

Prevalence of Musculoskeletal Disorders in Post-COVID-19 Patients - A Systematic Review

Seema Anilkumar Tharani¹, Pradeep Borkar²

¹PG Student, Department of Orthopaedic Physiotherapy, Dr. APJ Abdul Kalam College of Physiotherapy, Pravara Institute of Medical Sciences, Loni, Taluka- Rahata

²Associate Professor, Department of Orthopaedic Physiotherapy, Dr. APJ Abdul Kalam College of Physiotherapy, Pravara Institute of Medical Sciences, Loni, Taluka- Rahata

Corresponding Author: Seema Anilkumar Tharani

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ABSTRACT

Background and Purpose: SARS-COV-2 has become a pandemic disease causing the acute respiratory syndrome. Clinical presentation varies in every individual and had shown a majority of respiratory symptoms followed by musculoskeletal complications arising from the inflammatory and Immune responses. Understanding the epidemiology of musculoskeletal complications in post-COVID-19 is imperative for improvement of better rehabilitation strategies and quality of life. AIM was to assess the current evidence on prevalence of Musculoskeletal disorders in post-COVID-19 patients.

Methodology: The Systematic review was conducted using the data published from November 2019 onwards, articles (n=45) meeting the eligibility criteria were assessed from sources: PubMed, Google Scholar, Web of Science, EMBASE. Studies having a score of ≥ 15 on STROBE checklist, cross-sections studies, Observational/Survey were selected. Cases diagnosed COVID-19 for 6 weeks or more were included.

Results: We found that major musculoskeletal symptoms included are muscle fatigue(n=49.12%), arthralgia(n=33%), and myalgia(n=34.75%) followed by joint swelling (as reactive arthritis) and conditions such as joint limitations, tendon shortening, and muscle weakness due to prolonged bed rest.

Conclusion: Our findings revealed that focus on musculoskeletal rehabilitation of patients with post-COVID-19 is essential along with cardiorespiratory rehabilitation. Review suggests that it would be effective in reducing physical complications, improving functional independence and quality of life in patients.

Keywords: Musculoskeletal pain, Musculoskeletal disorders, Musculoskeletal consequences, Covid-19

INTRODUCTION

A new coronavirus was identified as the cause of heap of pneumonia cases in Wuhan, China, at the end of 2019. The World Health Organization recognized the disease COVID-19, which stands for coronavirus disease 2019, in February 2020^[1]. SARS-CoV-2 is a coronavirus that belongs to the beta coronavirus family and

is predominantly a disease of the human respiratory system ^[2].

Covid-19 symptoms range from no symptoms to severe pneumonia, with a wide range of symptoms including fever, shortness of breath, dry cough, nasal congestion, sore throat, nausea, vomiting, myalgia, arthralgia, lethargy, joint swelling, headache, diarrhea, and, in rare cases, arthritis ^[2].

The coronavirus disease pandemic had many effects on the lives and health of people all over the world. To combat the spread of COVID-19, the health care system took the initiative and implemented internment/ quarantine. While this was effective in reducing the spread of the virus, it had a significant impact on the community and people's lives, including decreased activity levels, a decline in mental health, and a decrease in quality of life [3].

Musculoskeletal disorders are problems that affect the locomotor system, namely the bones, muscles, joints, tendons, and ligaments, as described by the World Health Organization (WHO) [1].

Myalgia, arthralgia, tiredness, joint edema, and other musculoskeletal issues are common [2]. In the human body, the virus connects to the transmembrane protease serine 2 (TMPRSS2) and angiotensin-converting enzyme 2 (ACE2) receptors. Pathological alterations in the musculoskeletal system arise as a result of

viral infection or the impact of cytokines and pro-inflammatory chemicals on the muscle, synovium, and bone cells that possess these receptors [4].

