

Assessment of Musculoskeletal Problems in Post Covid-19 Subjects: An Observational Study Protocol

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Abstract:

Background: The severe acute respiratory syndrome corona virus 2 is the cause of the global pandemic known as Covid-19 (SARS-COV-2) seen by the whole world with major affection. The angiotensin-converting enzymes-2 (ACE-2) found in skeletal muscles has been shown to connect with the corona virus, making it more vulnerable to direct viral invasion. Muscle fibroblast's fibrotic activity to rise and the inflammatory response become exacerbated. Musculoskeletal symptoms such as exhaustion, myalgia, arthralgia, muscle weakness, decreased bone mineral density, and soft tissue abnormalities are found among the subjects. Additional research on COVID-19 patients revealed myositis and arthritic alterations, including myalgia, weakening in the muscles, and increased creatine phosphokinase levels. A long-term study discovered that the most prevalent musculoskeletal complaints between two weeks and one month following hospitalization were myalgia, arthralgia, and fatigue. The purpose of the current study is to evaluate different musculoskeletal issues in post-COVID-19 patients. **Outcome Measures:** Standard Nordic musculoskeletal questionnaire will be taken for all subjects. Depending on the problem and joint involved outcome measures like NPDI, SPADI, DASH, OLBQ, HHS, WOMAC, FADI, CFS, LEFS, FAS will be used. **Statistical Analysis:** Descriptive statistical analysis like mean, standard deviation will be done by using SPSS latest version software by taking the help of a Biostatistician after ensuring the normal distribution and analysis. To find out association between two variables Fisher's exact test and Pearson chi-square test will be used. **Conclusion:** This study will be helpful to find prevalence of musculoskeletal problems among post Covid-19 subjects. **Clinical Trial Registration:** The study is registered with Clinical Trials Registry- India (CTRI), with the registration number for the trial being CTRI/2022/08/044661.

Keywords: Musculoskeletal problems, Joint pain, covid-19, SARS-COV-2, myalgia

Introduction:

The severe acute respiratory syndrome corona virus 2 is the cause of the global pandemic known as Covid-19 (SARS-COV-2) seen by the whole world with major affection in the year 2020 & 2021. Corona virus mostly affects the respiratory tract. Patients with this viral infection experience compromised alveolar epithelium and viremias. Other systems, including the neurological, cardiovascular, digestive, and musculoskeletal systems, have also been documented to be impacted in the literature ^[1].

The angiotensin-converting enzymes-2 (ACE-2) found in skeletal muscles has been shown to connect with the corona virus, making it more vulnerable to direct viral invasion. Therefore, elevated

levels of cytokines and other inflammatory substances, such as IL-1 β and IL-6, in the musculoskeletal system are indicative of an aberrant immune response. This causes the muscle fibroblast's fibrotic activity to rise and the inflammatory response to become exacerbated. Muscle force output is hampered as a result, increasing the chance of injury. This turns as the primary mechanism in the patho-physiology of the clinical characteristics of the musculoskeletal system linked to COVID-19 [2, 3].

Corticosteroid medications widely used to stop the acute inflammatory alterations linked to arthralgia in virus-infected patients. Moreover, this medication has the direct ability to cause muscular weakening and atrophy. Depending on the severity and length of the medications used, this medication may lower bone mineral density [2]. Research demonstrates that patients with COVID-19 in the initial phase of hospitalization experience musculoskeletal symptoms such as exhaustion, myalgia, arthralgia, muscle weakness, decreased bone mineral density, and soft tissue abnormalities [4]. Another study discovered the effects of the post-acute COVID syndrome on participation; physical function, cognitive function, and health-related quality of life, in addition to persisting symptoms like exhaustion, dyspnea, and anxiety [5]. According to a quick examination of the impact of COVID-19 on skeletal muscle, viral myalgia and arthralgia are two of the most typical symptoms of COVID-19 infection. Another study noted that 30% of the patients experienced arthralgia, and that the side effects of medications such as corticosteroids made the condition worse [3, 6, 7].

According to a number of case studies, coagulopathy caused by SARS-COV-2 infection is linked to several symptoms, including peripheral vascular disease (PVD), which has underlying comorbidities including diabetes mellitus [7]. Osteoporosis and osteonecrosis, which have been discovered in CT reports of COVID patients, have also evolved. These conditions impact the major musculoskeletal structures, including the knee joint, the femur and humeral heads, and other anatomical sites [7, 8]. Additional research on COVID-19 patients revealed myositis and arthritic alterations, including myalgia, weakening in the muscles, and increased creatine phosphokinase levels [9, 10, 11].

