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Musculoskeletal Symptoms Following COVID-19 Infection and Vaccination: An Observational Study

Marwan H Adwan[1*], Sara O Rahhal[1], Jude J Abdulhameed[1], Ayman M. AbuHelal[1]

[1] Department of Medicine, Division of Rheumatology, The University of Jordan, Amman, Jordan

*Corresponding author:

mhad35@msn.com

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Abstract

Background: The global pandemic caused by COVID-19 has led to numerous reports of musculoskeletal (MSK) symptoms occurring after infection or vaccination. However, the precise prevalence of MSK symptoms in individuals following COVID-19 infection/vaccination remains uncertain.

Methods: This observational study involved 46 patients who developed MSK symptoms after experiencing COVID-19 infection or vaccination.

Results: The study group comprised 37 females (80.4%) and 9 males (19.6%) with an average age of 48.6±12.4 years (median 47.5 years). Among the participants, 25 patients (54%) developed symptoms after infection, while 21 patients (46%) reported symptoms after vaccination. The duration of symptoms ranged from 2 to 65 weeks, and the onset of symptoms occurred between 1-182 days following infection/vaccination (median 7 days). The small joints of the hands and feet were the most frequently affected (50%), followed by the wrists (47.8%) and knees (41.3%). Notably, approximately 50% of cases experienced complete resolution of symptoms. Additionally, individuals with pre-existing arthritis may experience exacerbation of their symptoms following infection/vaccination.

Conclusion: This study reveals that MSK symptoms can manifest after COVID-19 infection/vaccination, with the small joints being the most commonly affected. These findings emphasize the importance of comprehending and monitoring MSK symptoms in individuals post-COVID-19 infection/vaccination to provide appropriate medical care and management.

Keywords: COVID-19, Coronavirus, vaccination, arthritis.

INTRODUCTION

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the virus responsible for causing the COVID-19 pandemic, which emerged in Wuhan, China, in December 2019 and rapidly spread globally. The World Health Organization (WHO) declared it a pandemic in March 2020 [1].

While COVID-19 is primarily known for its impact on the respiratory system, it has become evident that the virus can affect other

systems in the body, including the musculoskeletal (MSK) system [2].

Notably, patients with COVID-19 have frequently reported experiencing musculoskeletal symptoms alongside respiratory issues. These symptoms often include fatigue, myalgia and arthralgia [3]. Furthermore, individuals who have received vaccinations against SARS-CoV-2 have also reported similar musculoskeletal symptoms [4, 5]. Additionally, cases of reactive arthritis and post-viral arthritis have been documented in some patients following COVID-19 infection [6, 7].

Understanding the underlying mechanisms behind the musculoskeletal manifestations in COVID-19 infection and vaccination is of great interest to the scientific community. One potential explanation lies in the angiotensin-converting enzyme 2 (ACE-2) receptor, known to be a key receptor for SARS-CoV-2 entry into cells. This receptor is expressed in various tissues outside of the lungs, including cartilage and synovial tissues, raising the possibility that direct viral damage in these tissues may contribute to arthralgia and arthritis [8, 9].

Another proposed mechanism for musculoskeletal symptoms after COVID-19 infection involves cytokine-mediated damage to MSK tissues. Cytokines are small proteins that play a crucial role in the body's immune response. In some severe COVID-19 cases, an excessive release of cytokines, known as a cytokine storm, can lead to systemic inflammation and tissue damage, potentially affecting the musculoskeletal system as well, resulting in conditions like rhabdomyolysis [10].

Despite the lack of full understanding regarding the mechanisms, it is clear that musculoskeletal symptoms following COVID-19 infection or vaccination can be significant and may persist long after the initial infection has resolved.

To shed light on this aspect, an observational study was conducted at a single center. The primary objective was to assess and determine the extent of musculoskeletal manifestations occurring in individuals after experiencing COVID-19 infection and vaccination.