Our study aimed to find out the prevalence of musculoskeletal pain and disorders in patients who have suffered from COVID-19

METHODOLOGY

Study design: Systematic review

Eligibility criteria: Studies done in the last 2 years (November-2019)

Inclusion criteria:

- Full-text articles having a score of ≥ 15 STROBE checklist.
 - Articles of cross-sections studies, Observational/Survey.
 - Population including both the genders
 - No restrictions regarding the country setting.
 - Studies assessing the outcome at 6 or more weeks after covid
- Article which did not present a specific percentage of disorders.

Exclusion criteria:

- Duplicate articles

PROCEDURE:

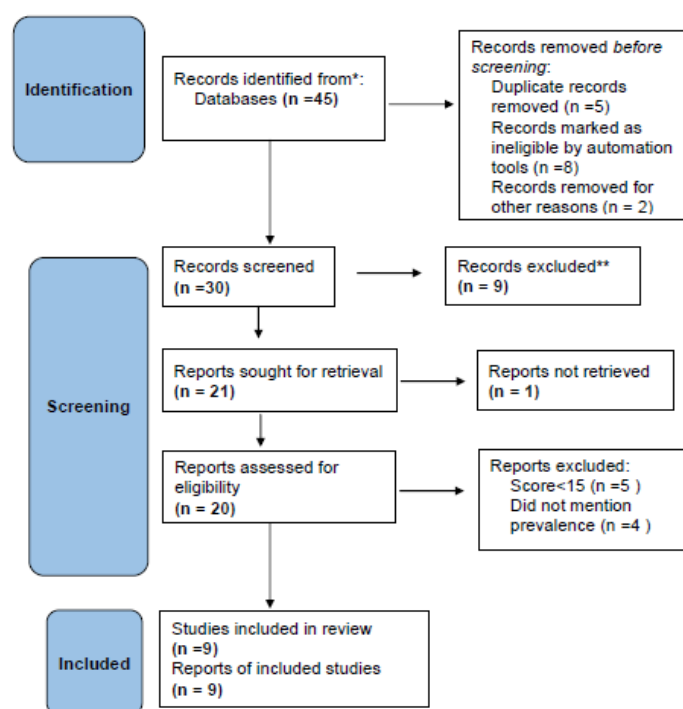


Figure 1: PRISMA flow chart

Table 1: Quality assessment of articles on STROBE checklist

Sr no.	Study Title	Location	Study Design	STROBE Score
1	Musculoskeletal pain and physical health status among confirmed COVID-19 patients of Bangladesh ^[5]	Sheikh Mujib Medical University, Bangladesh	Cross-sectional study	16
2	A relationship between musculoskeletal pain and prognosis in hospitalized COVID-19 patients ^[4] .	Erzurum Regional Training and Development Hospital, Turkey	Prospective longitudinal study	17
3	Long COVID: rheumatologic/musculoskeletal symptoms in hospitalized COVID-19 survivors at 3 and 6 months ^[6]	Gülhane Training and Research Hospital, Turkey	cohort study	16
4	Post-discharge rheumatic and musculoskeletal symptoms following hospitalization for COVID-19: prospective follow-up by phone interviews ^[7]	Gülhane Training and Research Hospital, Turkey	single-center cohort study	17
5	Clinical presentations of pain in patients with COVID-19 infection ^[8]	Goztepe Training and Research Hospital, Istanbul Medeniyet University, Istanbul, Turkey	Observational Study	18
6	Viral arthralgia a new manifestation of COVID-19 infection? A cohort study of COVID-19-associated musculoskeletal symptoms ^[9]	Woodlands Health Campus Singapore	A single-center retrospective cohort study	19
7	Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study ^[10]	Jinyintan Hospital in Wuhan, China.	retrospective, single-centre	16
8	Post-COVID-19 Syndrome: Nine Months after SARS-CoV-2 Infection in a Cohort of 354 Patients: Data from the First Wave of COVID-19 in Nord Franche-Comté Hospital, France ^[11]	Nord Franche-Comté Hospital in France.	observational retrospective study	20
9	Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China ^[12]	Jin Yintan Hospital (Wuhan, China)	Prospective Observational study	21