In a study where patients' grip strength was tested to determine the severity of COVID-19, it was discovered that women had weaker grip strengths than men [12]. Other study found that a high risk factor for COVID-19 patients in adults or those who are older is reduced muscle strength [13]. A long-term study discovered that the most prevalent musculoskeletal complaints between two weeks and one month following hospitalization were myalgia, arthralgia, and fatigue [14]. Following these results, the study was continued for six months in the hospital, during which time the same symptoms persisted. They also discovered that women were more likely than men to experience musculoskeletal complaints [15]. One study found that even after severe COVID, myopathic alterations are frequently the cause of physical exhaustion [16]. At 6 and 12 months, long-COVID fatigue was observed in 63% and 28% of COVID-19-infected persons, respectively. At the 1-year follow-up, the high prevalence was identical for those with severe and non-severe acute COVID-19 infection [17]. Prolonged COVID-19 infection and elevated ferritin levels have been identified as common indicators of post-infection fatigue syndrome development [18].

To the best of our knowledge, very few studies have been conducted to evaluate musculoskeletal issues in individuals who have recovered from COVID-19. Thus the purpose of the current study is to evaluate different musculoskeletal issues in post-COVID-19 patients.

Objectives of the study are to:

- To identify musculoskeletal problems like joint pain, myalgia, fatigue and functional performance in post covid-19 individual's first administration will be of "standard Nordic musculoskeletal questionnaire". Then for specific involvement of joint identification will be administered by respective outcome measures like
- To identify Neck pain with "Neck pain and disability index (NPDI)".
- To identify Shoulder pain with "Shoulder pain and disability index (SPADI)".

- To identify Arms and Hands pain with “Disability of arms, shoulder, hand (DASH)”.
- To identify Low back pain with “Oswestry low back disability Questionnaire (OLBDQ)”.
- To identify hip pain with “Harris hip score (HHS)”.
- To identify Knee pain with “Western Ontario and McMaster universities OA index (WOMAC)”.
- To identify ankle and foot pain with “Foot and Ankle disability index (FADI)”.
- To identify Fatigue with “Chalder fatigue scale (CFS)”.
- To assess lower extremity functional performance with “Lower extremity functional scale (LEFS)”.
- To assess Functional performance with “Functional assessment scale (FAS)”.

Ethical Approval:

All the procedures that will be involved in this trial had been taken approval from the Sumandeep Vidyapeeth Institutional Ethics Committee. The approval received from the Sumandeep Vidyapeeth Institutional Ethics Committee had the outward number, SVIEC/ON/Phys/BNMPT21/D22051 dated on 07/07/2022.

Clinical Trial Registration:

The study is registered with Clinical Trials Registry- India (CTRI), with the registration number for the trial being CTRI/2022/08/044661.

Sample size calculation:

Sample size calculation was done using the following formula,

$$n' = \frac{NZ^2P(1-P)}{d^2(N-1) + Z^2P(1-P)}$$

where n' = Sample size with finite population correction,

N = Population size,

Z = Z statistic for a level of confidence,

P = Expected proportion (If the prevalence is 20%, $P = 0.2$), and

d = Precision (If the precision is 5%, then $d = 0.05$)

After using the above formula for sample size calculation, the final sample size came to be minimum 107 subjects.

Method:

In this cross sectional, observational study, adults with age above 18 years from Constituents College's of Sumandeep Vidyapeeth, Dhiraj hospital and community surrounding the Institution will be approached and explained about the study.

Inclusion Criteria:

1. Age: Above 18 years
2. Gender: male and female
3. Post Covid-19 patients confirmed with the covid-19 positive reports (>3 months)
4. Laboratory reports related to covid-19.
5. Patients able to write and read languages (English, Hindi, Gujarati)

Exclusion Criteria:

1. Non covid-19 patients and patient with actue covid-19 affection < 3 months duration
2. Orthopedic conditions (like Fractures, tumours, etc.)
3. Cardiac conditions
4. Patients who have missing there documents related to covid-19 (reports)

The participants meeting the inclusion criteria and willing to participate will be included. Written informed consent form will be collected. Participant’s selection will be done from the population using convenient sampling technique. Routine musculoskeletal assessment will be done (fig. 1). All the participants will be assessed for different musculoskeletal problems using Nordic questionnaire, followed by particular outcome scale depending on the involvement of the joint (table 1).

