Original Article

Rheumatic and Musculoskeletal Complications after Covid-19 Infection

Mahbub-Uz-Zaman K[1], Haidar MS[2], Amin I[3], Mukit MA[4], Islam S[5], Alam MJ[6], Khan MAA[7]

DOI: https://doi.org/10.3329/jafmc.v21i2.84073

Abstract

Background: The persistence of symptoms after Covid-19 infection is a new area of interest for researchers.

Objective: To determine the frequency of persistence of rheumatic symptoms after Covid-19 infection.

Methods: This cross-sectional study was conducted at Combined Military Hospital (CMH), Dhaka from December 2021 to June 2022. A total of 173 patients who suffered from Covid-19 at least 6 months prior were enrolled. Data were collected using a pre-designed questionnaire over the phone regarding the persistence of symptoms and new rheumatic symptoms after Covid-19 infection.

Results: A total of 173 patients were enrolled; the average age was 43.5±18.2 years and 66% were male. Almost half of the study participants (44.5%) were serving military personnel and 87.9% of them were vaccinated against Covid-19. Among the study participants, 28.9% required supplemental oxygen to treat Covid-19. After Covid-19 suffering, 28.9% had persistent symptoms and 9.8% had persistent musculoskeletal symptoms. After Covid-19, 6(3.47%) developed new joint symptoms; of them, one was diagnosed with Rheumatoid Arthritis (RA), one with Osteoarthritis (OA) and 4 remained undifferentiated. Though the persistence of symptoms was numerically less in military personnel, it was not statistically significant (p 0.076).

Conclusion: Covid-19 infection may trigger the development of inflammatory arthritis. Further studies are needed to assess the molecular pathophysiological changes and to confirm causal relationship.

Keywords: Rheumatic Symptoms, Rheumatic Complications, Covid-19 infection, Coronavirus disease (COVID).

Introduction

Since the emergence of COVID in Wuhan of China in 2019, it has more than 3 years passed. It was declared as pandemic in 2020.[1] Though initially it was thought to be a short-lasting respiratory illness, with time many dimensions including long-term sequelae of the disease is unvealing.[2] COVID-19 has long-term effects on the neuropsychiatric, pulmonary, cardiovascular, hematologic, gastrointestinal, musculoskeletal, renal, endocrine and dermatologic systems.[2] Relentless efforts are being given to get rid of this illness. Vaccination against COVID-19 has improved survival and decreased the severity of the disease.[3] COVID-19 causes muscle and joint pain during acute illness[2,4-6] and cases of avascular necrosis of bone are also reported after acute illness.[7] COVID-19 can trigger autoimmunity[8] and can increase the risk of developing inflammatory arthritis.[9] Long-term and post-COVID-19 musculoskeletal complications are already reported in the literature; Persistent arthralgia, myalgia, fatigue, muscle weakness, cracking or popping sound in joints, joint stiffness, arthritis[10], reactive arthritis[11], avascular necrosis of bone[7], dermatomyositis[12], systemic lupus erythematosus (SLE)[13] are among them. This cross-sectional study was aimed to find out new rheumatic or musculoskeletal symptoms/ disease in patients who suffered from COVID-19 infection at least 6 months prior to enrollment.

Materials and Methods

This cross-sectional study was conducted at Combined Military Hospital, Dhaka from December 2021 to June 2022. Data were collected using a pre-designed questionnaire. Study population was patients who had positive covid-19 test result at Armed Forces Institute of Pathology (AFIP) at least 6 months back. A list of patients (name and contact number) affected with COVID-19 at least 6 months back was collected from the AFIP. We approached the first 300 from the list over the phone for enrollment in this study. Patients who suffered from Covid-19 within last 6 months were excluded (some of the patients in the list had further Covid-19 infection within last 6 months, tested in different lab). Other causes of exclusion were wrong phone number given, phone number given of some relative, not picking up the phone after at least 3 times calling spaced by time, and not interested to give personal information. Finally a total of 173 persons who suffered from Covid-19 at least 6 months prior to enrollment were enrolled. Data were collected by the authors of this study over the phone who also at the same time filled up the data sheet. Data imputation was done in SPSS (Statistical Package for the Social Sciences) version 25 to run the analysis. Numerical data were expressed in mean ± SD and categorical data in percentage. To compare two categorical variables chi-square test/Fisher's exact test was used. Before starting the research, ethical clearance was taken from the Ethical Committee of CMH Dhaka.

