

Long Covid-19, Radiological Findings, and Its Management: A Systematic Review

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ABSTRACT

Background: COVID-19 is a disease caused by SARS-CoV-2 and has numerous clinical spectrums. Mild respiratory infection is the common clinical manifestation of COVID-19, and the less common is pneumonia accompanied by fever, cough, and breathing difficulty. Long COVID can be defined as prolonged signs and symptoms which cannot be explained for other reasons 4 weeks after being diagnosed with SARS-CoV-2. This study aimed to describe the cause of illness is confirmed or suspected COVID-19 patients, specifically on long COVID.

Subjects and Method: We performed literature searches of the latest articles with Medline, CINAHL (EBSCO), Global Health (Ovid), WHO Global Research on COVID-19 database, LitCovid and Google Scholar databases published from 2019 to 2020. Two reviewers searched all articles independently (P and W, with 7 and 10 years of experience, respectively). We conducted a systematic review to provide recent evidence of symptoms and complications in long COVID. We followed PRISMA guidelines.

Results: A total of 22 papers was identified and screened for eligibility from medical databases. There were 15 papers included in this review. Reason for the continuous symptoms covid an extent of organ destruction, continuous response of chronic inflammation or immunology reaction, non-specific effect of hospital admission, some critical disease, post ICU syndrome, complications from COVID-19 infection, morbidities and adverse effects of medications used. Common symptoms are fatigue, shortness of breath, cough, chest pain, palpitations, dizziness, arthralgia, myalgia and weakness, sleep problems, sharp pain, gastrointestinal problems, rash and hair loss, impaired balance and ataxia, neurologic problems such as dementia, concentration disorders and poor quality of life.

Conclusion: The incidence of long-term manifestations of COVID-19 has been increasing and systemic clinical symptoms affect many organs and systems. This can be due to numerous reasons like post-ICU syndrome, post-viral fatigue syndrome, permanent organ deterioration or others.

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BACKGROUND

Worldwide pandemic due to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has started since 2019 (Proal et al., 2021). As COVID-19 widespread continues, long COVID understanding is progressively immense. Symptoms such as persistent fatigue, breathlessness, brain fog and depression seem to weaken millions of individuals globally. However, knowledge and research on this subject are still limited. "Long COVID" has become a phenomenon, a denomination described by the patient population, also as famous as Post COVID-19 disorder. Post-COVID-19 disease or Covid long-hauler. Current data from the United Kingdom revealed that the highest prevalence of long COVID after 3 months was people aged between 25 and 34 years old and lowest in those aged from 2 to 11 years old (7.4%) (Osmanov et al., 2021).

World Health Organization (WHO) stated that nearly 80-85% of COVID-19 infections are mild or without any symptom and relieve like common flu, 10-15% are serious, demanding hospitalization or oxygen supplementation and 5% have the need of intensive care and mechanical ventilation. Normally, most patients show fully recovery in 3-4 weeks of COVID-19 infection, but few of them continue to have its persistent effects and develop extended illness or complications, which can result in lasting health issues (Garg et al., 2021).

Scientific and clinical evidence has evolved in terms of subacute and long-term effects of COVID-19, affecting multiple organ systems. Previous reports suggest residual effects of SARS-CoV-2 infection, like myalgia, shortness of breath, chest pain, cognitive problems, arthralgia and impaired life quality (Nalbandian et al., 2021). Long COVID will affect most of the body's systems so that a diversified method is needed to efficiently handle the physical, cognitive,

psychological, and social aspects of this health problem (Berenguera et al., 2021). Fatigue or muscle weakness was common at 6 and 12 months, and nearly half of patients reported at least one symptom after 12 months, such as insomnia, palpitations, joint pain, or chest pain (The Lancet, 2021). In this systematic review, we describe the course of the disease of patients in the confirmed or suspected COVID-19 populations, specifically on the long COVID.

SUBJECTS AND METHOD

1. Study design

We performed literature searches of the latest articles with PubMed, Google Scholar, and Cochrane Library databases published from 2019 to 2020 (2-year span) for articles which explained prolonged COVID-19 symptoms, using Boolean search strategies with the keywords "Coronavirus", "COVID-19", "SARS-CoV-2", "long COVID". We included quantitative and qualitative studies of adults experiencing symptomatic COVID-19 or post-COVID syndrome.

2. Data collection

We retrieved additional articles by a manual screening of the included study reference list and relevant review articles.