Fig 1: Flowchart summarising the overall trial design

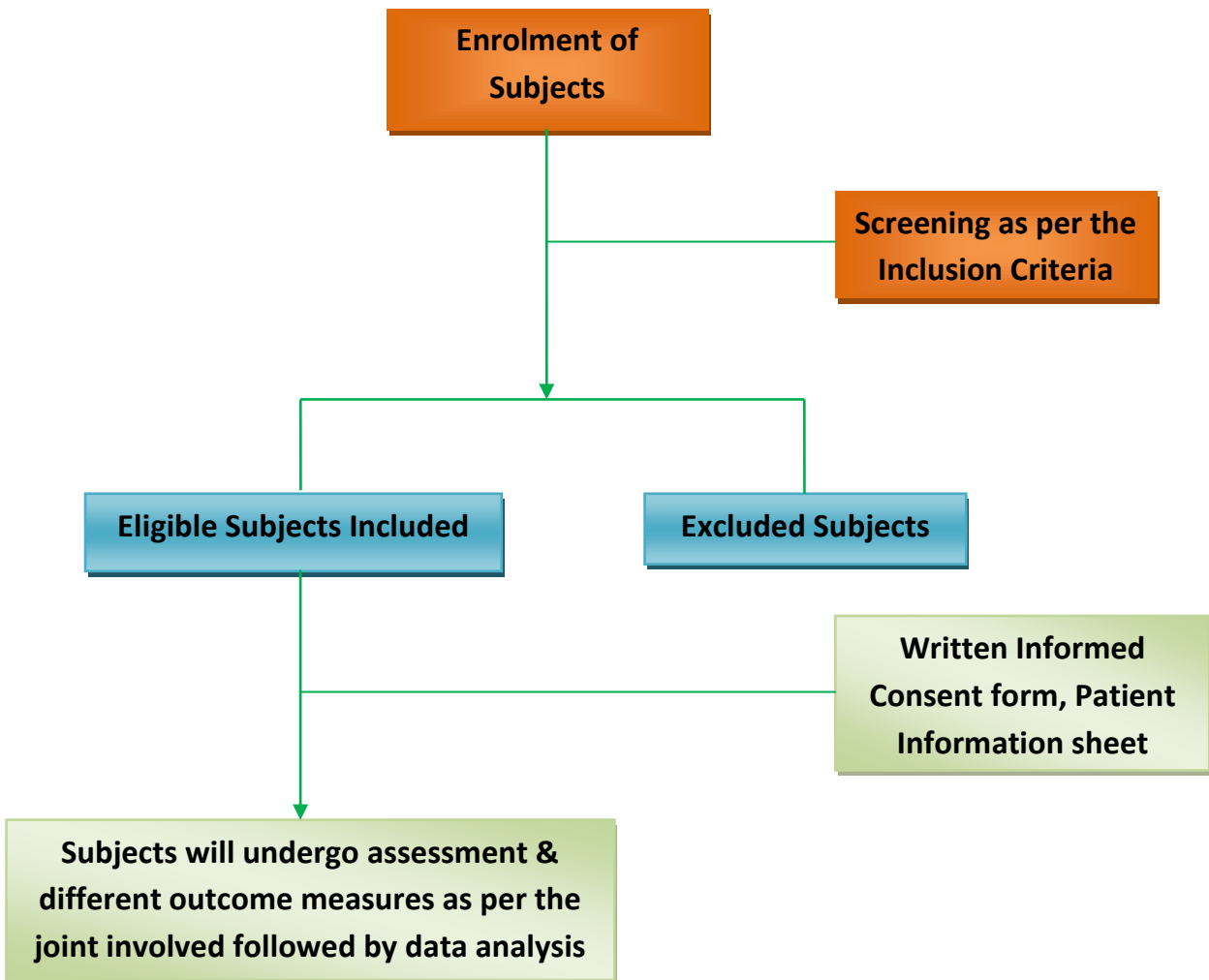


Table 1: the schedule of enrolment, interventions and assessments in accordance with the Standard Protocol Items: Recommendation for Interventional Trials (SPIRIT) for the Observational Study

| Time Point | Study Period | | | |
|--------------|--|-----------|----------------|---------------------|
| | | Enrolment | Day 1 | Later if applicable |
| Enrolment | Eligibility Screen | x | | |
| | Informed Consent | x | | |
| | Patient Information Sheet | x | | |
| Intervention | Intervention if any | | Not applicable | |
| Assessments | Baseline | x | | |
| | Nordic Musculoskeletal Questionnaire | | x | |
| | NPDI, SPADI, DASH, OLBDQ, HHS, WOMAC, FADI, CFS, LEFS, FAS whichever is/are applicable per patient | | x | |

Statistical Analysis:

The data will be collected and entered in Microsoft excel sheet and descriptive statistic like mean, standard deviation after ensuring the normal distribution and analysis will be done by using SPSS latest version software by taking the help of a Biostatistician. As the data which will be obtained is qualitative and having categorical variable, to find out association between two variables Fisher’s exact test and Pearson chi-square test will be used.

Discussion:

On completion of this observational study, the results of the study will give better understanding of musculoskeletal problems like joint pain, myalgia, fatigue, etc. in post covid-19 subjects as the study aims to evaluate them. To the best of our knowledge very few studies have been done which assessed musculoskeletal problems in post covid-19 patients. The results of this study will also be important for subjects affected with Covid-19 symptoms to better understand their long term musculoskeletal problems with duration of more than 3 months from affection with the virus which may or may not affect their functional performance and physical activity levels.

The strength of this study protocol is that it follows the SPIRIT protocol. The study also follows all the recommendations for observational studies considered in the Strengthening the Reporting of Observational studies in Epidemiology (STROBE) statement.

Conclusion: This observational study will be helpful to find prevalence of musculoskeletal problems among post Covid-19 subjects. If any particular symptoms are found to be more prominent than strategies to cope and manage those symptoms in Covid-19 subjects can be developed in the future by doing further research.

Conflicts of Interest:

The authors hereby state that we have no potential conflicts of interest to declare.

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