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**Musculoskeletal complications in long COVID-19: A systematic review**

Swarnakar R *et al*. Long COVID-19 musculoskeletal complications

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**Abstract**

BACKGROUND

Coronavirus disease 2019 (COVID-19) has crippled humanity since early 2020. Various sequelae of COVID-19 have been reported in different body systems. Musculoskeletal symptoms are widely reported during COVID-19 infection, but musculoskeletal complications in long COVID-19 are underreported. However, post-COVID-19 survivors have reported complaints of persisting or new-onset fatigue, myalgia, arthralgia, arthritis, muscle weakness, *etc* in clinical practice. The well-known detrimental effects of steroids on the musculoskeletal system coupled with their over-the-counter availability can also be anticipated since they were the cornerstone of life-saving management in this pandemic.

AIM

To determine the musculoskeletal complications in long COVID.

METHODS

We performed a systematic review of ‘systematic reviews and meta-analyses’.

RESULTS

Of the 63 articles screened, 24 articles were included. Two articles specifically discussed children and adolescents. One article discussed rehabilitation intervention. No article addressed rehabilitation of musculoskeletal issues in long COVID-19 in particular. Fatigue was the most common musculoskeletal complication.

CONCLUSION

Fatigue is found to be very common along with myalgia and arthralgia. There were no studies on rehabilitation intervention in musculoskeletal complications specifically. Considering the lacuna in literature and the needs of the current situation, further studies are warranted to standardize effective rehabilitation interventions in musculoskeletal complications. More homogenous studies are needed. Studies on functional impairment due to musculoskeletal involvement are essential.

**Key Words:** Musculoskeletal complications; COVID-19; Long COVID-19; Post-COVID-19 syndrome; Rehabilitation; SARS-CoV-2

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**Core Tip:** Though musculoskeletal involvement is reported in severe acute respiratory syndrome coronavirus 2 infection, the literature is limited for musculoskeletal symptoms in long coronavirus disease 2019 (COVID-19). Moreover, rehabilitation of each musculoskeletal complaint is not addressed in most reviews. We highlighted those keys areas through our review article. Fatigue is the most common musculoskeletal issue in long COVID-19. Considering the gaps in literature and current needs, future studies are warranted to standardize effective rehabilitation interventions in musculoskeletal complications.

**INTRODUCTION**

Since 2020 the world has witnessed multiple waves of the coronavirus disease 2019 (COVID-19) pandemic caused by different variants of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) at different times and places. As of September 1, 2022, 599 million confirmed cases and more than 6 million deaths have been reported[1]. The loss of lives, superimposed by the deterioration of the quality of life of a significant number of survivors, made this pandemic a huge hurdle for the whole world. A range of long-term effects or complications involving different body systems have been reported. The respiratory sequelae of COVID-19 have been widely investigated, but musculoskeletal complications are underreported. Here we performed a systematic review of systematic reviews and meta-analyses to find musculoskeletal complications caused by long COVID-19 conditions.

**MATERIALS AND METHODS**

Here a systematic review of systematic reviews and meta-analyses was conducted (Figure 1). We also cited high-quality articles in *Reference Citation Analysis* (https://www.referencecitationanalysis.com).

***Eligibility criteria***

PICOS model: (1) Studies that considered patients with long-term COVID-19 symptoms at least > 4 wk of COVID-19 infections (population); (2) Studies where the primary aim was to evaluate long-term COVID-19 symptoms in mild, moderate, severe, and critical patients that have a follow-up of at least 14 d (interventions); (3) Studies with or without a control group (comparisons); (4) Studies that reported the long COVID-19 symptoms (outcomes); and (5) Systematic review and meta-analyses (study designs). From January 2020 to mid-July 2022, any relevant studies that followed the above mentioned PICOS model and that reported musculoskeletal complications in long COVID-19 were eligible for inclusion.

***Search strategy***

The search was carried out by two independent researchers in all electronic databases, mainly MEDLINE, EMBASE, Web of Science, and Google Scholar with this time period. We combined search terms and key words related to the population (*e.g.,* “COVID-19”, “SARS-CoV-2”, “long Covid-19”, “long Covid”, “long haulers”) and outcomes (*e.g.,* “fatigue”, “pain”, “musculoskeletal”, “myalgia”, “myopathy”, “arthralgia”, “arthritis”, “rheumatic”, “joint”). We additionally filtered study designs “systemic review” and “meta-analyses” in humans.

