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Chronic musculoskeletal symptoms following COVID-19 in a cohort of Sri Lankan patients

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Abstract

Introduction and objectives: Musculoskeletal symptoms of myalgia and arthralgia after recovery of COVID-19 is a pressing issue. Objective of this study was to assess the prevalence of persistent myalgia and arthralgia and likelihood of developing rheumatoid arthritis (RA), six weeks following COVID-19.

Methods: A descriptive longitudinal study was conducted in selected private sector hospitals in Colombo, Sri Lanka. PCR positive COVID-19 patients were recruited by consecutive sampling until required sample size of 333 was fulfilled. They were contacted over the phone six weeks after the discharge. Interviewer administered questionnaire was used to evaluate the presence of symptoms of myalgia and arthralgia. Those with positive symptoms were invited for a consultation to conduct further investigations.

Results: Of the 333 patients, 96 (28.8%) had persistent arthralgia, myalgia or both, six weeks after recovery from COVID-19. Among them, 56.3% had only arthralgia, 10% had only myalgia and 33% had both myalgia and arthralgia. Two patients (4.8%; 95% CI: 0.6-16.2%) were confirmed of having RA.

Conclusions: More than one fourth of patients, suffered with persistent symptoms of myalgia and arthralgia six weeks following COVID-19 and 2 patients (4.8%) were confirmed to have rheumatoid arthritis.

Key words: COVID-19, arthralgia, myalgia, rheumatoid arthritis, rheumatic musculoskeletal disease

Introduction

Coronavirus disease-2019 (COVID-19) pandemic has affected healthcare systems across the world.[1] The persistence of musculoskeletal symptoms following COVID-19 has been reported. Myalgia and arthralgia are among the common musculoskeletal symptoms following recovery from COVID-19.[2, 3]

Rheumatic musculoskeletal diseases (RMDs) are a diverse group of conditions which affects joints, connective tissue, cartilage, ligaments, tendons and muscles.[4] Many of these are long term diseases which worsen over time.[3] Rheumatoid arthritis (RA), a main type of RMD, is a disabling disease. Persistent myalgia and arthralgia need further investigations as these symptoms indicate ongoing pathology related to RMDs. The objective of the study was to assess the prevalence of persistent myalgia and arthralgia and prevalence of rheumatoid arthritis six weeks following COVID-19 in a cohort of patients recruited from two selected private sector hospitals in Colombo, Sri Lanka.

Methods

A descriptive longitudinal study was conducted over three months from 1st July to 30th September 2021. The sample size of 333 was computed using the formula for the sample size calculation for a single proportion, where critical value for confidence level was 1.96, considered population proportion was 27% and precision was 5% with a non-response rate of 10%. Consecutive PCR positive, symptomatic COVID-19 patients above the age of 18 years, were recruited during the hospital stay and written informed consent

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was obtained. Those with mental disorders, thyroid diseases or known rheumatological diseases were excluded. They were contacted over the telephone six weeks after the discharge from the hospital. A pretested, interviewer-administered questionnaire consisting of eight questions (demographic data, past history of arthritis and musculoskeletal symptoms) were used for data collection. Those with symptoms of arthralgia and myalgia were sent a request for erythrocyte sedimentation rate (ESR) and rheumatoid factor to be obtained from a private laboratory and the expenses were reimbursed. The hospital consultations were arranged free-of charge. Those who had severe synovitis at the time of consultation, were subjected to x-ray imaging and the x-rays were reported by two independent radiologists.

The 2010 American College of Rheumatology/ European League Against Rheumatism (ACR/EULAR) criteria[5] were used to diagnose rheumatoid arthritis. The criteria include: tender or swollen joint count, positive serology (rheumatoid factor titer or anti-citrullinated protein antibody level), elevation of acute phase reactants (erythrocyte sedimentation rate or C-reactive protein). The duration of symptoms of equal and more than six weeks with a score of ≥6 out of a total of 10 is considered for diagnosis of RA.

SPSS version 22.0 was used for statistical analysis. The results are presented as proportions expressed as percentages with 95% confidence intervals where applicable.

Ethical clearance was obtained from the Ethics Review Committee of the Faculty of Medicine of the University of Kelaniya.