Table 2: Characteristics of the studies included in the review

Sr. No.	Study Title	Name of the journal	Country	Sample size	Outcome measure	Result/ Conclusion
1.	Musculoskeletal pain and physical health status among confirmed COVID-19 patients of Bangladesh ^[5]	Bangabandhu Sheikh Mujib Medical University Journal	Bangladesh	380	Cognitive ability -brief cognitive rating scale (BCRS). musculoskeletal (MSK) pain intensity -visual analog scale. Bangla version of short form-12 V2 (SF-12v2) survey instrument10 - to assess physical global health. A telephonic interview was conducted. RT-PCR tests results.	younger age group (aged ≤50 years), 37.59%-moderate pain, 6.77% -severe pain, 13.91% - mild pain, older respondents aged >50 years) 47.37%- moderate pain, 25.44% - severe pain, 13.15% - mild pain,
2	A relationship between musculoskeletal pain and prognosis in hospitalized COVID-19 patients ^[4]	HEALTH SCIENCES MEDICINE	Turkey	154	Visual Analog Scale (VAS)-pain The pain diagram by Margolis- myalgia. Arthralgia, arthritis	71.4% (n=110) had myalgia, 55.8% (n=86) had arthralgia. Mean VAS value on admission was 6.39 ± 2.04. The majority of hospitalized patients in this study who were diagnosed with COVID-19 had musculoskeletal system pain.
3	Long COVID: rheumatologic/musculoskeletal symptoms in hospitalized COVID-19 survivors at 3 and 6 months ^[6]	International League of Associations for Rheumatology (ILAR)	Turkey	300	rheumatic and musculoskeletal symptoms fatigue, myalgia, joint pain, low back pain, back pain, and neck pain. Additionally, the other COVID-19 fever, cough, lack of appetite, dyspnea, diarrhea, sore throat, headache, dizziness, absence of taste, and absence of smell. the severity of all these symptoms through a 5-point Likert-type scale	31.6% had fatigue, 18.6% had joint pain, and 15.1% had myalgia. Approximately 3 in 5 patients had at least one symptom with ≈2 in 5 patients having at least one rheumatic and musculoskeletal symptom. Fatigue, joint pain, and myalgia were the most frequent rheumatic and musculoskeletal symptoms.

Table 2 Continued...						
4	Post-discharge rheumatic and musculoskeletal symptoms following hospitalization for COVID-19: prospective follow-up by phone interviews [7]	Rheumatology International	Turkey	300	Demographic characteristics, musculoskeletal symptoms Severity of all musculoskeletal symptoms_ level Likert scale (i.e. none; mild; moderate; severe; and very severe). Statistical method	fatigue (44.3% ,back pain (22.7%), arthralgia (22.0%), myalgia (21.0%), low back pain (16.3%), and neck pain (10.3%);
5	Clinical presentations of pain in patients with COVID-19 infection [8]	Irish Journal of Medical Science	Ireland	193	Demographic characteristics, musculoskeletal symptoms - VAS	Complaints of the patients were 76.6% fatigue, 69.3% pain. Among 133 patients reporting pain, the distribution of site was 92 (69.2%) myalgia/arthralgia; 67 (50.4%) headache; 58 (43.6%) back pain; 44 (33.1%) low back pain; The most common pain symptoms were myalgia/arthralgia and headache (69.17% and 50.37%) a
6	Viral arthralgia a new manifestation of COVID-19 infection? A cohort study of COVID-19-associated musculoskeletal symptoms [9]	International Journal of Infectious Diseases	Singapore	294	development of pneumonia-radiologically and clinically requirement for supplemental oxygen was defined as finger oxygen saturation 93% on room air, or arterial blood oxygen partial pressure (PaO2)/oxygen concentration (FiO2) 300 mmHg VAS	Of 294 hospitalised patients with COVID-19, 88 (30%) reported musculoskeletal complaints. Among these 88 patients, 37.5% had myalgia, 5.7% arthralgia, 6.8% new-onset backache, and 50% generalized body ache.
7	Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study [10]	The Lancet	China	99	demographics; signs and symptoms on admission; comorbidity; laboratory results; co-infection with other respiratory pathogens; chest radiography and CT findings; treatment received for 2019-Nov; and clinical outcomes	Patients had clinical manifestations of muscle ache (11 [11%] patients), headache (eight [8%] patients),
8	Post-COVID-19 Syndrome: Nine Months after SARS-CoV-2 Infection in a Cohort of 354 Patients: Data from the First Wave of COVID-19 in Nord Franche-Comté Hospital, France [11]	Microorganisms	France	354	demographic variables, comorbidities, COVID-19 characteristics, and persistence or no persistent symptom were collected through an online questionnaire sent by email. In case of hospitalization, hospitalization characteristics (duration of hospitalization, intensive care unit admission (ICU), outcome, and treatment) were collected through the medical record.	pain symptoms (26.8% (n = 34), 26.0% (n = 33), 24.4% (n = 31); headache, arthralgia, and myalgia, respectively).
9	Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China [12]	The Lancet	China	41	standardized data collection forms: WHO the researchers also directly communicated with patients or their families to ascertain epidemiological and symptom data	Common symptoms at onset of illness were fever (40 [98%] of 41 patients), cough (31 [76%]), and myalgia or fatigue (18 [44%]); less common symptoms were sputum production (11 [28%] of 39), headache (three [8%] of 38), ETC)

