reviews[9,11,12,14,28,29,30,31,32], 22.22% (n=6) are literature reviews[10,13,15,33,34,35] and 3.70% (n=1) are case series[36]. As for the year of publication, 81.48% (n=22)[9.-14,18-24,28,29,30-36] of the studies were published in 2020 and 18.52% (n=5)[7,15,25,26,27] were published in 2021.

As for the place where the research was carried out, 18.52% (n=5) of the studies took place in Italy[9,22,28,32,33] while 18.52% (n=5) were conducted in the United Kingdom[7,10,26,27,30], followed by the United States[13,19,21,36] with 14.81% (n=4) of the publications. Spain[18,20], China[11,24], and Brazil[14,35] accounted for 7.41% (n=2) of the articles each. Germany[23], Australia[31], Colombia[15], South Korea[12], United Arab Emirates[25], Philippines[29] and Sweden[34] contributed with 3.70% of the studies each (n=1).

The sequelae of COVID-19 identified in the studies include neurological[12,13,19,20,22,26,29,33,34], mental health[7,27,28,30], cardiac[9,23,25,35], smell and taste[14,18,31], vascular[21,32], cutaneous[15,36], respiratory[10,24], and gastrointestinal manifestations[11]. The vast majority of studies (88.89%) portray these conditions in patients who presented moderate to severe cases and only a portion of them, 11.11% (n=3)[14,18,31], reported these manifestations in patients with mild to moderate cases.

Within the population covered by the studies, the manifestations ranged from mild to severe symptoms in patients who presented neurological sequelae[12,13,19,20,22,26,29,33,34]. The highest prevalence rates of these sequelae were found in women[13,19,26,29] and individuals aged between 30 and 50 years[12,22,26,29,33,34] who needed admission to intensive care units (ICU).

As for mental health, there was no difference in the prevalence of symptoms between men and women[27,28,30], and the predominant age range of people with this condition was between 30 and 50 years old[7,27,28]. Also, the diagnoses of sequelae that involved mental health were more common in those patients who had been hospitalized. However, studies emphasize that the incidence of diagnoses of some mental health problem increased even in cases of COVID-19 that did not require hospitalization[7,27,28,30].

As for cardiac sequelae[9,23,25,35], there was a higher prevalence of this condition in men[23,25] aged between 30 and 50 years with moderate to severe COVID-19. These sequelae result from several mechanisms, ranging from direct injury to secondary complications triggered by SARS-CoV-2 infection, which must be quickly identified for proper management[9,23,25,35].

Changes related to smell and taste[14,18,31] were mostly present in patients with mild to moderate COVID-19, with a higher prevalence rate among women aged 30 to 50 years.

Vascular sequelae[21,32] prevailed in men aged between 30 and 50 years[21], with cases reported in individuals up to 77 years of age[32]. This condition was a frequent complication in patients with COVID-19 who required hospitalization.

With regard to cutaneous alterations[15,36], the selected articles did not report any difference in prevalence rates between men and women, but the age ranges with the highest occurrence of these manifestations were between 30 and 50 years old[15] and up to 77 years old[36].

The prevalence of respiratory sequelae[10,24] and gastrointestinal complications[11] did not differ between men and women, but there was a predominance of patients aged between 30 and 50 years. Table I depicts the main characteristics of the selected studies.

Table I - Characteristics of the studies included in the review until March 2021.

Identification of the studies	Title	Study place	Study design	Sequelae assessed
Evans RA, McAuley H, Harrison EM, Shikotra A, Singapuri A, Sereno M, et al., 2021	Physical, cognitive and mental health impacts of COVID-19 following hospitalization – a multi-centre prospective cohort study[7]	United Kingdom	Observational	Mental health: anxiety, depression, post-traumatic stress, sleep quality and fatigue
Sabatino J, Rosa S, Salvo GD, Indolfi C, 2020	Impact of cardiovascular risk profile on COVID-19 outcome. A meta-analysis[9]	Italy	Systematic Review	Cardiac: acute myocardial infarction, and possible
Ahmed H, Patel K, Greenwood DC, Halpin S, Lewthwaite P, Salawu A, et al., 2020	Long-term clinical outcomes in survivors of severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS) coronavirus outbreaks after hospitalization or ICU admission: a systematic review and meta-analysis[10]	United Kingdom	Systematic Review	Respiratory: reduced lung capacity and lower exercise capacity due to respiratory effort

Table I - Characteristics of the studies included in the review until March 2021. (Continuation)

