

ORIGINAL ARTICLE

RHEUMATOLOGICAL MANIFESTATIONS IN PATIENTS HOSPITALIZED WITH COVID-19 IN A TERTIARY CARE SETTING

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Background: Corona virus disease 2019 (COVID-19) is a pandemic affecting over 150 million people worldwide since its emergence in Wuhan, China in December 2019, and is leading to over 600 thousand deaths. Severe acute respiratory syndrome novel coronavirus 2 (SARS-nCoV-2) causes a wide range of symptoms by affecting different organ systems of the body. This study was designed to specifically look for its rheumatological manifestations. **Methods:** It was a cross-sectional study conducted in the corona complex MTI Lady Reading Hospital Peshawar. A total of 141 COVID-19 positive hospitalized patients requiring oxygen therapy and having no previous rheumatological diseases were enrolled and studied for any rheumatological manifestations. **Results:** There were 88 (62.4%) males and 53 (37.6%) females, with age range from 27–88 years, and mean age of 58.5±11.5 SD. Arthralgia and myalgia were found very common, occurring in 128 (90.8%) and 119 (84.4%) of patients. Arthritis was not found in any patient. **Conclusion:** Arthralgia and myalgia were reported frequently in patients with severe COVID-19 requiring oxygen therapy, while arthritis was not present even in a single patient as is reported in other viral infections.

Keywords: Arthralgia, Arthritis; COVID-19; Myalgia; Rheumatological Manifestations

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INTRODUCTION

Corona virus disease 2019 (COVID-19) is a pandemic affecting over 150 million people worldwide since its emergence in the city of Wuhan, China in December 2019, and is leading to over 600 thousand deaths.¹ COVID-19 is caused by a novel corona virus strain, Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) which belongs to the Nidovirales family.²

Transmission of the disease is from person to person through infected droplets from human saliva.³ Once inside the human body, its primary site of infection is the upper respiratory track and/or lungs. Therefore, in addition to fever, respiratory symptoms are the most common presenting symptoms in patients with COVID-19. Some of these include cough, sore throat, nasal congestion, chest pain and shortness of breath.⁴

However, in addition to involving the lungs, the SARS-nCoV-2 is now known to affect other systems of the body as well, thus causing a wide range of symptoms.⁵ For example, it is now known to cause gastrointestinal symptoms causing anorexia, nausea, vomiting, abdominal pain, diarrhoea and dysentery in a subset of patients. Similarly, stroke, dizziness, confusion and other neurological symptoms have also been reported so far.⁵

Musculoskeletal symptoms like arthralgia and myalgia of other corona viruses like Middle east respiratory syndrome coronavirus (MERS-CoV) and severe acute respiratory syndrome coronavirus (SARS-CoV) have been well documented.⁶ Similarly, COVID-19 is also known to cause musculoskeletal symptoms like generalized body aches and fatigue in a minority of patients.⁷ However, no study has been performed that focuses primarily on the rheumatological manifestations of COVID-19. Therefore, the aim of this study was to determine the frequency of different musculoskeletal and rheumatological manifestations in COVID-19 infected hospitalized patients.

MATERIAL AND METHODS

This cross-sectional study was conducted in the corona complex MTI Lady Reading Hospital Peshawar from 1st May 2020 to 1st August 2020. A total of 141 COVID-19 patients who were Reverse Transcriptase-Polymerase Chain Reaction (RT-PCR) positive on throat/nasal swab and were requiring oxygen therapy, were included in the study. Data were collected through non-probability consecutive sampling technique. A written informed consent was obtained from the patients and ethical approval was taken from the institutional ethical committee of the hospital before starting the study. Patients under 16

years of age, those with negative PCR, patients on mechanical ventilation, confused/unconscious patients, those with pleural effusion on chest X-ray and patients who were previously diagnosed with any rheumatic disease were excluded from the study to control confounding factors. Rheumatological symptoms were defined as;

1. Arthralgia: patients complaining of pain in one or more joints during the present illness.
2. Myalgia: patients complaining of generalized pain in his/her muscles
3. Arthritis: patients with swollen and/or tender joint during the present illness with morning stiffness of more than 30 minutes
4. Myositis: myositis was then divided into 2 types:
 - Suspected Myositis: Patient have power less than 4 –in his limb muscles on Medical Research Council (MRC) scale during neurological examination together with raised CPK levels (more than 500U/l)
 - Confirmed Myositis: suspected Myositis patient with Electromyographic studies suggestive of myositis.
5. Rash: patients with palpable or non-palpable purpura in the absence of thrombocytopenia
6. Anaemia: patients with Hb% less than 11.5gm/dl
7. Thrombocytopenia: patients with platelets counts less than 150,000/ μ l

Detailed history of the patient illness was recorded and demographic information related to the study like name, age, gender and address was recorded in a pre-designed proforma. The inclusion and exclusion criteria were strictly followed to control confounders and bias in the study results.

All the data were stored and analysed in SPSS version 16. Mean \pm SD was calculated for numerical variables like age. Frequencies and percentages were calculated for categorical variables like gender, arthralgia, myalgia, arthritis, oral ulcers, anaemia and thrombocytopenia. All rheumatological findings were stratified among age and gender to see the effect modifications. Post stratification Chi-Square test was applied and *p*-value of ≤ 0.05 was considered statistically significant.