***Inclusion and exclusion***

All the systematic reviews and meta-analyses on long COVID-19 following our above-mentioned PICOS model were included. After the preliminary search, we extracted the musculoskeletal complications that were reported in long COVID-19 studies or in post COVID-19 studies (at least 4 wk after COVID-19 active infection). We excluded any musculoskeletal issues that occurred after any neurological sequelae of long COVID-19 and excluded any myocarditis or issues related to smooth muscle dysfunction.

***Study selection and data extraction***

Titles and abstracts were screened for potentially eligible studies. Following an initial screening, full texts of potentially eligible studies were acquired for detailed evaluation eliminating all duplicates. Manual scanning of key articles and review papers was conducted to identify additional articles missed by the search strategy. Two reviewers assessed the articles independently and in case of any disagreements, the opinion of the third reviewer was consulted.

***Analysis***

We performed a descriptive analysis of the included reviews.

**RESULTS**

Of the 63 articles screened; 24 articles were included[2-25]. Two articles specifically discussed children and adolescents. One article discussed rehabilitation intervention. No article addressed rehabilitation on musculoskeletal issues in long COVID-19 in particular. Details of the selected articles are listed in Table 1.

**DISCUSSION**

According to the National Institute of Health and Care Excellence guidelines, post-acute COVID-19 and post-COVID-19 syndrome are included in long COVID. Post-acute-COVID-19 means ongoing symptomatic COVID-19 for people who still have symptoms 4 wk and 12 wk after acute COVID-19. On the other hand, post-COVID-19 syndrome means that patients are having persisting symptoms for > 12 wk after acute symptoms[26]. According to the World Health Organization, post-COVID-19 conditions generally occur 3 mo from the onset of COVID-19 with symptoms lasting for at least 2 mo and should be unexplained by any alternative diagnosis[27].

Another definition consists of “not recovering several weeks or months following the start of symptoms that were suggestive of COVID-19, regardless individuals were tested or not”[28]. Common symptoms reported are fatigue, shortness of breath, cognitive dysfunction/attention disorder, hair loss, and dyspnea[29,30]. Musculoskeletal symptoms of skeletal muscle, neurological, bone, and joint disorders have also been reported. The proinflammatory responses can impact nearly every organ system, including the musculoskeletal system. Myalgias, arthralgias, fatigue, exercise, and intolerance are some of the common musculoskeletal sequelae.

***Why musculoskeletal system affected?***

SARS-CoV-2 has three structural proteins (membrane protein, spike protein, and envelope protein). Spike glycoprotein through its subunits S1 and S2 helps in entering the host cells[31]. The angiotensin-converting enzyme 2 (ACE2) receptor acts as the entry receptor using the serine protease transmembrane protease, serine 2 (TMPRSS2) for spike protein priming[32]. Following the binding of the receptor, viral spike protein is broken down by TMPRSS2 proteolytically, which exposes a fusion peptide signal that helps in the fusion of viral and human membranes. It leads to the cytoplasmic release of viral RNA. Interestingly, ACE2 is found in the lung, heart, kidney, liver, gastrointestinal, and musculoskeletal systems.

In humans, endothelial cells, smooth muscle cells, pericytes, muscle stem cells, macrophages, B cells, T cells, natural killer cells, and myonuclei express TMPRSS2. Furthermore, several cells in the synovium including fibroblasts, monocytes, B cells, and T cells express ACE2 and TMPRSS2. However, only smooth muscle cells and pericytes express ACE2. Articular cartilage (proliferative, hypertrophic, and effector chondrocytes) express ACE2, and only homeostatic chondrocytes (which control circadian rhythm in cartilage) express TMPRSS2. In the meniscus, a few cartilage progenitors and regulatory fibrochondrocytes express ACE2 (no TMPRSS2 is detected). ACE2 is also found to be present in composite unenriched cortical and trabecular bone and osteoblast enriched tissues. TMPRSS2 was almost absent in composite bone tissue, and TMPRSS2 was detected in all osteoblast-enriched samples.

The presence of these receptors implies that skeletal muscle, synovium, and cortical bone may serve as potential areas of direct SARS-CoV-2 infection and its probable long-term sequelae[33]. The cytokines and signaling molecules are induced by the infection [C-X-C motif chemokine 10, interferon-gamma, interleukin (IL)-1β, IL-6, IL-8, IL-17, and tumor necrosis factor-alpha (TNF-α)]. They play a crucial role in the pathogenesis of clinical signs and symptoms and long-term sequelae of COVID-19. Interferon-gamma, IL-1β, IL-6, IL-17, and TNF-α show a negative impact on skeletal muscle (fiber proteolysis and decreasing protein synthesis). IL-1β and IL-6 may lead to fibrosis after inducing increased muscle fibroblast activity. IL-1β and TNF-α induce muscle fiber growth by inhibiting the differentiation and proliferation of satellite cells, the progenitor cells[34].

