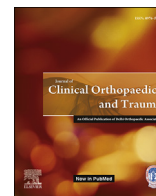




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## Editorial

### Musculoskeletal manifestations of COVID-19



COVID-19 is a predominantly respiratory illness caused by the novel Coronavirus SARS-CoV-2.<sup>1</sup> Extra-pulmonary involvements, including musculoskeletal manifestations of the disease, have now become evident.<sup>2</sup> Musculoskeletal (MSK) symptoms of fatigue, myalgia, and arthralgia are common with COVID-19. Although the exact incidence of MSK affliction is unclear, Cipollaro et al. have reported clinical data on 12,046 patients (54% male and 46% females) ascertaining the prevalence of MSK symptoms and epidemiological characteristics in patients with COVID-19.<sup>3</sup> The total prevalence of fatigue symptoms was 25.6% while, the prevalence of arthralgia and myalgia was 15.5%. Interestingly, eight studies have reported a higher prevalence of fatigue in more than 50% of patients. Some European studies have reported an even higher incidence of myalgia (59%) and arthralgia (31%).<sup>4</sup>

The exact mechanism leading to the development of MSK manifestations in COVID-19 remained unclear. It is postulated that Angiotensin-Converting Enzyme 2 (ACE-2) receptor found in the central, peripheral nervous systems, smooth muscles, and TMPRSS2 (Trans Membrane Protease, Serine) expression in skeletal muscles and the synovium may act as a portal of entry for the novel Coronavirus SARS-CoV-2.<sup>5,6</sup> Co-fusion of viral structural spike (S) protein with the host cells results in subsequent viral replication, cell inflammation, cell death, altered immune response, and release of pro-inflammatory cytokine mediators. Direct viral toxicity, endothelial cell damage, and dysregulation of the immune response lead to an abnormal, exaggerated inflammatory response (the “cytokine storm”). It appears to be the key mechanism in the pathophysiology of the variety of MSK clinical features associated with COVID-19.

Several short and long-term MSK manifestations of COVID-19 are reported in the literature. MSK manifestations are described in one-quarter to one-half of symptomatic patients with COVID-19.<sup>3,4,6</sup> These are usually present early in the course of the disease. Most of these symptoms are not severe but are disabling and manifest as fatigue, myalgia, or transient arthralgia. It appears to be found more commonly in females and associated with disease activity.<sup>7</sup> A more extended hospitalization period of about three weeks seems to increase Intensive Care Unit (ICU) acquired muscle weakness and deconditioning.

Soft tissue abnormalities such as limb gangrene, “COVID-19 toes,” hematoma and pressure sores have been described primarily in patients with associated comorbidities such as diabetes mellitus.<sup>8</sup> Inflammatory-mediated thrombosis and endothelial injury are the responsible factors for it. Bone and joint involvement in COVID-19 also has a broad spectrum, with viral arthralgias being commoner rather than clinical arthritis. The arthritis is usually a reactive or crystalline type instead of a viral arthritis type. Therefore, one must search for other causes of arthritis by performing serological tests and fluid sampling. The presence of MSK

symptoms is problematic, especially in the elderly and middle-aged population, with or without comorbidities. It may lead to increased use of non-steroidal anti-inflammatory drugs (NSAIDs) for symptom relief. Reduced bone mineral density (BMD), osteoporosis, and osteonecrosis at various anatomical sites seem dependent on the extent and duration of corticosteroids in the treatment of COVID-19.<sup>6</sup>

“Long COVID” is a term used to describe the long-term effects of COVID-19 in people who have either suspected or confirmed COVID-19. These are seen in a group of people recovering from the disease but are still demonstrating ongoing symptoms of COVID-19 far longer than expected for the disease pattern. The commonly reported symptoms in these patients include fatigue (53%), dyspnoea (43%), joint pain (27%), and chest pain (22%).<sup>9</sup>

Routine laboratory investigations to rule out other inflammatory joint pathology need to be carried out. Besides, multimodality imaging may be required for the diagnosis and evaluation of MSK disorders in COVID-19 patients. Ramani et al. have reported MSK findings at various anatomical levels in patients with COVID-19 with characteristic abnormalities detected in soft tissues, muscles, bones, and joints.<sup>10</sup>

The management of MSK symptoms requires NSAIDs for pain relief and multi-disciplinary support, including orthopaedic rehabilitation. Patients may seek online therapy support to avoid face-to-face consultation. Exercise-based regimes should be recommended to all patients following an in-hospital stay to reduce stiffness and disuse atrophy of muscles. Prevention of osteoporosis and osteonecrosis is crucial in every admitted patient, especially on high doses of steroids. Surveillance of symptoms is of paramount importance to minimize any progressive and long-term disability. We need to wait and see if there are any long-term and permanent effects of COVID-19 on the bones and joints like conversion to inflammatory arthritis, and closed monitoring of these patients is therefore required.

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