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Clinicodemographic Characteristics of COVID-19 Infection Among Patients with Rheumatic Diseases

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Abstract:

Background: The occurrence of COVID-19 infection in rheumatic patients and their evaluation are of global interest. The purpose of this study was to determine the clinicodemographiccharacteristics of COVID-19 infection among rheumatic patients.

Methods: In this observational cross-sectional study, 167 consecutive patients of both genders from online consultancy were enrolled from 13th June to 12thOctober 2020 conducted in a tertiary level rheumatology consultation center, Modern One Stop Arthritis Care & Research Center®, Dhanmondi, Dhaka. The WHO case definition of COVID-19 and disease severity scoring tool were used for diagnosis and assessment of the patients.Suspected cases were interviewed in detail and investigated with RT-PCR for COVID-19, HRCT of the chest, X-ray chest P/A view, and other necessary tests. The prevalence of COVID-19 infection was expressed in percentage.

Results: Out of 167 rheumatic subjects,64 and 103 were men and women respectively, witha mean age of 42.15±13.04 years. The prevalence of COVID-19 infection was 7.78% (13/167). RT-PCR was positive in 9 (69.23%) patients and the remaining weresuspected cases (RT-PCR was negative but positive clinical features and X-ray chest findings.All COVID-19 positive patients presented with fever (100%).Among COVID-19 cases,spondyloarthritis (SpA), osteoarthritis of knee(OA),psoriatic arthrtis (PsA), rheumatoid arthritis (RA) and systemic lupus erythematosus(SLE)were5 (38.46%), 3 (23.08%), 2 (15.38%), 2 (15.38%) and 1 (7.69%) respectively.DMARDs/biologics wereongoingin 3 (tofacitinib), 1 (etanercept), 1 (methotrexate), 1 (sulphasalazine), 1(hydroxychloroquine) and 1 (leflunomide) patients.The use of non-specific drugs forCovid-19 treatment were azithromycin, ivermectin, doxycycline, and hydroxychloroquin. Among these rheumatic patients, the elderly group of patients with the comorbidities like diabetes5 (38.46%), hypertension 5 (38.46%)and bronchial asthma 3 (23.08%)were infected with COVID-19.

Conclusion: The prevalence of COVID-19 was 7.78% among the rheumatic patients. Fever was the universal presentation in this study. The commonest rheumatic diseases were SpA . Diabetes and hypertension werethe most common comorbidities in patients with rheumatic diseases with COVID-19 infection.

Keywords:COVID-19 infection, rheumatic diseases, DMARDs, arthritis.

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Introduction:

COVID-19 infection has become a global health crisis, since its detection in December, 2019[1-2].WHO declared a pandemic on March 11, 2020, and to date the number of confirmed cases has exceeded >121 million with an increasing number of deaths (>2.5 million) worldwide[2].A study among rheumatic patients in northern Italy had shown the prevalence of COVID-19 infection to be 8%, whereas a retrospective hospital-based study reported the rate of COVID-19 confirmed by PCR to be 0.76% in Spain[3-4]. A study conducted by Favalli et al, 2020, showed that the incidence of confirmed COVID-19 cases among adult rheumatic patients attending an out-patient clinic in Italy was 0.62%[3]. A phone survey in Spain conducted by Michelena et al, 2020, showed that the incidence of COVID-19 confirmed cases among rheumatic patients on tDMARDs was 0.48%[4].Grainger, Machado, and Robinson, 2020, found that the meta-analysis of prevalence of COVID-19 estimated by systemic review and meta-analysis was 0.9% for rheumatic disease; 3.4% for systemic lupus erythematosus (SLE), Sjögren's syndrome (SS), or

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systemic sclerosis (SSc); and 0.3% for inflammatory bowel disease (IBD) among patients with autoimmune disease[5].A study by Quartuccioet al, 2020, determined the rate of COVID-19 in an Italian province among adult rheumatic patients on small molecules or biologic agents was 4.3%[6]. A hospital-based study in Spain showed that the prevalence of RT-PCR confirmed COVID-19 among rheumatic patients was 0.76%[7].