***COVID-19 therapy sequelae in the musculoskeletal system***

Corticosteroids, a lifesaving medication in the management of COVID-19, has been overused in many cases. Additionally, long-term corticosteroid use has been known to cause a variety of effects on the bone, including osteonecrosis, reduced bone mineral density (BMD), avascular necrosis of the hip joint, and osteoporosis with or without fracture. It implies that steroids might be an important cause of multiple musculoskeletal complications.

***Skeletal muscle and fatigue***

Many studies have reported fatigue myalgia and generalized weakness as some of the common persisting complaints in symptomatic infections of the disease[35]. In the previous epidemics of SARS, extensive myalgias and muscle dysfunction were also reported. Direct viral infection and/or the cytokine storm could lead to pathological changes in skeletal muscle tissue in addition to deconditioning due to prolonged disuse during the hospitalization or disease period.

Mayer *et al*[36] showed that a long intensive care unit stay is linked with a rapid and significant reduction in the volume of the rectus femoris muscle (average: 18.5%), until the 7th d of hospitalization. Carfì *et al*[37], in a study to follow up the post-COVID-19 patients in a hospital in Italy, found that in recovered patients, 87.4% responded with at least one persistent symptom, especially fatigue. Paneroni *et al*[38] evaluated the muscle strength of the quadriceps and biceps femoris of patients in post-discharge recovered COVID-19 cases. They found that 86% of cases had quadriceps weakness and 73% had biceps femoris weakness. These findings proved muscle dysfunction in individuals with long COVID-19. Jacobs *et al*[39] in their study to assess the persistence of symptoms and quality of life at 35 d after hospitalization of COVID-19 infection found fatigue as the most common persisting symptom.

Fatigue was found to be the most common symptom followed by shortness of breath (31%), loss of smell (22%), and muscle ache (21%) by the Office for the National Statistics, census 2021, in the estimates of the prevalence of self-reported long COVID-19 and associated activity limitation using United Kingdom Coronavirus (COVID-19) Infection Survey data[40]. Compared with age-matched healthy controls, approximately 2-3 mo after discharge, moderate to severe cases had a 32% reduction in grip strength and a 13% reduction in the distance walked in 6 min[41].

Aiyegbusi *et al*[42] did a review on symptoms, complications, and management of long COVID-19 and found that 47% reporting fatigue as the most common, myalgia (muscle pain) in 25%, and joint pain in 20%. Varghese *et al*[43] found that 54% of the patients reported fatigue as one of the persisting symptoms. Huang *et al*[44] did a follow-up study from June 16, 2020 to September 3, 2020 to assess 6 mo consequences of COVID-19 in patients discharged from the hospital, and they reported fatigue (63%) and sleep difficulties (26%) as the most common symptoms. Miyazato *et al*[45] also reported fatigue as one of the prolonged and late-onset symptoms conducted in patients admitted for COVID-19 to the Disease Control and Prevention Center and National Center for Global Health and Medicine from February to June 2020. Daher *et al*[46] conducted a follow-up study on 33 confirmed COVID-19 positive patients 6 wk post-discharge to assess the pulmonary and extrapulmonary disease sequelae and found a significant tendency among the patients to suffer from fatigue symptoms with significant limitations of their mobility, which was reflected by reduced 6-min walking test distance among the extrapulmonary sequelae. In their study, characterizing long COVID-19 in an international cohort over 7 mo of symptoms and their impact, Davis *et al*[47] also reported the patients who have had or were suspicious of COVID-19 reported fatigue as the most common persisting symptom even after 6 mo.

Multiple etiologies of fatigue (physical, mental, emotional) could be present. Therefore, fatigue should be researched according to the accompanying symptoms or more specific features[48]. Another sequelae is intolerance to physical activities associated with a chronic fatigue condition and difficulty in returning to normal daily life[49]. Eighteen people living with long COVID-19 in the United Kingdom were interviewed with a semi-structured questionnaire in a qualitative study by Humphrey *et al*[50] showing people faced reduced physical function, compounded by the cognitive and psychological effects of long COVID-19.