3. Data analysis

All articles are searched independently by two reviewers. They examined the appropriate study abstracts and assessed the eligibility criteria of the full paper. The consensus was carried out to resolve any disagreements. We used PRISMA guidelines in this systematic review.

RESULTS

1. Long COVID

Long COVID can be defined as patients who still have signs and symptoms that cannot be explained for other reasons 4 weeks after being diagnosed with SARS-Cov-2. Its approximate incidence is about 10%, and

signs as well as symptoms can persist for several months (Sisó-Almirall et al., 2021). This term, long COVID, was coined by Perego on the internet to represent the prolongation effects for weeks, even months after first being infected by beginning SARS-CoV-2, while 'long-hauler' is a term first introduced by Watson and Yong (Raveendran et al., 2021). CDC-10 defines long covid individuals or covid long haulers as people suffer from continuous side effects of covid-19 persisting more than 1 month after being infected.

2. Pathophysiology of “Long COVID”

Reason for continuous symptoms can be organ damage, extended injury and prolonged duration of organ recovery, continuous chronic inflammation (convalescent stage) or immune reactions/autoantibody production, infrequent continuous finding of the virus in the body, hospitalization's impact, some critical illnesses, post ICU syndrome, COVID-19 complication, morbidities, and adverse effects of medications used (Raveendran et al., 2021).

In the alveoli, chronic inflammation occurs because of continuous forming inflammatory cytokines and reactive organ species (ROS) released to adjacent tissue and blood flow. Endothelial impairment activates fibroblasts, leading to fibrotic alterations, endothelial injury, complement and platelet activations, platelet-leukocyte interlinkage inflammatory cytokines released, abnormal coagulant pathways, and hypoxia result in prolonged hyper inflammation and hypercoagulability, which increases the risk of thrombosis (Crook et al., 2021).

In the heart, a chronic inflammatory state results in myositis and leads to cardiomyocytes death. Postural orthostatic tachycardia syndrome caused by afferent autonomic nervous system disorder is the complication. Fibrosis results from long-term inflammation and cellular damage. Reduced

cell to cell adhesion results from damaged desmosomal proteins, while fibrotic alterations are followed by an increase in cardiac myofibroblasts (Crook et al., 2021).

The long term immune response leads to prolonged damaging neurons in the central nervous system. Hyperinflammation and hypercoagulability lead to an expanded chance of thrombotic occurrence. Damaging in the blood-brain barrier leads to pathological permeability, permitting blood acquired materials and leukocytes to invade brain parenchyma. Conclusion this outcome of chronic inflammation in the brain and brainstem are not only autonomic dysfunction but also cognitive impedance.

There are various processes promoting post-COVID-19 fatigue. A set of central, peripheral, and psychological components can generate persistent fatigue in long COVID. Long term fatigue can be due to chronic inflammation within the brain. In skeletal muscle, fatigue was caused not only by sarcolemma harm and fibre atrophy but also by various mental and social factors (Crook et al., 2021).

3. Common Symptoms in “Long COVID”

Extreme fatigue, shortness of breath, cough, chest pain, palpitations, dizziness, arthralgia, muscle ache as well as general weakness, sleep problems, sharp pain, gastrointestinal problems, rash or hair loss, impaired balance and ataxia, neurologic issues like dementia, concentration problems, and aggravated quality of life are commonly found in "Long COVID" patients (Raveendran et al., 2021). Sustained symptoms were also experienced by 64% of those suffering from COVID-19 (Aiyegbusi et al., 2021).

A study conducted by the UK government reported that fatigue was the most common symptom of individuals experience of long COVID, followed by breathing shortness, muscle ache, and smell loss

(Ayoubkhani et al., 2021). An international cohort study by Davis et al. (2021) in distinguishing long COVID shows that there are several symptoms of long COVID which are not commonly encountered, such as anaphylaxis and new allergic reactions, seizures, suicidality, alterations in sensitivity to medication, vision loss, hearing loss, and facial paralysis (Davis et al., 2021). A study performed in nurses with mild COVID-19, 26% had moderate to severe symptoms for 2 months, and 15% had moderate to severe symptoms for 8 months (Solomon et al., 2021).

In pediatric patients, Osmanov et al. (2021) revealed that a quarter of children and adolescents had persistent symptoms during follow-up, the most common being fatigue, insomnia and sensory problems. Nearly one in ten people suffered from a multi-system effect, with two or more types of prolonged symptoms at follow-up. Middle-aged children (6-18 years old) are at greater risk of sustained symptoms during follow-up (Osmanov et al., 2021).

