



Orthopedic Manifestations in Patients of Long COVID-19 Syndrome

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Abstract

The effects of the new coronavirus on the musculoskeletal system have been widely reported. The aim of this study was to determine the prevalence of musculoskeletal symptoms in patients with prolonged covid syndrome. This was a retrospective cohort review of 100 admitted patients who tested positive for COVID-19 after admission to a medical institute in Sitapur. Based on the COVID-19 questionnaire prepared by ourselves, we recorded complaints about new myalgias, joint pains, back and muscle weakness, bone inflammations and compiled a table of all accompanying diseases. Statistical analyzes were performed to examine the association between various comorbidities and orthopedic manifestations in patients with COVID-19. Of the 100 patients who tested positive for COVID-19, 27 had at least one orthopedic problem (27.0%). Patients with orthopedic diseases were significantly younger at 53.7 years than 58.1 years ($p=0.003$) and their incidence was significantly higher in obese than non-obese patients ($p=0.022$). Patients with diabetes had significantly more orthopedic symptoms than patients with cardiac or pulmonary complications. Obese and diabetic patients had significantly more orthopedic symptoms during COVID-19 infection. Further studies are needed in these populations to determine whether these diseases present during COVID infection affect the musculoskeletal system during active disease and after recovery from infection.

Keywords: COVID-19; Diabetic; Myalgia; Obese; Orthopedic

Introduction

The global spread of the novel coronavirus SARS-CoV-2 has raised many questions about the pathophysiological and clinical course of COVID-19. Since the emergence of the virus, there has been talk of introduction of the virus and effects on various organ systems have been reported. The clinical features of this disease vary from an asymptomatic patient to acute respiratory distress and multiple organ dysfunction, while the most common symptoms are fever, cough and dyspnea. Some musculoskeletal symptoms such as muscle pain, joint pain and general muscle fatigue have also been reported [1]. Although these symptoms are not uncommon in viral infections, the extent to which this new virus affects the musculoskeletal system is not fully known, as the literature is limited on the prevalence of these symptoms and their association with multiple comorbidities.

Musculoskeletal manifestations in viral diseases have been associated with an inflammatory immune response through the D-dimer of various cytokines, especially Interleukin (IL)-6 and Tumor Necrosis Factor (TNF), CRP [2]. Levels of IL-6 and TNF- α in both plasma and airway secretions have been directly correlated with severity in COVID-19-positive patients, especially in patients with common comorbidities, which may further contribute to their increased inflammatory state [3,4]. Some recent studies also suggest that the mechanism of myalgia in COVID-19 may differ from the cytokine storm seen in typical viral infections. When lactate dehydrogenase is elevated and creatine kinase is absent, one study suggested that myalgia from COVID-19 may be exacerbated by a novel mechanism involving muscle ischemia [5].

Various concomitant diseases, which prolong the course of the infection and increase the severity of the disease, can also aggravate musculoskeletal symptoms (myalgia, joint pain, etc.). Many comorbidities, such as type 2 diabetes, coronary artery disease, and chronic obstructive pulmonary disease, are thought to lead to chronic inflammation and dysregulation of the immune system, especially under viral infection [6,7], are much more susceptible to complications of COVID-19, because the cytokine storm caused by the virus amplifies immune system disorders and leads to

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worse outcomes.

In the clinical assessment of disease progression, it may be useful to identify which comorbidities are associated with increased musculoskeletal symptoms. We know very little about the viral pathogenesis of COVID-19 and its impact on the musculoskeletal system, and whether orthopedic procedures should be of concern in patients with active or recent infection. Our goal is to provide an overview of the incidence of musculoskeletal disorders in patients with COVID-19 and to find out possible connections between various comorbidities and their symptoms [8-10].

Material and Methods

This was a retrospective cohort review of 100 admitted COVID-19 positive patients at HIMS. Ethical clearance was permitted by institutional review board with target population was of covid patients. We included all patients who were found to be positive for COVID-19 at any time, regardless of whether they had symptoms of COVID or those who were otherwise positive without symptoms. The cohort spanned the period from May 2020 to November 2021. Patients who did not respond to treatment for COVID questionnaire focused on the following: Demographics, orthopedic symptoms, medical treatment for COVID-19, PPE, and others (e.g., intubated on arrival) were excluded from this study along with exclusion criteria extending to patients with previous history of seronegative arthritis, previously diagnosed degenerative arthritis and previous bony infection and including patients who tested COVID-19 positive and patients with co morbidities like DM, CAD, obesity, hypothyroidism, and hypertension.