***Arthralgia and myalgia***

Arthralgia is pain localized to the joints, while myalgia is pain localized to muscle. They are typically present in the early course of the disease and in patients experiencing long-term effects of COVID-19 or a prolonged disease course. Studies have described how SARS-CoV-2 infection induces systemic elevations of cytokines and signaling molecules. This ‘cytokine storm’ is thought to be implicated in musculoskeletal manifestations, among many others. Myalgia and arthralgia are reported as one of the most common persistent symptoms in patients with post-acute sequelae of COVID-19 and are more notable in patients who were prone to being positioned during intensive care unit admission[51].

In a study of 294 patients hospitalized with COVID-19, Hoong *et al*[52] observed that 30% of patients reported musculoskeletal complaints; 37.5% had myalgia, 5.7% had arthralgia, 6.8% had new-onset backache, and 50% had generalized body aches. Elhiny *et al*[53] reported that physical decline was the most common symptom reported in musculoskeletal complications. Patients who also had mild to moderate forms of the infection can experience exacerbated muscle and joint pain. Petersen *et al*[54] in their study of long COVID-19 in a longitudinal study in the Faroe Islands found out arthralgia is one of the most persistent symptoms following fatigue and loss of smell and taste.

Follow-up of adults with non-critical COVID-19 after symptom onset in a study by Carvalho-Schneider *et al*[55] found that 13% of the patients who never had arthralgia at the onset of the disease reported arthralgia 30 d after discharge and 21% after 60 d. The study by Chopra *et al*[56] on clinical predictors of long COVID-19 symptoms in patients with mild COVID-19 at 30 d post-discharge (long COVID-19) found myalgia as one of the most common persistent symptoms following fatigue and cough. Stavem *et al*[57] also reported myalgia as one of the most common persisting symptoms 1.5-6.0 mo after infection in non-hospitalized patients. Ghosn *et al*[58] in a large prospective cohort study in France among the post-discharge patients at 3 mo and 6 mo observed mostly fatigue, dyspnea, joint pain, and myalgia. COVID-19 has also been found to cause reactive arthritis and new-onset inflammatory arthritis typically occurring within a month after its diagnosis[59].

There were reported cases of reactive arthritis post discharge from COVID-19[60]. Derksen *et al*[61] in a Dutch study of 5 patients who presented with inflammatory arthritis 6.6 wk post COVID-19 infection, found that 2 patients had strongly positive and another patient had weakly positive anti-CCP antibodies, suggesting post-COVID-19 rheumatoid arthritis development.

***BMD***

C-X-C motif chemokine 10, IL-17, and TNF-α induce osteoclastogenesis and inhibit osteoblast proliferation and differentiation causing increased bone fragility[34]. Berktaş *et al*[62] assessed the BMD of hospitalized COVID-19 patients at diagnosis and follow-up visits using chest computed tomography. BMD was retrospectively measured by quantitative computed tomography. BMD decreased by a mean of 8.6% (± 10.5%) from diagnosis to follow-up. The osteoporosis ratio increased two-fold after hospitalization for COVID-19 because of this substantial bone loss.

An animal experimental study characterized the effects of SARS-CoV-2 infections on bone metabolism in an established golden Syrian hamster model for COVID-19. SARS-CoV-2 caused significant multifocal loss of bone trabeculae in the long bones and lumbar vertebrae of all infected hamsters implicating the same could happen in humans post-COVID-19. A multicenter study by Kottlor *et al*[63] showed that COVID-19 patients requiring intensive care had significantly lower BMD than those who were managed in non-intensive care settings.

Researchers at Indiana University School of Medicine discovered that the mouse models infected with the novel coronavirus lost nearly 25% of their bone mass within 2 wk of infection. They also found mouse models with a 63% increase in osteoclasts, the cells that cause the bone to break down.

***Neuromuscular***

Musculoskeletal manifestations can be a result of underlying neurological disturbances. The central and peripheral nervous systems control our movements *via* the spinal motor neurons, which act as the final common pathway to the muscles[64]. Many studies have reported peripheral neuropathy, most commonly Guillain-Barre and related symptoms. Guillain-Barre syndrome and critical illness-induced polyneuropathy/myopathy are two important peripheral neuropathies seen in COVID-19[65].

A follow-up study conducted for 8 mo in Denmark performed electromyography and conventional nerve conduction study of 20 patients with persistent fatigue. They found that all patients with myopathic electromyography reported physical fatigue; 8 patients reported about myalgia while 3 patients without myopathic changes complained about physical fatigue. Long-term COVID-19 does not cause large fiber neuropathy, but myopathic changes were seen[66]. Acute myopathies are reported in acute COVID-19 infection[67], which may have a detrimental effect in the muscle in the post infective stages.