By examining a cohort of patients who had developed such symptoms, it was hoped to contribute to a better understanding of the impact of SARS-CoV-2 on the musculoskeletal system and provide valuable insights for clinical management and care.

STUDY METHODS

This observational study aimed to investigate musculoskeletal (MSK) symptoms in patients following COVID-19 infection or vaccination. The study period ranged from July 2021 to May 2022. Patients attending the rheumatology clinic with such symptoms during this time frame were included in the research.

To ensure the accuracy of COVID-19 infection cases, the inclusion criteria required confirmation of infection through conventional polymerase chain reaction (PCR) tests performed on nasopharyngeal swabs. All patients included in the study were interviewed and examined by qualified physicians to gather comprehensive data.

The data recorded for each patient encompassed various aspects, including age, sex, co-morbidities, duration of joint symptoms, presence of morning stiffness and synovitis, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), rheumatoid factor (RF), and anti-cyclic citrullinated peptide (anti-CCP).

These factors were critical in

understanding the progression and characteristics of MSK symptoms in the studied cohort.

To evaluate the development and resolution of symptoms over time, a follow-up was conducted three months after the initial clinic visit. The follow-up was conducted through telephone calls, allowing researchers to assess any changes or persistence in the reported MSK symptoms.

Ethical considerations were strictly adhered to throughout the study. Approval was obtained from the Institutional Review Board (IRB) at Jordan University Hospital to ensure the protection of patients' rights and privacy. Additionally, the study was conducted in accordance with the ethical standards outlined by the World Medical Association Declaration of Helsinki, which serves as a global guideline for medical research involving human participants.

Statistical Analysis

To analyze the data collected, researchers employed Microsoft Excel 2007 and the Statistical Package for the Social Sciences (SPSS) version 17.0. These tools facilitated the organization and interpretation of the data, providing valuable insights into the trends and associations within the patient cohort.

Continuous variables, such as age and symptom duration, were expressed using the mean and standard deviation, giving an overall representation of the data distribution. On the other hand, categorical variables, including gender and presence of specific symptoms, were expressed as percentages to highlight their prevalence within the studied group.

Statistical tests were applied to assess the significance of certain findings. For categorical variables, Fisher's exact test was employed, while an independent sample t-test was used for continuous variables. The critical threshold for statistical significance was set at a two-tailed p-value of ≤ 0.05.

RESULTS

The study cohort consisted of 46 patients who experienced MSK symptoms following either COVID-19 infection or vaccination. Among these patients, 25 (54%) developed symptoms after infection, while 21 (46%) reported symptoms after vaccination.

The demographic distribution of the group was predominantly female, with 37 female patients (80.4%) and 9 male patients (19.6%). The overall mean age of the patients was 48.6±12.4 years, with a median age of 47.5 years.

The duration of MSK symptoms varied among patients, ranging from 2 to 65 weeks. The onset of symptoms following infection or vaccination ranged from 1 to 182 days, with a median onset of 7 days.

Among the patients, 76.1% reported experiencing early morning stiffness, and this symptom's prevalence did not differ significantly between those who developed symptoms after infection and those who did so after vaccination.

Regarding the affected joints, the small joints of the hands and feet were the most frequently involved, affecting 50% of the patients. This was followed by the wrists (47.8%) and knees (41.3%).

The nature and distribution of MSK symptoms were diverse among the patients. Arthralgia/arthritis was the most common, present in 42 patients, while 3 patients reported diffuse bone ache, and 2 patients experienced Achilles tendon rupture. Of the total, 33 patients had purely peripheral joint involvement, whereas 10 patients exhibited a combination of peripheral and axial

involvement.

Nearly half of the patients (47.8%) had an underlying rheumatic disease, with rheumatoid arthritis being the most prevalent. Other underlying rheumatic diseases included systemic lupus erythematosus (SLE), disc prolapse, osteoarthritis, systemic sclerosis, overlap syndrome, gout, pseudogout, fibromyalgia, and Behcet's disease.