Identification of the studies	Title	Study place	Study design	Sequelae assessed
Mao R, Qiu Y, He JS, Tan JY, Li XH, Liang J, et al. , 2020	*Manifestations and prognosis of gastrointestinal and liver involvement in patients with COVID-19: a systematic review and meta-analysis*[11]	China	Systematic Review	Gastrointestinal: possible liver damage
Choi Y, Lee MK, 2020	*Neuroimaging findings of brain MRI and CT in patients with COVID-19: A systematic review and meta-analysis*[12]	South Korea	Systematic Review	Neurological: stroke, intracranial hemorrhage, encephalopathies
Ghannam M, Alshaer Q, Al-Chalabi M, Zakarna L, Robertson J, Manousakis G, 2020	*Neurological involvement of coronavirus disease 2019: a systematic review*[13]	United States	Literature review	Neurological: stroke, intracranial hemorrhage, encephalopathies and Guillain-Barré syndrome
Costa KV, Carnaúba ATL, Rocha KW, Andrade KCLD, Ferreira S, Menezes PDL, 2020	*Olfactory and taste disorders in COVID-19: a systematic review* [14]	Brazil	Systematic Review	Smell and taste: anosmia and ageusia
González GF, Correa CC,Contreras P, 2021	*Manifestaciones cutáneas en pacientes con COVID-19: características clínicas y mecanismos fisiopatológicos postulados* [15]	Colombia	Literature review	Cutaneous: viral rashes, generalized urticaria
Barón-Sánchez J, Santiago C, Martin GG-S, Arca R, Fernandez R, 2020	*Afectación del sentido del olfato y el gusto en la enfermedad leve por coronavirus (COVID-19) en pacientes espanoles*[18]	Spain	Observational	Smell and taste: anosmia and ageusia
Sweid A, Hammoud B, Bekelis K, Missios S, Tjoumakaris SI, Gooch MR, et al., 2020	*Cerebral ischemic and hemorrhagic complications of coronavirus disease 2019*[19]	United States	Observational	Neurological: stroke
Abenza-Abildua MJ, Ramírez-Prieto MT, Moreno-Zabaleta R, Arenas-Valls N, Salvador-Maya MA, Algarra-Lucas C, et al. 2020	*Complicaciones neurológicas en pacientes críticos por SARS-CoV-2*[20]	Spain	Observational	Neurological: stroke, encephalopathies
Al-Samkari H, Leaf, RSK, Dzik WH., Carlson JC, Fogerty AE, Waheed A, et al., 2020	*COVID-19 and coagulation: bleeding and thrombotic manifestations of SARS-CoV-2 infection*[21]	United States	Observational	Vascular: venous thromboembolism
Pilotto A, Cristillo V, Piccinelli SC, Zoppi N, Bonzi G, Sattin D, et al., 2020	*COVID-19 severity impacts on long-term neurological manifestation after hospitalization*[22]	Italy	Observational	Neurological: fatigue, headache, memory impairment, and focal deficits
Puntmann VO, Carerj ML, Wieters I, Fahim M, Arendt C, Hoffmann J, et al., 2020	*Outcomes of cardiovascular magnetic resonance imaging in patients recently recovered from coronavirus disease 2019 (COVID-19)*[23]	Germany	Observational	Cardiac: myocarditis, acute myocardial infarction, and possible arrhythmias
Liu K, Zhang W, Yang Y, Zhang J, Li Y, Chen Y, 2020	*Respiratory rehabilitation in elderly patients with COVID-19: A randomized controlled study*[24]	China	Observational	Respiratory: reduced lung capacity and lower exercise capacity due to respiratory effort
Liaqat A, Ali-Khan RS, Asad M, Rafique Z, 2021	*Evaluation of myocardial injury patterns and ST changes among critical and noncritical patients with coronavirus19 disease*[25]	United Arab Emirates	Observational	Cardiac: right ventricular dilation, acute myocardial infarction, and possible arrhythmias
Sigfrid L, Drake TM, Pauley E, Jesudason EC, Olliaro P, Lim WS, et al, 2021	*Long COVID in adults discharged from UK hospitals after COVID-19: A prospective, multicentre cohort study using the ISARIC WHO Clinical Characterization Protocol* [26]	United Kingdom	Observational	Neurological: Fatigue, myalgia, weakness, reduced mobility
Taquet M, Geddes JR, Harrison PJ, 2021	*Six-month neurological and psychiatric outcomes in 236,379 survivors of COVID-19*[27]	United Kingdom	Observational	Mental health: fatigue, headache, memory impairment, focal deficits, mood swings

Table I - Characteristics of the studies included in the review until March 2021. (Continuation)