Results

Response rate was 100% when contacted after six weeks of discharge. Among the 333 individuals, 96 (28.8%), had either myalgia, arthralgia or both. There were 52/96 (54.2%) women. Their age was 42.5 years (SD=14.9 range of 20-87) in women and 40.7 years (SD=11.7, range of 20-73) in men (Table 1).

Table 1. Distribution of persistent musculoskeletal symptoms by sex and age

Age - years	*Persistent musculoskeletal symptoms (N=96)*	
	Women *n*	*Men* *n*
18 - 39	27 (51.9%)	20 (45.5%)
40 - 59	17 (32.7%)	22 (50.0%)
≥60	08 (15.4%)	02 (04.5%)
Total	**52 (100.0%)**	**44 (100.0%)**

Of the 96 symptomatic patients, 86 (89.6%) had arthralgia and it was common among women (49.0%; n=47) than in men (40.6%; n=39). Considering a single symptom, 56.3% (n=54) had only arthralgia and 10.4% (n=10) had only myalgia.

Table 2. Type of musculoskeletal symptoms

Rheumatic & musculoskeletal symptoms	*N = 96*	
	Men (N=44) *n*	*Women (N=52)* *n*
Overall total with arthralgia	39 (88.6%)	47 (90.4%)
Total with only arthralgia	22 (50.0%)	32 (61.5%)
Overall total with myalgia	22 (50.0%)	20 (38.5%)
Total with only myalgia	05 (11.4%)	05 (09.6%)
Presence of both arthralgia & myalgia	17 (38.6%)	15 (28.8%)

Commonly affected joints

The commonly affected joints were the knees (49.0%; n=47), spine (36.5%; n=35) and ankles (24%: n=23), and elbow was the least affected joint (3.1%; n=3) [Table 3].

Table 3. Distribution of arthralgia

No.	*Joints affected*	*N=96 n*
01.	Elbow	03 (03.1%)
02.	Shoulder	04 (04.2%)
03.	Foot	05 (05.2%)
04.	Cervical spine	06 (06.3%)
05.	Hip	10 (10.4%)
06.	Hand	13 (13.5%)
07.	Wrist	14 (14.6%)
08.	Ankle	23 (24.0%)
09.	Spine	35 (36.5%)
10.	Knee	47 (49.0%)

Overall total with arthralgia = 86; *Had more than one joint affected

Distribution of myalgia

The most commonly involved muscle groups were the calf (31.3%; n=30) followed by thighs and feet (11.5%; n=11) and the least were chest, abdomen, forearm and hand having one patient each (1%; n=1) [Table 4].

Table 4. Distribution of myalgia by affected sites

No.	*Site*	*N=96 n*
01.	Scalp	0
02.	Face	0
03.	Chest	01 (01.0%)
04.	Abdomen	01 (01.0%)
05.	Forearm	01 (01.0%)
06.	Hand	01 (01.0%)
07.	Thoracic area	04 (04.2%)
08.	Lumbosacral area	04 (04.2%)
09.	Cervical area	05 (05.2%)
10	Upper arm	06 (06.3%)
11.	Thigh	11 (11.5%)
12.	Foot	11 (11.5%)
13.	Calf	30 (31.3%)
Total		**75***

Overall total with myalgia = 42; *Had more than one site affected

Forty-eight patients out of 96 symptomatic patients attended the follow up clinic (response rate of 50%). Mean ESR level of 48 patients was 35.4 mm/hour (SD=21.4 range of 5-72). ESR was elevated above 10 mm 1st hour in 41/48 (85.4%) patients. High ESR values ranged from 11-72 mm/hour with a mean of 40.3 mm/hour (SD=19.2). Rheumatoid factor was positive in 3/42 (7.1%) patients. X rays were done in four patients and they were reported as normal.

Rheumatoid factor was positive in 3 patients and 2 of them were confirmed as RA according to the clinical features of ACR/EULAR criteria. This gives a prevalence of 4.8% (95% CI: 0.6-16.2%). Both these patients were females aged 47 and 68 years.