The presence of rheumatoid factor was positive in 10 out of 44 patients (22.7%), but it was noted that 90% of those with a positive result had an underlying rheumatic disease. Additionally, 5 out of 36 patients (13.8%) tested positive for anti-cyclic citrullinated peptide (anti-CCP), with no significant difference observed between those with and without an underlying rheumatic disease.

Comparison of patients who developed symptoms post-infection and those with post-vaccination symptoms showed no significant differences in age, sex, symptom duration, number of involved joints, morning stiffness, ESR, CRP, or resolution/persistence of symptoms. However, there was a statistically significant difference in the presence of synovitis between the two groups.

A comparison between patients with transient symptoms and those with persistent symptoms revealed that the latter group had significantly higher CRP levels.

Due to the limited sample size, a detailed comparison between different vaccine types could not be performed.

Treatment

The management of patients' MSK symptoms varied depending on the severity and underlying conditions. Approximately 25 patients were managed conservatively using analgesia, 7 patients received disease-modifying anti-rheumatic drugs (such as sulfasalazine, methotrexate, or hydroxychloroquine), 7 patients were prescribed oral corticosteroids, and 3 patients received intra-articular steroid injections to address specific joint-related issues.

DISCUSSION

Findings were presented from a comprehensive study involving 46 patients who developed musculoskeletal (MSK) symptoms following either COVID-19 infection or vaccination. To the best of our knowledge, this study represents the largest investigation conducted to date on this particular subject.

The connection between autoimmunity, autoimmune diseases, infection, and vaccination has been well-established in scientific literature [11, 12]. Both infection and vaccination can trigger autoimmunity through various mechanisms, including molecular mimicry, epitope spreading, bystander activation, and cryptic antigens [12, 13].

Of particular significance in vaccine-induced autoimmunity is the bystander activation mechanism, which involves the release of self-antigens from infected tissue, leading to an auto-reactive T-cell response [13].

Numerous studies have highlighted the presence of molecular epitopes in SARS-CoV-2 that share similarities with human proteins, potentially resulting in cross-reactivity and the initiation of autoimmune disorders. The occurrence of acute local inflammation due to the presence of mimicking epitopes in the synovial membrane has been proposed as a plausible explanation for arthritis observed after recovering from COVID-19 infection, manifesting as reactive arthritis, acute arthritis, and post-viral arthritis [15].

Regarding patient demographics, our

study revealed a higher proportion of female patients, suggesting their heightened susceptibility to autoimmune diseases. Intriguingly, there was no significant sex difference between patients with underlying rheumatic diseases and those without. Furthermore, symmetric symptoms were predominant among the patients, regardless of whether the symptoms manifested after infection or vaccination. These findings align with a study by Mukarram et al., which reported five patients who developed polyarthritis with symmetrical joint distribution and synovitis [16].

The small joints of the hands and feet, along with the wrists, were the most commonly affected in our patient cohort, accounting for 56% of joint involvement. Additionally, nearly half of the patients experienced complete resolution of symptoms, irrespective of the presence of an underlying rheumatic disease.

Notably, a noteworthy correlation was observed between higher mean serum C-reactive protein (CRP) levels and the persistence of symptoms. This association with inflammatory markers, including erythrocyte sedimentation rate (ESR) and CRP, indicates that the underlying mechanism of post-COVID-19 arthritis primarily results from the hyper-inflammatory process triggered by COVID-19 infection, rather than an autoimmune reaction [17].

Furthermore, our study highlighted that patients aged 50 years or older were more likely to experience an exacerbation of an underlying rheumatic disease after infection/vaccination rather than developing de novo arthritis.