Identification of the studies	Title	Study place	Study design	Sequelae assessed
Cipriani G, Danti S, Nuti A, Carlesi C, Lucetti C, Fiorino MD, 2020	*A complication of coronavirus disease 2019: delirium*[28]	Italy	Systematic Review	Mental health: delirium
Collantes MEV, Espiritu AI, Sy MCC, Anlacan VMM, Jamora RDG, 2020	*Neurological manifestations in COVID-19 infection: a systematic review and meta-analysis*[29]	Philippines	Systematic Review	Neurological: fatigue, headache, memory impairment, focal deficits, myalgia, encephalopathies, and Guillain-Barré syndrome
Rogers JP, Chesney E, Oliver D, Pollak TA, McGuire P, Fusar-Poli P, et al., 2020	*Psychiatric and neuropsychiatric presentations associated with severe coronavirus infections: a systematic review and meta-analysis with comparison to the COVID-19 pandemic*[30]	United Kingdom	Systematic Review	Mental health: mood swings, anxiety, irritability
Agyeman AA, Chin KL, Landersdorfer CB, Liew D, Ofori-Asenso R, 2020	*Smell and taste dysfunction in patients with COVID-19: A systematic review and meta-analysis* [31]	Australia	Systematic Review	Smell and taste: anosmia and ageusia
Porfidia A, Valeriani E, Pola R, Porreca E, Rutjes AW, Di Nisio M, 2020	*Venous thromboembolism in patients with COVID-19: Systematic review and meta-analysis*[32]	Italy	Systematic Review	Vascular: venous thromboembolism
Leonardi M, Padovani A, McArthur JC, 2020	*Neurological manifestations associated with COVID19: a review and a call for action*[33]	Italy	Literature review	Neurological: headache, stroke
Almqvist J, Granberg T, Tzortzakakis A, Klironomos S, Kollia E, Öhberg C, et al., 2020	*Neurological manifestations of coronavirus infections – a systematic review*[34]	Sweden	Literature review	Neurological: fatigue, headache, memory impairment, focal deficits, stroke, intracranial hemorrhage, encephalopathies, and Guillain-Barré syndrome
Costa IBSDS, Bittar CS, Rizk SI, Araújo-Filho AED, Santos KAQ, Machado TIV, et al., 2020	The heart and COVID-19: what the cardiologist needs to know[35]	Brazil	Literature review	Cardiac: possible arrhythmias, myocarditis
Lee DS, Mirmirani P, McCleskey P, Mehrpouya M, Gorouhi F, 2020	*Cutaneous manifestations of COVID-19: a systematic review and analysis of individual patient-level data*[36]	United States	Case series	Cutaneous: viral rashes, generalized urticaria

DISCUSSION

This review shows the little knowledge about the sequelae developed by patients after COVID-19 infection and many aspects of the disease. However, we found that injuries that have already been identified are highly likely to impact the population's quality of life[22,26]. Studies have estimated that the global prevalence of post-COVID-19 infection ranges 43% to 80%[8,37,38].

Of the studies included in this review, those addressing neurological problems were frequent and described the presence of fatigue, headache, memory and mood alterations, reduced mobility, myalgia and focal deficits[22,26,27,29,34]. In other recently published studies, fatigue was the most reported symptom in patients with post-COVID-19 symptoms, with a prevalence of circa 23%, followed by dyspnea – approximately 18% – and memory problems – around 14%[8,37,38].

In addition, there are reports of the presence of some possible serious complications, such as stroke, intracranial hemorrhage, encephalopathies and Guillain-Barré syndrome[12,13,29,34]. These situations should be highlighted as they compromise patients' daily activities. These complications may be related to the direct effect of infection, cerebrovascular disease (including hypercoagulation), physiological impairment (hypoxia), medication side effects, and social aspects of having a potentially fatal disease[8].

It should be noted that the rates of prevalence of neurological sequelae were higher in women[13,18,19], and the mean age of patients was above 57 years[12,13,18,19]. These findings are in agreement with the age range of the most severe cases of COVID-19, which is close to 60 years, and which explains the higher frequency of complications[39].

Abnormal findings on echocardiography, right ventricular dilation, myocarditis, acute myocardial infarction, tachycardia[37] and possible arrhythmias[9,25,35] were the most reported cardiac sequelae, which highlights the need for of a persistent follow-up of this patient after the acute phase of COVID-19.

With regard to smell and taste, cases of anosmia and ageusia were identified in some patients who had already recovered from COVID-19[14,18]. This situation, as reported in several studies, was more persistent in women with mild to moderate disease and with a mean age of 50 years[14,18,31,8]. Little is known about how olfactory dysfunction can become a sequela[8]. However, the symptom is largely reported. Studies indicate that more than 20% of the patients studied presented loss of smell after approximately three months[38,40]. But everything indicates that olfactory dysfunction is more common in patients (approximately 13%) with a mild form of COVID-19 and that symptoms persist longer in this group (on average 30 days)[8,37].