1. **Maj Khandker Mahbub-Uz-Zaman**, MBBS, MD, Classified Specialist in Medicine (Rheumatology), Combined Military Hospital (CMH) Dhaka, Dhaka (*E-mail:* khmahbub21@gmail.com) 2. **Maj Gen Md Shameem Haidar**, MBBS, FCPS, Consultant Physician General, Bangladesh Armed Forces 3. **Maj Ikramul Amin**, MBBS, CMH Dhaka, Dhaka 4. **Maj Md. Abdul Mukit**, MBBS, CMH Dhaka, Dhaka 5. **Maj Saiful Islam**, MBBS, MPH, CMH Dhaka, Dhaka 6. **Maj Md. Jayedul Alam**, MBBS, MCPS, CMH Dhaka, Dhaka 7. **Maj Md Asif Ashfaque Khan**, MBBS, GSO-II (R&D), AFMC, Dhaka.

Results

A total of 173 patients were enrolled. The mean age of the study participants was 43.5±18.2 years, 66% were male. Among them, 77(44.5%) were serving in any of the military forces of Bangladesh. Among the remaining 96 persons 41 were homemakers, 8 students, 5 businessmen, 38 retired personnel and 4 others (teacher, banker and freelancer). Among the participants, 123(71.1%) were non-smokers, 19(11%) were smokers and 31(17.9%) were ex-smoker. Regarding comorbidity of the study participants, 28.3% were hypertensive, 23.7% were diabetic, 9.8% had ischemic heart disease, 7.5% had chronic kidney disease, 4.6% asthmatic, 2.9% had cerebrovascular disease, 2.3% hypothyroid, 1.7% had prostatic enlargement, 1.2% had chronic liver disease, 0.6% had each of psoriasis, pemphigus vulgaris, hemorrhoid, multiple myeloma, carcinoma lung.

Out of 173 study participants, 152(87.9%) were vaccinated against Covid-19 (Figure-1). Regarding suffering from Covid-19, 156(90.2%) suffered from Covid-19 once, and the rest 17(9.8%) suffered twice. Hospital admission was required in 154(89%) to treat Covid-19; 50(28.9%) needed supplemental oxygen; 1(10.4%) needed HDU or ICU support.

Table-I: Persistent symptoms (n=173)

Symptom	Persisted in n (%)
Constitutional symptom	35 (20.2)
Fatigue	23 (13.3)
Generalized weakness	13 (7.5)
Persistent joint pain	14 (8.1)
Persistent mild shortness of breath	9 (5.2)
Persistent cough	5 (2.9)
Myalgia	5 (2.9)
Weight loss	3 (1.7)
Muscle weakness	2 (1.2)
Persistent chronic low back pain	2 (1.2)
Persistent loss of appetite	2 (1.2)
Chest pain	1 (0.6)
Reduced smell	1 (0.6)
Feverish feeling	1 (0.6)
Insomnia	1 (0.6)
Hearing difficulty	1 (0.6)

Six (3.5%) developed new joint symptoms after being suffered from Covid-19. One was diagnosed with Rheumatoid arthritis (RA), one was osteoarthritis (OA) and 4 of them suffered from pain in multiple joints where the diagnosis is not confirmed. The comparison of the persistence of symptoms between those who are serving in the military and non-military personnel is shown in Table-II.

Table-II: Comparison of Persistence of symptoms between military and non-military personnel (n=173)

		Military personnel, n=77, n (%)	Non-military personnel, n=96, n (%)	*p*
Any Persistence of Symptoms post-Covid-19	Yes	17 (22.1)	33 (34.4)	.076*
	No	60 (77.9)	63 (65.6)	
Persistent constitutional symptoms	Yes	14 (18.2)	21 (21.9)	.548*
	No	63 (81.8)	75 (78.1)	
New Rheumatic symptoms after Covid-19	Yes	3 (3.9)	3 (3.1)	1.000#
	No	74 (96.1)	93 (96.9)	

**Chi square test, # Fisher's exact test*

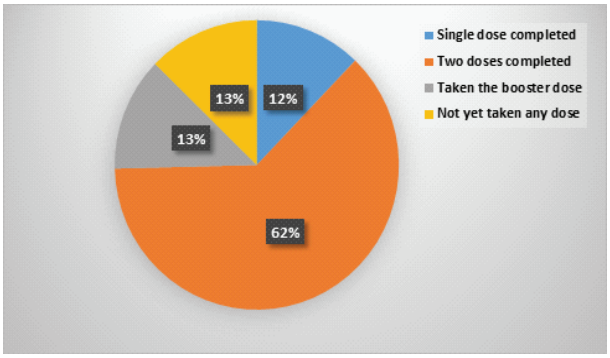

Figure-1: Covid-19 vaccine taking among study participants (n=173)