***Rehabilitation perspectives***

COVID-19 has multisystem effects including physical as well as psychological effects. The wholesome evaluation and rehabilitation of such patients require a multifaceted and interdisciplinary approach to cover all aspects properly. Identification of the pre-existing disabling conditions contributing to the cumulative effect of long COVID-19 is also an important aspect. Reinfection, post-viral bacterial and fungal infections, baseline routine investigations along with C-reactive protein, fibrinogen, D-dimer, troponin, and ferritin can also be considered if clinically indicated. Cardiac function tests (echocardiography) should be done to check cardiopulmonary status before framing the exercise program.

Rehabilitation should be addressed holistically following the domains of the International Classification of Functioning, Disability, and Health. Studies have shown that early mobilization helps in the reduction of the harmful effects of the disease, especially on muscle and cardiopulmonary function, mobility, and function[68], implying rehabilitation of long COVID-19 should start from the beginning. Physical exercise should be individualized specifying intensity, frequency, duration, and type of exercise. Exercise should be gradually increased according to one’s capacity. The patient should be educated with an emphasis on self-management. The patient should respect the pain and their own capabilities. Energy conservation techniques such as simplifying tasks, pacing the activities over time, and taking breaks should be followed. Repeated practice of functional activities and a set of specific actions according to the patient’s priorities, needs, and goals may improve the functional aspects. All such activities need to be evaluated regularly to determine whether they should be continued, changed, or stopped[69].

However, no studies on rehabilitation intervention have been investigated in long COVID-19 for musculoskeletal complications in particular[70]. In our systematic reviews, we did only descriptive analysis. We did not address the individual cases or case series study or any cohort or trials, which may miss the characteristics of the individual cases in particular. However, performing a systematic review of all systematic reviews and meta-analyses provided a stronger evidence-based study.

**CONCLUSION**

Musculoskeletal involvement is common during active SARS-CoV-2 infection. Fatigue is very common during this phase. Here we have highlighted the musculoskeletal complications in long COVID-19 syndrome. Again, fatigue is found to be very common along with myalgia and arthralgia. There is a lack of studies on these aspects. Moreover, all the studies are heterogeneous, especially in terms of the duration of post-COVID and the definition of long COVID. There are no studies for rehabilitation intervention in musculoskeletal complications specifically. This study reinforced the gravity of the current situation. Considering the lacuna in literature and the needs of the current situation, further studies are warranted to standardize effective rehabilitation interventions in musculoskeletal complications. More homogenous studies are needed using proper case definition and duration of long COVID. Studies on functional impairment due to musculoskeletal involvement are needed.

**ARTICLE HIGHLIGHTS**

***Research background***

Research is lacking in musculoskeletal complications in long coronavirus disease 2019 (COVID-19).

***Research motivation***

Currently, many long COVID-19 patients are coming to outpatient departments of rehabilitation for musculoskeletal issues.

***Research objectives***

To find musculoskeletal complications in long COVID-19 and relevant rehabilitation interventions.

***Research methods***

A systematic review of systematic reviews and meta-analyses was done.

***Research results***

Among many musculoskeletal issues, fatigue was found to be the most common complication. Rehab intervention is severely lacking in literature.

***Research conclusions***

Rehabilitation need identification is of the utmost importance in musculoskeletal aspects of long COVID. Fatigue was found to be the most common complication.

***Research perspectives***

Identification of rehabilitation needed following identification of musculoskeletal complications is crucial in long COVID-19 cases.