Discussion

More than one fourth of (28.8%) patients had symptoms of myalgia, arthralgia or both, after six weeks of recovery from COVID-19. Rheumatoid arthritis was diagnosed among 4.8% of patients based on the ACR/EULAR criteria.[5]

Among the symptomatic patients, 49% were younger than 40 years, and 57.4% were women. Commonest symptom observed among the study population was arthralgia (90%); men (41%) and women (49%). The prevalence of persistent arthralgia and myalgia similar to the present study (28.8%) was reported by Singh et al. (27.3%)[2] and by Hasan et al. (27%)[6] following COVID-19. Karaarslan et al reported arthralgia in 22% and myalgia in 21% of patients as a consequence of COVID-19.[7] There is a dearth of literature even globally, as COVID-19 pandemic is a novel disease and long term follow up studies are yet to be conducted.[8]

The response rate was 100% for the initial survey conducted via telephone to assess the presence of RMDs which is considered a strength of the study. The narrow 95% CI observed for those positive with symptoms (28.8%; 95% CI: 24.2-33.9%) reflects the adequacy of sample size. However, the response rates were low for the investigations (50% for ESR and 44% for rheumatoid factor) which is a limitation of the study. This study was conducted during the height of COVID-19 infection with the Delta variant, during which time frequent lockdowns were enforced. Therefore, we believe that the travel restrictions and financial difficulties would have led to the low response rate observed.

The ESR was elevated in 85.4% (n= 41/48), and the rheumatoid factor was positive in 7.1% (n=3/48) patients. Only 2 of them, fulfilled the ACR/EULAR criteria[5] (score of >6) for the diagnosis of RA. According

to the ACR/EULAR 2010 criteria, it is either the rheumatoid factor or the anti CCP antibodies and either the ESR or the CRP that is required for the diagnosis of RA.[5] Anti CCP antibodies and CRP were not considered due to the high costs involved. Elevated ESR suggests a possibility of underlying inflammation. Thus, all patients with high ESR were given a trial of oral steroids for which they responded well. The two patients who fulfilled the criteria for rheumatoid arthritis were treated with a multi-disciplinary approach.[8]

X-ray imaging was indicated only in 4 patients with severe synovitis and they were reported as normal. Imaging is not required for the diagnosis of rheumatoid arthritis according to the ACR/EULAR criteria.[5] Ultrasonography of the hands is unlikely to provide additional information which would be of relevance for the diagnosis of RA, and is costlier as compared to an X-ray.

Rheumatic musculoskeletal diseases comprise degenerative, inflammatory and auto immune conditions.[7] COVD-19, as a severe viral infection, can potentially lead to long term consequences such as RMDs due to the severe disruption of the immune system.[3] In addition, some of the anti-viral agents such as remdesivir used in the treatment of COVD-19 are also reported to cause severe adverse reactions mimicking RMDs.[3]

RA is known to be precipitated when a genetically susceptible host encounters specific environmental triggers, such as a viral infection.[3,8,9] The global prevalence of RA is reported as 460 per 100,000 population (0.46%; 95% CI: 0.06-1.27%) during the years between 1980 and 2019.[11] Prevalence of early rheumatoid arthritis have been reported as 0.7%. in a suburb of Colombo in Sri Lanka.[12] Thus, the prevalence of RA in the present study (4.8%) which is much greater than the global prevalence of RA may suggest that COVID-19 acts as a strong triggering factor for development of rheumatoid arthritis.

Conclusions

Approximately one fourth of patients, suffered with persistent symptoms of myalgia and arthralgia six weeks following COVID-19. Out of those presented for consultation, 2 patients (4.8%) were confirmed to have rheumatoid arthritis. Patients with elevated acute phase reactants need close monitoring to ascertain whether they will progress to RMDs such as rheumatoid arthritis. Further studies on a larger sample of patients focused on symptoms of rheumatic musculoskeletal diseases is recommended to obtain a better picture related to the magnitude of RMDs especially rheumatoid arthritis as a consequence of COVID-19.

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Conflicts of Interest

None.

Criteria for inclusion in the authors' list

SAK – Substantial contributions to the conception, collection of data, analysis of data and drafting the manuscript and final approval. KAL – Design of the study, revision of the draft and final approval of the version to be published.

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