RESULTS

Out of 141 COVID-19 patients, there were 88 (62.4%) male and 53(37.6%) were females. The age range of patients was 27–88 years, and the mean age was 58.5 \pm 11.5 SD as shown in table-1.

Arthralgia and Myalgia were the commonest symptoms, occurring in 128 (90.8%) and 119 (84.4%) of patients respectively. The frequencies of other manifestations were less common as shown in table-2.

When compared, there was no statistically significant difference of rheumatological manifestations in both genders as shown in the table-3.

Table-1: Age and gender distribution of the study population (n=141)

Age Range		
Minimum age (Year)	Maximum age (Years)	Mean (Year)
27	88	58.5 (\pm 11.5)
Gender	Frequency	Percentage
Male	88	62.4
Female	53	37.6

Table-2: Rheumatological findings in patients with COVID-19 (n=141)

Rheumatological Manifestations	Frequency	Percentage
Arthralgia	128	90.8
Myalgia	119	84.4
Thrombocytopenia	44	31.2
Anaemia	13	9.2
Rash	1	0.7
Myositis	1	0.7
Arthritis	-	-

Table-3: Corelation of rheumatological manifestations across gender (n=141)

Rheumatological Manifestations	Male	Female	Total	<i>P</i> -value
Arthralgia	80	48	128	0.58
Myalgia	73	46	119	0.36
Thrombocytopenia	27	17	44	0.5
Anaemia	5	8	13	0.06
Rash	1	0	1	0.6
Myositis	1	0	1	0.6

DISCUSSION

Viral infections usually have multi-system involvement. Rheumatological manifestation are usually present in different viral infections. Corona viruses also have other systemic manifestations along with the respiratory symptoms. The present study provided several important insights and associated rheumatological involvement was confirmed. One of the striking finding was that arthralgia and myalgia were found in 90.8% and 84.4% of patients respectively. This was in contrary to the other studies performed previously which reported a frequency of 7–35%.^{8,9} One explanation for this may be due to the fact that they included all COVID-19 positive patients in their study group, while we studied only severe cases requiring oxygen therapy. Though Guan *et al.*¹⁰ observed that there does not exist any relationship between the severity of the disease and frequency of arthralgia, Zangh *et al.*¹¹ reported an 87% frequency of myalgia in patients with severe COVID-19 disease which was in accordance with our study.

Thrombocytopenia in patients with COVID-19 is thought to be due to numerous possible causes. Although reduced production due to bone marrow

suppression has been suggested to be one reason, development of autoantibodies against platelets has also been proposed; thus, suggesting a possible rheumatological cause.¹² In our study, thrombocytopenia was present in 31.2% of patients. Similar results were reported by Huang *et al.* who showed that 35% of patients with severe disease were thrombocytopenic.¹³

In our study, 9.2% of patients were found to have anaemia. Though autoimmune haemolytic anaemia has been reported in patients with SARS-nCoV- 2 infection,¹⁴ we were not sure as to whether anaemia in our study population was due to autoimmune disease or due to other reasons. Though in our study group, patients had high serum LDH levels, we did not rule out iron deficiency anaemia or other causes of anaemia by performing specific tests which is one of the limitations of the present study.

Other rheumatological manifestations like rash and myositis were found in only one patient (0.9%). Rash was a palpable purpura found on the lower limbs only. Similar purpuric rash were also reported by Henry *et al.*¹⁵ and Joob *et al.*¹⁶ but the results were non-significant and could be a chance presentation.

One of the limitations of this study is that we did not confirm our suspected case of myositis with further investigations. In literature, cases of myositis secondary to COVID-19 have been reported. Maxime *et al.*¹⁷ report on such case; however, in their case report, patient was complaining of weakness in their upper limbs while in our case, lower limb was affected COVID-19. Another similar case is reported by Qian *et al.*¹⁸.

Arthritis or inflammation of the joints is a common finding following viral infections like Hepatitis-B virus, Hepatitis-C virus, and other alpha viruses like Chikungunya, Ross river, Barmah Forest virus infections.¹⁹ However, none of our patients in the study group demonstrated any history of arthritis.

Our study has certain strengths. Firstly, after extensive literature review, we found that no study has been specifically designed to look for the rheumatological manifestations of patients with COVID-19. Secondly, we provided insight into the symptoms of patients with severe disease. Other studies performed on severe patients either had small sample size or were more directed towards respiratory symptoms. Thirdly our results provided some very important information. Arthralgia and myalgia were found to be a very common clinical feature in COVID-19 patients requiring oxygen therapy; arthritis was not associated with COVID-19. This study was not without limitations like other studies. Patients studied were all on oxygen therapy and thus had severe disease. Therefore, these results

cannot be generalized to all COVID-19 positive patients. Secondly, we could not ascertain the exact cause of thrombocytopenia and anaemia, as we did not perform specific investigations to rule out causes other than autoimmune; nor could we find out whether the patients had them before contracting corona virus disease. And finally, we did not confirm our case of myositis by performing muscle biopsy or by doing the electromyographic tests.

CONCLUSION

This study concludes that Arthralgia and Myalgia are the commonest rheumatological manifestations in patients with severe COVID-19 disease having low oxygen saturation requiring oxygen therapy. We also conclude that inflammatory joint disease, like arthritis is not a manifestation of COVID-19 as is present in patients having some other viral infections. Similarly, this study concludes that Arthralgia and Myalgia are present in COVID-19 patients irrespective of their age and gender, a single patient can present with more than one manifestation.

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