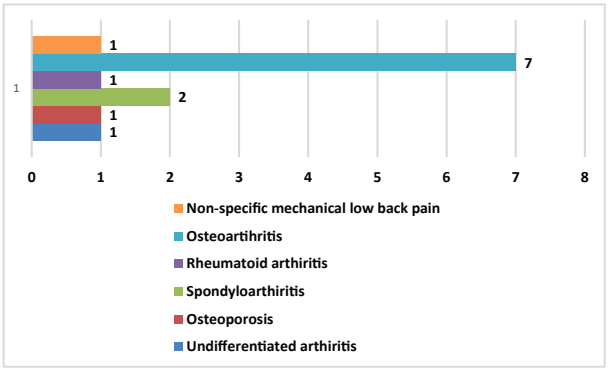

Figure-2: Frequency of Rheumatic disease in study participants

Discussion

This study was probably the first study on this topic conducted in a military hospital where a significant number of military personnel were the study subject. Nearly half of the study participants are serving military personnel. A quarter of the study participants were homemakers (23.7%). Among the study participants, 11% of the subjects were smokers; 13.1% were smokers reported in another study in Bangladesh.[14]

Among the participants, 10% have suffered from COVID-19 twice before. As already 3 years have passed, a good number of participants suffered more than once. Regarding treatment, 89% were hospitalized to treat COVID-19. The frequency of hospitalization is 15.3%[15] and 37.91% reported in another study.[16] The higher rate of hospitalization is probably due to the practice of defensive medicine in military hospitals. During treatment, 28.9% of subjects needed supplemental oxygen in this study; the proportion is higher than that reported by others (14.9%).[17] 10.4% needed HDU/ICU support; this is again higher than that reported (4.9%) by others.[17]

In this study, 28.9% had persistent symptoms after Covid-19 and 17(9.8%) had persistent musculoskeletal and rheumatic symptoms. After more than 6 months of Covid-19 infection, 13.3% had fatigue, 7.5% had generalized weakness and 8.1% had persistent joint pain. A much higher proportion of patients had persistence of these symptoms in another study[10] where 55% had fatigue, 25% had arthralgia and 12% had muscle weakness within 6 months. This may be due to differences in

study design. In this study, we have enrolled persons who have suffered from Covid-19 at least 6 months prior, whereas Gulzar et al[10] enrolled patients within 6 months of Covid-19 infection. So with time probably symptoms disappear. Among the participants of this study, one developed rheumatoid arthritis (RA), one developed osteoarthritis OA and 4 developed arthritis which is still undifferentiated. The development of inflammatory arthritis resembling RA after suffering from Covid-19 was reported in other studies.[18,19]

In this study, the rate of persistence of MSK and non-musculoskeletal symptoms was numerically more among non-military personnel than that of currently serving military personnel, though the difference was not statistically significant. This might be due to the difference in lifestyle as serving military personnel has to do regular physical activity and exercise which affects immune system and body homeostasis.[20,21] Regular exercise has anti-inflammatory effects on central and peripheral organs[22] that may act positively to wash out the inflammatory triggers by Covid-19.

In conclusion, a portion of patients suffered from Covid-19 develops masculoskeletal symptoms. Regular exercise is a potential non- pharmacological intervention to manage these issues which needs further research.

References

1. Cucinotta D, Vanelli M. WHO declares COVID-19 a pandemic. Acta Biomed. 2020; 91(1):157–60.

2. Desai AD, Lavelle M, Boursiquot BC, Wan EY. Long-term complications of COVID-19. Am J Physiol- Cell Physiol. 2022; 322(1):1–11.

3. Bernal JL, Andrews N, Gower C, Robertson C et al. Effectiveness of the Pfizer-BioNTech and Oxford-AstraZeneca vaccines on covid-19 related symptoms, hospital admissions and mortality in older adults in England: Test negative case-control study. BMJ. 2021; 373(n1088):1-11.

4. Abdullahi A, Candan SA, Abba MA, Bello AH, Alshehri MA, Afamefuna Victor E et al. Neurological and musculoskeletal features of COVID-19: A systematic review and meta-analysis. Front Neurol. 2020; 11(687):1-16.

5. Alexander AJ, Joshi A, Mehendale A. The Musculoskeletal Manifestations of COVID-19: A Narrative Review Article. Cureus. 2022; 14(9):1-5.