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**Figure Legends**



**Figure 1 Flow diagram of the study.**

**Table 1 Included systematic reviews and meta-analyses in this systematic review**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Serial no.** | **Ref.** | **Reported musculoskeletal complications** | **Type of study** | **Types of patients** | **Rehabilitation intervention** |
| 1 | Ludvigsson[2], 2021 | Fatigue, muscle weakness | Systematic review | Children | No |
| 2 | Akbarialiabad *et al*[3], 2021 | Fatigue (63%), muscle weakness | Systematic scoping review | All age groups | No |
| 3 | Michelen *et al*[4], 2021 | Weakness (41%; 95%CI: 25%-59%), general malaise (33%; 95%CI: 15%-57%), fatigue (31%; 95%CI: 24%-39%) | Living systematic review | All age groups | No |
| 4 | Iqbal *et al*[5], 2021 | 48% fatigue in >12 wk | Systematic review and meta-analysis | All age groups | No |
| 5 | Vollbracht and Kraft[6], 2021 | Vitamin C improved in post-COVID-19 fatigue; the IV vitamin C doses administered ranged from 3.5 g to > 75 g/d | A systematic review on intervention | All age groups | No |
| 6 | Jennings *et al*[7], 2021 | Arthralgia 13% (6%-29%), myalgia 34% (2%-86%), fatigue 44% (10%-71%) | Systematic review | All age groups | No |
| 7 | Fernández-de-Las-Peñas *et al*[8], 2021 | Fatigue (58%), headache (44%), joint pain (15%-20%) | Systematic review | All age groups | No |
| 8 | Malik *et al*[9], 2022 | Fatigue (64, 54-73), arthralgia (24.3, 14.0-36.0), headache (21, 3-47) | Systematic review and meta-analysis | All age groups | No |
| 9 | Ceban *et al*[10], 2022 | Fatigue in 30% of cases | Systematic review and meta-analysis | All age groups | No |
| 10 | Chen *et al*[11], 2022 | Fatigue prevalence 0.23 (95%CI: 0.17-0.30) | Systematic review and meta-analysis | All age groups | No |
| 11 | van Kessel *et al*[12], 2022 | Fatigue most common | Systematic review | All age groups | No |
| 12 | Alkodaymi *et al*[13], 2022 | Fatigue 3-6 mo follow-up 32%, 36% 6-9 mo, 37% 9-12 mo, > 12 mo, 41% | Systematic review | All age groups | No |
| 13 | Fernández-de-Las-Peñas *et al*[14], 2022 | Prevalence of post-COVID-19 myalgia, joint pain, and chest pain ranged from 5.65% to 18.15%, 4.6% to 12.1%, and 7.8% to 23.6%, respectively, at different follow-up periods during the 1st yr postinfection. Almost 10% of individuals infected by SARS-CoV-2 will suffer from musculoskeletal post-COVID-19 pain symptomatology at some time during the 1st yr after the infection | Systematic review | All age groups | No |
| 14 | Han *et al*[15], 2022 | Fatigue/weakness (28%, 95%CI: 18%-39%), arthromyalgia (26%, 95%CI: 8%-44%) | Systematic review | All age groups | No |
| 15 | d’Ettorre *et al*[16], 2022 | 63% of fatigue reported | Systematic review | All age groups | No |
| 16 | Behnood *et al*[17], 2022 | 47% fatigue, 25% myalgia, 35% headache, females with higher pain symptoms | Systematic review | In children and young people | No |
| 17 | Nguyen *et al*[18], 2022 | Fatigue (16%-64%), arthralgia (8%-55%), thoracic pain (5%-62%), myalgia (1%-22%), headache (9%-15%) | Systematic review | All age groups | No |
| 18 | Lopez-Leon *et al*[19], 2022 | Fatigue (9.66%) | Systematic review | Children and adolescents | No |
| 19 | Abdel-Gawad *et al*[20], 2022 | Fatigue (72.8%) and joint pain (31.4%) | Systematic review | All age groups | No |
| 20 | Almas *et al*[21], 2022 | Fatigue (54.11%), arthralgia (16.35%), myalgia (5.78%), chest pain (10.37%) | Systematic review | All age groups | No |
| 21 | Maglietta *et al*[22], 2022 | Fatigue and female sex association statistically significant, with OR = 1.54, 95%CI: 1.32-1.79 | Systematic review | All age groups | No |
| 22 | Healey *et al*[23], 2022 | fatigue (37%; 95%CI: 23%-55%), myalgia (12%; 95%CI: 5%-25%), headache (7%; 95%CI: 3%-16%), chest pain (3%; 95%CI: 1%-8%) | Systematic review | All age groups | No |
| 23 | de Oliveira Almeida *et al*[24], 2022 | Fatigue. COVID-19 survivors can have a reduction in physical function, ability to perform activities of daily living and their health-related quality of life 1-6 mo post-infection | Systematic review | All age groups | No |
| 24 | Fugazzaro *et al*[25], 2022 | Muscle strength, walking capacity, sit-to-stand performance improvements | Systematic review of rehabilitation interventions | All age groups | Yes |

CI: Confidence interval; COVID-19: Coronavirus disease 2019; IV: Intravenous; OR: Odds ratio; SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2.



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