Siso-Almirall et al. (2021) reported that fatigue was one of the commonest extra-respiratory symptoms of acute SARS-CoV-2 infection (41%). The study estimates that the incidence rates after 4, 8, and 12 weeks of infection were 35-45%, 30-77%, and 16-55%, respectively. The deep and persistent fatigue of some COVID-19 patients is characterized by chronic fatigue syndrome (CFS), which is experienced after other infections, such as SARS, MERS, and community-acquired pneumonia (Sisó-Almirall et al., 2021).

4. Radiological Findings of Patients with Long COVID

Studies of other viral infections involving lungs indicate that functional and radiological deterioration persists after hospital discharge (Solomon et al., 2021). Most patients will have deformities on the chest X-ray upon discharge, and it remains a

question when the best time to take a follow-up X-Ray and assess the resolution of this abnormality (Alarcón-Rodríguez et al., 2021). Han et al. (2021) study found that 40 of 114 participants (35%) recovering from severe pneumonia in COVID-19 experienced fibrotic changes in their lungs within 6 months; in this group, most fibrotic changes (22 of 40 [55%]) were observed in the 6-month follow-up CT (Solomon et al., 2021). In another study, 71% (39/55) of previously admitted patients for COVID-19 were found to have radiological abnormalities of varying degrees of severity on chest CT scans approximately 3 months after discharge (Aiyegbusi et al., 2021).

A recent meta-analysis of 60 studies on follow-up examinations after hospitalization for SARS-CoV-2, MERS, or influenza pneumonia showed inflammatory alterations (GGO or consolidation) in 40% and “fibrosis” (reticulation, distortion of pulmonary architecture, interlobular septum thickening, traction bronchiectasis, or honeycombing) in 56% of the examinations. The findings of few emphysema, cysts, and mosaic attenuation in some post COVID-19 patients indicate infection can occasionally lead to airflow obstruction (Solomon et al., 2021).

5. Management of Long COVID Patients

Therapy for long COVID patients needs a multidisciplinary approach, comprising assessment, symptomatic therapy, solving potential issues, physical therapy, occupational therapy, and psychological support. Symptomatic treatment can be cough suppressant and oral antibiotic for secondary infection with some symptoms like cough, pain, myalgia and another minor complaint. If any, the underlying cause of symptoms, such as lung embolism, stroke, coronary artery disease, must be treated according to standard protocols. Thorax physical therapy

and neurorehabilitation are important for those with lung and neuromuscular complications. As it is a novel disease, the understanding of long-term effects and alternative therapies continues to evolve. After being infected with SARS-CoV2, people may experience exacerbations of potential comorbidities such as diabetes, hypertension, and cardiovascular disease, requiring optimized treatment (Raveendran et al., 2021).

In a guideline approved by the British Thoracic Society, the algorithms for assessing COVID-19 survivors in the first 3 months after hospitalization are based upon the COVID-19 severity and ICU admission, and the therapy protocol for the severe and mild to moderate COVID-19 recommends a clinical evaluation and thorax radiograph after 12 weeks for all patients, along with consideration of PFT, 6MWT, sputum samples, and echocardiograms after clinical evaluation. Based on this 12-week examination, it is further suggested that chest high-resolution CT scan, CT pulmonary angiography, or an echocardiogram are required to be done, and patients are discharged based on follow-up care.

Follow-up chest examinations are not recommended to be performed in patients who did not show signs of pneumonia on imaging studies or in whom complete lung parenchyma complete resolution was documented during hospitalization (Alarcón-Rodríguez et al., 2021).

Conclusion

The long-term manifestations of COVID-19 are increasing, and systemic clinical symptoms affect many organs and systems. This can be due to numerous reasons like post-ICU syndrome, post-viral fatigue syndrome, permanent organ deterioration or others. Definite clinical evaluation can support the establishment of the diagnosis and management. Fibrosis and inflammatory changes are the two most common findings in post

COVID-19 infection patients. Since it is a novel disease, it is too soon to know the actual outcome.

AUTHOR CONTRIBUTION

All authors had equal contribution in collecting the articles about long COVID-19, radiological findings, and its management, and wrote the manuscript.

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CONFLICT OF INTEREST

None.

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