6. Disser NP, De Micheli AJ, Schonk MM, Konnaris MA, Piacentini AN, Edon DL et al. Musculoskeletal Consequences of COVID-19. J Bone Jt Surg. 2020; 102(14):1197–204.

7. Sulewski A, Sieroń D, Szyluk K, Lukoszek D, Christe A, Dabrowski M et al. Avascular necrosis bone complication after active COVID-19 infection: Preliminary results. Med. 2021; 57(12):1–8.

8. Rodríguez Y, Novelli L, Rojas M, Santis M De, Acosta-ampudia Y, Ansari AA et al. Autoinflammatory and autoimmune conditions at the crossroad of COVID-19. Journal of Autoimmunity. 2020; 114:1-19.

9. Joo Y Bin, Lim YH, Kim KJ, Park KS, Park YJ. Respiratory viral infections and the risk of rheumatoid arthritis. Arthritis Res Ther. 2019; 21(1):1–8.

10. Gulzar R, E Haque Mahmud T, Rasheed A, Riaz S, Adnan WA, Hafeez U et al. Musculoskeletal symptoms in patients recovering from COVID-19. Muscles Ligaments Tendons J. 2022; 12(1):9–16.

11. Mukarram MS. Post COVID-19 Reactive Arthritis: An Emerging Existence In the spectrum of musculoskeletal complications of SARS-CoV-2 Infection. Clin Stud Med Case Reports. 2020; 7(3):1–4.

12. Gokhale Y, Patankar A, Holla U, Shilke M, Kalekar L, Karnik ND et al. Dermatomyositis during COVID-19 pandemic (A Case Series): Is there a cause effect relationship? J Assoc Physicians India. 2020; 68(11):20–4.

13. Bonometti R, Sacchi MC, Stobbione P, Lauritano EC, Tamiazzo S, Marchegiani A, Novara E, Molinaro E, Benedetti I, Massone L, Bellora A BR. The first case of systemic lupus erythematosus (SLE) triggered by COVID-19 infection. Eur Rev Med Pharmacol Sci. 2020; 24(18):9695–7.

14. Khalil MM, Mahbub-Uz-Zaman K, Hossain A-S, Ahmed F, Chowdhury MFK, Khan ST et al. Adverse Events Following COVISHIELD Vaccination Among Adult Population in Bangladesh. SN Compr Clin Med. 2021; 3(11):2207–13.

15. Mahbub-Uz-Zaman K, Debnath D, Khalil MM, Tahmid MS, Monir S, Munmun ST et al. Socio-demographic Profile of COVID-19 Patients and Difficulties Faced by Them while Testing RT-PCR: A Multi-center Cross-sectional Study. Mymensingh Med J. 2021; 30(3):796–802.

16. Carrillo-Vega MF, Salinas-Escudero G, García-Peña C, Gutiérrez-Robledo LM, Parra-Rodríguez L. Early estimation of the risk factors for hospitalization and mortality by COVID-19 in Mexico. PLoS One. 2020; 15:1–11.

17. Kamal M, Abo Omirah M, Hussein A, Saeed H. Assessment and characterisation of post-COVID-19 manifestations. International Journal of Clinical Practice. 2021; 75(3):1–5.

18. Mukarram MS, Ishaq Ghauri M, Sethar S, Afsar N, Riaz A, Ishaq K. COVID-19: An Emerging Culprit of Inflammatory Arthritis. Case Rep Rheumatol. 2021; 2021:1–8.

19. Deeb M, Moloney PB, McCarthy G, Stack J, Lynch T, Osorio YL. Inflammatory Arthritis Post Covid-19 Infection. Journal of the Irish Medical Association. 2022; 115(1):1–4.

20. Cook MD, Allen JM, Pence BD, Wallig MA, Gaskins HR, White BA, et al. Exercise and gut immune function: Evidence of alterations in colon immune cell homeostasis and microbiome characteristics with exercise training. Immunol Cell Biol. 2016; 94(2):158–63.

21. Martin KS, Azzolini M, Ruas JL. The kynurenine connection: How exercise shifts muscle tryptophan metabolism and affects energy homeostasis, the immune system, and the brain. American Journal of Physiology-Cell physiology. 2020; 318(5):C818–30.

22. Scheffer D da L, Latini A. Exercise-induced immune system response: Anti-inflammatory status on peripheral and central organs. Biochim Biophys Acta Mol Basis Dis. 2020; 1866(10):1-16.