Reduced lung capacity and lower exercise capacity due to respiratory effort[10,24] were also some of the reported respiratory sequelae. This is in agreement with data presented in a study carried out in the United Kingdom with 327 participants, mostly women under 50 years old, which reinforced the need for interventions and rehabilitation for these conditions. This is because 93% of the population persisted with some respiratory symptoms, the most reported being shortness of breath and dyspnea[26,37]. A systematic review showed that a large percentage of patients still had respiratory symptoms after three months: 71% of patients still had shortness of breath, 29% had cough and 24% had chest pain[40].

Mood changes, anxiety, irritability and possible delirium were symptoms of mental health impairment[27,28,30]. This corroborates recent studies that point out that in the period after Severe Acute Respiratory Syndrome (SARS) and Middle East Respiratory Syndrome (MERS) there were also reports of possible changes related to mental health[30,41]. These situations highlight the need and importance of psychological follow-up for these patients[42].

The reporting of vascular alterations, with a high incidence of patients with venous thromboembolism (VTE)[21,32], should also be highlighted. In addition, there is also presence of cutaneous manifestations, such as viral rashes and generalized urticaria, persistent in the trunk[15,36]. Finally, gastrointestinal changes, such as diarrhea and possible liver damage, also occurred in patients who had COVID-19 and should be evaluated[11].

Recently, the sequelae of COVID-19 described in this work could characterize the “long COVID” (or chronic COVID-19), which has a heterogeneous definition of subacute and/or chronic symptoms and signs after the acute phase of the infection and whose duration may vary (usually 12 weeks or more). However, it should be noted that the presence of this syndrome in an individual does not depend on the initial severity of the infection[40,43,44]. Due to the extreme clinical heterogeneity of long-term COVID and also the lack of a shared and specific definition of the disease, it is very difficult to know the real prevalence and incidence of this condition. However, the most common clinical symptoms reported are fatigue, dyspnea, cough, chest pain, headache, altered mental and cognitive status, and olfactory dysfunction. These symptoms corroborate the present review[40,43,44].

Some risk factors for the development of long-term COVID-19 were advanced age, high body mass index, comorbidities, specific symptoms of acute COVID-19 (especially dyspnea), number of symptoms in the acute phase, and female gender[40,43,44].

The present study had some limitations, such as the non-inclusion of gray literature, the non-saturation of the literature on the subject, and the lack of knowledge of many aspects of the pathology of the disease. Also, the scientific literature on COVID-19 is updated very quickly, so some descriptors used in the work may no longer reflect the best search. In addition, there are low-quality publications with very small populations, the duration of the identified sequelae differs greatly from one study to another or is not yet clarified, and there is also not enough follow-up time to determine whether these conditions are really irreversible, thus not allowing a conclusion to be made at this time.

However, this seems to be reasonable as the COVID-19 pandemic started recently and several studies are still ongoing. More long-term observational studies are needed to reach reliable conclusions with regard to helping general practitioners recognize more of the sequelae of COVID-19. But the evidence summarized in this work, which has been published in relevant journals, describes the information available so far.

This review highlighted the importance of long-term follow-up of people who have had COVID-19 since the symptoms developed are not uncommon and can affect the quality of life of these people in addition to economically impacting health systems. Therefore, the need for long-term follow-up of patients, with a view to health promotion and prevention actions, is very important. Access to this knowledge by health professionals and affected populations allows each individual to have greater control over their own health and its determinants, which is at the heart of health promotion[44]. Such information can also help the planning of health policies and the care of this population, adding better quality to the service provided by the health system.

Based on these findings, the importance of long-term follow-up of people who have had COVID-19 is emphasized since the symptoms developed are not exclusive to this disease and can impact the quality of life of these individuals. Thus, more studies are needed to better understand the pathophysiology, symptoms and correct management of patients.

CONCLUSION

The evidence gathered in this research allowed us to synthesize the knowledge of the sequelae developed after the COVID-19 infection, the main ones being neurological, cardiac, smell and taste, vascular, cutaneous, respiratory, gastrointestinal and mental health alterations. In most of the studies analyzed, the most affected by some change in health were patients who presented moderate to severe disease, with women being the most affected.

CONTRIBUTIONS

Bianca Fontana Aguiar and **Jolline Lind** contributed to the study conception and design; acquisition, analysis and interpretation of data; and writing and/or revision of the manuscript. **Moacir Pires Ramos, Harli Pasquini-Netto, Beatriz Böger** and **Jaime Luis Lopes Rocha** contributed to the acquisition, analysis and interpretation of data; and writing and/or revision of the manuscript. **Rafaella Tiepo Borges Abatti** contributed to the acquisition, analysis and interpretation of data. All authors have approved the version to be published and are responsible for its content and integrity.

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