Of particular interest were two cases of Achilles tendon tear identified in the study, both occurring after COVID-19 vaccination. Notably, neither of these cases had an underlying rheumatic disease. The onset of tendon tears was reported 20 days after vaccination in a 28-year-old male and 91 days after vaccination in a 41-year-old female. As far as we are aware, no cases of tendon rupture following coronavirus vaccination have been reported in the literature to date.

Conclusion: This study concludes that MSK symptoms, encompassing arthralgia, arthritis, and tendinopathy/tendon tear, can develop following either COVID-19 infection or vaccination. The small joints were most frequently affected, and close to half of the patients experienced complete resolution of symptoms. However, prospective studies are essential to precisely determine the prevalence of MSK symptoms and their associations with different types of vaccines.

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

Funding: This research study did not receive specific funding from any public, commercial, or not-for-profit organizations to carry out the investigations described in this article.

Ethics Statement: The Institutional Review Board at Jordan University Hospital approved this study, and all procedures adhered to the ethical standards defined by the institutional and/or national research committee, in accordance with the principles outlined in the World Medical Association Declaration of Helsinki for this type of study.

Informed Consent: Informed consent was diligently obtained from all participating patients, ensuring their full understanding and voluntary participation in the research study.

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الأعراض العضلية الهيكلية بعد مرض ومطعوم كوفيد-19

مروان حمود العدوان[1]، سارة الرحال[1]، جود عبد الحميد[1]، ايمن ابو هلال[1]

[1] قسم الامراض الباطنية، شعبة الروماتزم، الجامعة الاردنية، عمان، الاردن

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الملخص

الخلفية والأهداف : أدى الوباء العالمي الناجم عن كوفيد-19 إلى العديد من التقارير عن أعراض الجهاز العضلي الهيكلي (MSK) التي تحدث بعد الإصابة أو التطعيم. ومع ذلك، لا يزال دقة حدوث أعراض الجهاز العضلي الهيكلي لدى الأفراد بعد إصابتهم بعدوى كوفيد-19 أو التطعيم له غير مؤكد.

منهجية الدراسة : شملت هذه الدراسة الرصدية 46 مريضًا ظهرت عليهم أعراض الجهاز العضلي الهيكلي بعد إصابتهم بعدوى كوفيد-19 أو تطعيمهم.

النتائج: تألفت مجموعة الدراسة من 37 أنثى (80.4٪) و 9 ذكور (19.6٪) بمتوسط عمر 48.6 ± 12.4 سنة (متوسط 47.5 سنة). من بين المشاركين، ظهرت أعراضٌ على 25 مريضًا (54٪) بعد الإصابة، بينما أبلغ 21 مريضًا (46٪) عن أعراضٍ بعد التطعيم. تراوحت مدة الأعراض من أسبوعين إلى 65 أسبوعًا، وحدث ظهور الأعراض بين 1-182 يومًا بعد الإصابة/التطعيم (متوسط 7 أيام). كانت المفاصل الصغيرة في اليدين والقدمين الأكثر تأثرًا (50%)، تليها مفاصل المعصم (47.8%) والركبتين (41.3%). والجدير بالذكر أن حوالي 50% من الحالات شهدت اختفاءً تامًا للأعراض. بالإضافة إلى ذلك، قد يعاني الأفراد المصابون بالتهاب المفاصل الموجود مسبقًا من تفاقم أعراضهم بعد العدوى/التطعيم.

الاستنتاجات : تكشف هذه الدراسة أن أعراض الجهاز العضلي الهيكلي يمكن أن تظهر بعد الإصابة/التطعيم بكوفيد-19، حيث تُعد المفاصل الصغيرة الأكثر تأثرًا. تؤكد هذه النتائج على أهمية فهم أعراض الجهاز العضلي الهيكلي ومراقبتها لدى الأفراد بعد الإصابة/التطعيم بكوفيد-19 لتوفير الرعاية الطبية المناسبة والإدارة المناسبة.

الكلمات الدالة: كوفيد 19، فيروس كورونا، تطعيم، التهاب مفاصل.