We collected various demographic data for each patient, including age, race, sex, smoking status, length of stay, reason for admission, ICU (Intensive Care Unit) admission, intubation, and death. Orthopedic diseases were recorded and scored using a designed questionnaire such as myalgia, arthralgia, back pain and general fatigue/weakness, and bone infections.

Results

Of the 100 patients with a positive COVID-19 test, 27 patients had at least one orthopedic disease (27.0%). Table 1 shows the demographics of the patient cohort. Patients with musculoskeletal symptoms were significantly younger at 53.7 years than at 58.1 years ($p=0.003$). No significant association was found between race, sex, ICU stay, death, or smoking.

Of those 100 positive tests, 67 patients had symptoms of COVID-19. The incidence of new orthopedic symptoms in patients with symptoms of COVID-19 was 32 patients. 36 patients were diagnosed with diabetes, 56 with hypertension and 27 with coronary artery disease. A total of 15 patients were diagnosed with Chronic Obstructive Pulmonary Disease (COPD) and/or asthma.

Table 2 shows the prevalence of orthopedic symptoms in patients with COVID-19 by comorbidities. Patients with obesity, type 2 diabetes, heart disease, and COPD/asthma were at significant risk of developing musculoskeletal symptoms associated with COVID-19. Overall, 32% of patients with type 2 diabetes had orthopedic symptoms compared to only 25% of patients in the non-diabetic population ($p=0.03$). We also found that 20% of patients with heart disease had orthopedic disorders compared to 29% of patients without heart disease ($p=0.02$). 28.0% of non-COPD/asthmatics developed orthopedic problems compared to 1% of COPD/asthmatics

Table 1: Demographics of all admitted COVID-19 patients.

Population Demographics (Age and Sex)			
N = 100	Ortho Manifest (-) (n= 73)	Ortho Manifest (+) (n= 27)	p-Value
Sex	M = 54	M = 53	0.78
	F = 46	F = 47	
Age*	Average = 58.1	Average = 53.7	0.006

Table 2: Orthopedic manifestations of COVID-19-positive patients by comorbidity.

Orthopedic Manifestations Based on Comorbidity, n (%)			
Comorbidities	Population Size (N = 100)	Exhibited Orthopedic Manifestations	p-value
Hypertension			
No HTN	44	12	0.73
HTN	56	15	
Type II Diabetes*			
No Diabetes	64	16	0.029
Diabetes	36	12	
Heart Disease*			
None	73	21	0.02
CHF/CAD	27	6	
COPD*			
None	91	26	0.012
COPD	9	1	
Smoking			
History of Smoking	40	10	0.61
No History of Smoking	60	17	

Table 3: Odds ratio by comorbidity for risk factors.

Odds Ratio Based on Comorbidity				
Odds Ratio	Orthopedic Manifestations			
	Yes, (%)	No, (%)	Odds Ratio	Confidence Interval
Obesity	38.00%	62%	2.19	1.54–3.12
Diabetes	32%	68%	1.47	1.04–2.07
Heart Disease	21%	80%	0.62	0.4139 0.9310
COPD	14%	86%	0.41	0.1963 0.8373

($p=0.012$).

Table 3 shows the odds ratios for patients with obesity and diabetes (1.47 and 2.19, respectively). The odds ratios for patients with heart disease and COPD/asthma were 0.62 and 0.41 respectively.

Most common orthopedic manifestation among different comorbidity was arthralgia being 11% among total of 27%.

Discussion

As a result of the COVID-19 pandemic, concerns have been raised about the pathogenesis of the disease and its effects on various organ systems, including the musculoskeletal system. Very few studies have reported musculoskeletal symptoms in the positive population of COVID-19. In the study presented above, a total of 27% of orthopedic manifestations were found to be more common in diabetic and obese patients [11-15].

Obesity, diabetes is established risk factors for viral diseases,

Table 4: Orthopedics manifestations.