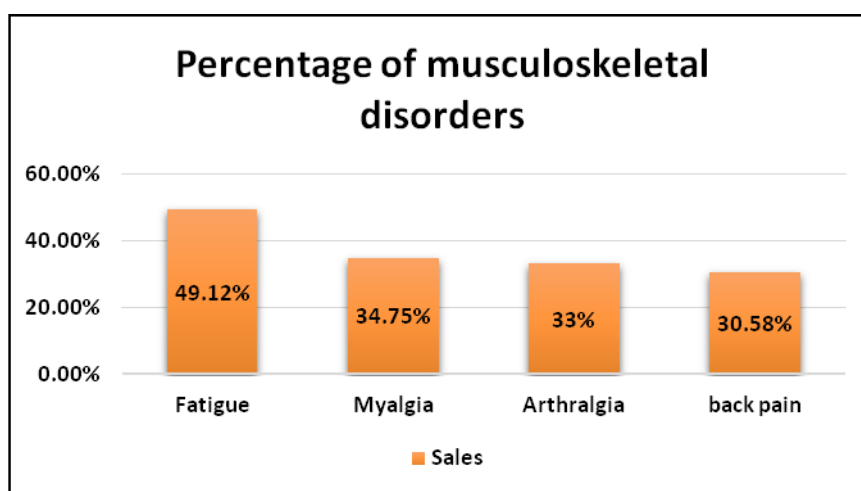
RESULT

We identified 45 full text articles, Articles of observational studies were chosen for this analysis, sources including PubMed (n=8), Google Scholar (n=30), ResearchGate(n=5), Sci-Elo(n=2). The studies included patients of COVID-19 post 6weeks of diagnosis. After removing duplicates and based on inclusion criteria 18 articles were selected. The methodological quality of 18 articles was assessed using the STROBE checklist, out of which 8 studies had shown low evidential value, 5 studies have shown moderate evidential value, 4 have shown high evidential value. So, a total of 9 studies was included in qualitative synthesis.

The sample size included in the study ranged from 50-400 diagnosed COVID-19 patients. The subjects reported with age ranging from 18-90, including male- 1309, and female- 803.

The major musculoskeletal symptoms faced by the patients were Fatigue, arthralgia, and myalgia and other symptoms were back pain, headache, neck pain, hip pain.

The mean percentage were: fatigue (49.12%) 4 studies, myalgia (34.75%) 8 studies, arthralgia (33%) 6 studies, headache (28.4%) 3 studies, back pain (30.58%) 5 studies.



Graph 1: Percentage of musculoskeletal disorders

DISCUSSION

This systematic review focused on the Prevalence of musculoskeletal disorders in post-COVID-19 patients. COVID-19 patients. The review revealed a wide range of prevalence of musculoskeletal symptoms in post-COVID-19 patients, with the most common being myalgia, arthralgia, and tiredness, and the least common being headache and back discomfort.

Myalgia

Myalgia is the most prevalent symptom in patients with viral infections; it represents general inflammation and cytokine response (immune response); COVID-19-induced myalgia is longer and

more severe than other viral infections' myalgia. The capacity of the tissue cell to deliver oxygen to the cell is compromised in hyperlactatemia, and the tissue stays hypoxic. This musculoskeletal disease can result in ischaemia and discomfort in ischemic muscle tissue. As a result of elevated lactate levels, low pH, and low oxygen levels, muscular discomfort may be enhanced [13]. The mouse model of SARS-COV-2 has shown 20% decrease in muscle mass after 4 days of infection. Muscle atrophy is also seen, as well as random and localized muscle fiber necrosis and immune cell infiltration. Infection-induced cytokines and proinflammatory signalling molecules may cause degenerative alterations in

skeletal muscle tissue [14]. The studies reviewed in this qualitative analysis showed the percentage of myalgia from (11% to 69%) mean (34.75%).

Arthralgia

The known cause of Arthralgia is varied from de-generative and destructive process such as osteoporosis and sports injuries to inflammation of the tissue around the joints such as bursitis [14]. It is also an important clinical complaint seen in many people with viral infections, including the COVID-19 disease [13]. Systemic inflammation may also play a role in bone and joint tissue physiology in patients with COVID-19. Of the cytokines known to be induced as a result of COVID-19, CXCL10, IL-17, and TNF- α have established roles in inducing osteoclastogenesis and decreasing osteoblast proliferation and differentiation, leading to a net reduction in BMD74-76. IL-1b, IL-6, and TNF- α can lead to chondrolysis, which could result in arthralgias or progression of osteoarthritis in some patients. Similarly, IL-1b, IL-17, and TNF- α are hypothesized to induce inflammation in tendinopathy and can impede the normal biological activity of tenocytes, resulting in poor matrix remodelling and probable worsening of degenerative tendon diseases [14]. The studies reported the occurrence of arthralgia from (5.9% to 69.2%) mean (33%).

Fatigue

Persistent fatigue is caused by many viral infections and has been documented in COVID-19 patients. According to the WHO report, COVID-19 caused fatigue in 38% of the patients. Fatigue can be identified in a variety of clinical settings, ranging from cancer therapy to inflammatory arthritis. The presence of chronic viral infection in the lungs, brain, adipose, and other tissues is the most likely cause of tiredness in COVID-19. Aside from that, the immune response is afflicted, which is another cause. The immune system is harmed after eradicating the infection, which is referred

to as cytokine storm. It is a type of immune system overreaction in which the immune system targets the body's tissue and causes further harm. The occurrence of the fatigue ranges from 31 to 76% mean being 49.12%. [2,13]

In addition, vitamin D is involved in the maintenance of a healthy skeleton by regulating calcium and phosphate metabolism. Low levels of serum 25-hydroxy vitamin D have been linked to a variety of immune-related illnesses and ailments, including psoriasis, type I diabetes, multiple sclerosis, rheumatoid arthritis, TB, sepsis, respiratory infection, and COVID-19. Vitamin D also has a deleterious impact on the outcome of COVID-19 pneumonia [4].

CONCLUSION

Our findings revealed that focus on musculoskeletal rehabilitation of patients with post-COVID-19 is essential along with cardiorespiratory rehabilitation. Review suggests that it would be effective in reducing physical complications, improving functional independence and quality of life in patients.

Clinical Implication: Understanding the prevalence of MsK disorders and its epidemiology in post-COVID-19 patients will help the clinician in planning better rehabilitation strategies and improve the quality of life of patients

Conflict of Interest: The authors declare that they have no conflict of interest.

Ethical Clearance: Taken from Institutional ethical committee with letter number: PIMS/Dr. APJAKCOPT2021/731. It is an exempted review

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