Manifestations	Number of cases (N=100)	% age
Myalgia	8	8%
Arthralgia	11	11%
AVN	1	1%
Backache	5	5%
Extra muscular symptoms	2	2%
Total	27	27%

including COVID-19. Several studies have reported higher rates of ICU admission, ventilator use, and mortality in patients with diabetes; this rate can be 3.1 times higher than in non-diabetic patients infected with other respiratory viral diseases such as SARS.6 [16,17]. Similarly, data published in this latest pandemic showed that diabetics have a much higher mortality and severe illness disease according to an Italian study, up to two-thirds of patients who died from COVID-19 were diagnosed with diabetes [18]. In addition, these authors showed that diabetes can be an independent risk factor for high levels of IL-6, serum ferritin, erythrocyte sedimentation rate and C-reactive protein, suggesting a higher inflammatory state in diabetics. Diabetes is an independent risk factor for severe progression of COVID-19 due to a higher inflammatory state [19]. This was clearly evident in our current cohort of patients, as significantly more orthopedic symptoms were observed in patients diagnosed with diabetes.

Heart disease has been documented as the most common form of disease in hospitalized and deceased patients with COVID-19 [20]. Studies have also reported that patients with heart disease have higher levels of inflammatory markers; however, there are no studies showing heart disease as an independent risk factor for elevated cytokines in these patients. Although heart disease is a disease with a high inflammatory state [21], our study did not report higher levels of inflammation in muscle tissue based on patient-reported muscle pain. In fact, this study showed significantly less myalgia in patients with heart disease. This may be due to the local pathophysiology of heart disease, as it primarily affects the coronary microvasculature. Similarly, COPD has been recognized as an independent risk factor for severe pneumonia and poor outcomes. Studies have suggested that this is probably due to poor pulmonary reserve and increased expression of angiotensin-converting enzyme 2 in diseased lungs [22]. ICU reports in patients with COVID vary widely [23-25]. Like heart disease, COPD is a localized inflammatory condition with minimal systemic symptoms. This study documented significantly fewer musculoskeletal symptoms in patients with documented COPD compared to patients without COPD.

Musculoskeletal pain complaints have been widely reported in the literature, particularly in initial reports during the COVID-19 pandemic. One study reported an incidence of myalgia of 21%; However, a study that focused on patients with diabetes as the only comorbidity had a small sample size of only 21 patients [19]. It is likely that musculoskeletal complaints are caused by an elevated systemic inflammatory state, as shown by the higher prevalence of muscle pain in obese and diabetic patients. However, our study found no association between reported muscle pain and length of ICU stay or total stay. In addition, we suspect that the lower number of myalgias in patients with heart disease and COPD may be due to the relatively localized nature of these diseases and the faster exacerbations in these patients. Based on our research and review of the literature,

we suspect that obese and diabetic patients have a greater incidence of COVID-19 orthopedic disease due to their chronic inflammatory state.

This retrospective study was based primarily on physician notes and patient-reported symptoms from a single large academic institution. Therefore, the study has limitations. Patients may not have been adequately screened for musculoskeletal conditions or were too unwell to respond. In addition, this study may have been limited by errors in the documentation provided. The diversity of patient populations was limited to one geographic location and institution. Despite these limitations, this is the first study to analyze the incidence of orthopedic disorders in patients who tested positive for COVID-19, while accounting for common comorbidities.

Orthopedic symptoms of COVID-19 are more often seen in patients with comorbidities such as diabetes mellitus. Overweight and diabetics are at higher risk for more severe symptoms of COVID-19 due to an increased inflammatory response. Myalgia may indicate a poor prognosis in these patients; however, more detailed investigation is needed. Future studies may focus on orthopedic surgical outcomes in patients with positive perioperative tests and whether complaints of frequent myalgia, joint pain, and bone infections may have an additional effect in this surgical group. Another aspect of the future is the long-term impact of COVID-19 on the musculoskeletal system.

Conclusion

This retrospective cohort study of COVID-19 patients with long-term covid progression at HIMS, Sitapur showed a significant (27%) increase in the incidence of orthopedic conditions such as myalgia, arthralgia, low back pain, bone infection, AVN and joint disease accompanying patients. Further studies are now warranted to determine whether muscle pain is an indicator of poor prognosis and whether these patients are at increased risk, particularly for orthopedic procedures and injuries. Identifying medical comorbidities and their effects on other diseases plays an important epidemiological role and may provide future treatment options for at-risk populations diagnosed with COVID-19.

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