To date, there is no specific treatment available for COVID-19 infection, and treatment recommendations vary from country to country[5-6]. Patients with comorbidities like diabetes, hypertension, asthma, chronic diseases such as chronic heart or kidney diseases, rheumatic diseases, immunocompromised patients and on immunosuppressive medications are at higher risk of COVID-19 infection and its complications[2]. Autoimmune rheumatic diseases are characterizedby irregularfunctioningofthe immune system and immune-mediated inflammation in target tissues[7].Patients with rheumatic diseases rely on immunosuppressive drugs such as disease-modifying anti-rheumatic drugs (DMARDs) and NSAIDs to control symptoms and disease progression, thus become immunocompromised and more vulnerable to infections than the general population[8]. The immune system has an important role to protect against viruses and virus-related tissue damage. It was reported that most of the patients with SARS-CoV-2 infection recovered completely due to effective immune responses[9-10].Different reports on COVID-19 infection in patients with the rheumatic disease have been limited to case reports and small case series. Thosestudies indicated mixed outcomes, though results are difficult to generalize with a given variable of COVID-19 case definitions and small sample sizes[11-14].The outcome of COVID-19 infection in rheumatic disease treated with several types of medications (e.g., interleukin-6 receptor inhibitors) is currently being studied[15-17].Monti et al, reported that two immune cells namely, antibody-secreting cells and activated follicular helper T cells, are mainly responsible for antiviral immunity[11]. The circulating concentration of these two cells notably increased before symptomatic recovery of a patient with COVID-19 and concurrent with the clearance of SARS-CoV-2[11]. The antiviral immune response is crucial for viral clearance. However, hyper-activation of the immune response in COVID-19 might also cause tissue damage in the lungs and other organs[2, 12]. Therefore, several immune-modulating drugs including corticosteroids, hydroxychloroquine (HCQ), and anti-cytokine agents are being used for the treatment of severe cases of COVID-19[16]. This ongoing pandemic demands timely research to evaluate COVID-19 infection and their subsequent consequences in rheumatic patients for early diagnosis, identifying disease severity, starting early treatment, and to minimize post-infection complication. Therefore, this study aimed to determine the clinicodemographic characteristics of COVID-19 infection among rheumatic patients.

Methods:

Study population and case identification

This observational cross-sectional study was conducted in a tertiary level rheumatology consultation center, Modern One Stop Arthritis Care & Research Center®, Dhanmondi, Dhaka, Bangladesh from 13th June to 12thOctober 2020. Patients were attended via online consultation either over telephone or video call over social apps. A total of167 consecutivepatients were included in the study who had differentrheumatological diseases. The rheumatological diagnosis was made using diagnostic criteria of respective diseases. COVID-19 cases were diagnosed by WHO criteria andRT-PCR[17]. Assessment of severity was done by the severity scoring tool of WHO[17].Events related to the COVID-19 infection were also obtained and recorded.

Data Collection

Data of demography, characteristics of rheumatic diseases, comorbidities, symptoms of COVID-19 infections, treatment, and any event following COVID-19 infection(e.g. hospitalization, ventilation, death) were collected during an online consultation. Data of medications such as immunosuppressive therapy for rheumatic diseases as well as for COVID-19 infection were taken. Data of laboratory investigations like complete blood count, C-reactive protein, D-dimer, and radiological investigations like a plain chest x-ray and high-resolution computerized tomography of chest were taken.

Statistical analysis

The prevalence was expressed in percentage.Categorical variables were presented as numbers (percentage).

Results:

A total 167 study patients comprised 54 males (mean age 39.24 ± 14.17 years) and 113 females (mean age 45.0 ± 12.01 years). Among the study patients who were

consulted online, 13 (7.78%) were COVID-19 positive rheumatic patients (4 males and 9 females). Among these COVID-19 positive patients, 9 were diagnosed by RT PCR test while the remaining 4 were diagnosed based on symptoms. Demographic characteristics of COVID-19 cases have shown in table I.

Table-I

Demographic characteristics of COVID-19 casesin rheumatic patients (n=13)

Age range	n (%)
20-29	1 (7.7)
30-39	5 (38.46)
40-49	2 (15.38)
50-59	4 (30.77)
e"60	1(7.7)
Gender	
Male	4 (30.77)
Female	9 (69.23)
Occupation	
House wife	9 (69.23)
Service	2 (15.38)
Business	1(7.7)
Retired	1(7.7)

Among the rheumatic patients, SpAwas the most common pevalen disease (38.46%). Perevalence of otherrheumatic diseasesin patient with COVID-19 infection are shown in table II.

Table-II

Different rheumatic diseasesin patient with COVID-19 infection(n=13)

Rheumatic diseases	n(%)
Spondyloarthritis	5 (38.46)
Osteoarthritis of knee	3 (23.07)
Psoriatic arthrtis	2 (15.38)
Rheumatoid Arthritis	2 (15.38)
Systemic Lupus Erythematosus	1 (7.7)

Perevalence of diabetes mellitus,hypertensionand bronchial asthma was 38.46% ,38.46% and 23.07% in patientswith rheumatic diseaseswith COVID-19 infection respectively. Perevalence of other comorbidities in rheumatic patients with COVID-19 infection are shown in table III.

Table-III

Different comorbidities in rheumatic patient with COVID-19 infection(n=13)

Comorbid diseases	n(%)
Diabetes mellitus	5 (38.46)
Hypertension	5 (38.46)
Bronchial Asthma	3 (23.07)
Hypothyroidism	2 (15.38)
Chronic Kidney Disease	1 (7.7)
Chronic obstructive pulmonary disease	1 (7.7)

All COVID-19 positive patients presented with fever (100%). Other symptoms have shown in table IV.

Table-IV

Symtoms of COVID-19 infectionin rheumatic patient (n=13)

Serial No.	DiagnosisSymptoms of COVID-19					
	Fever	Sore throat	Dry cough	Shortness of Breath (SOB)	Loose motion	Others
1 Psoriatic arthritis (PsA)	+	+	+	+		
2 Spondyloarthritis (SpA)	+		+	+	+	Weakness, Chest pain
3 Osteoarthritis (OA) knee	+	+	+			Headache, Myalgia
4 SpA	+	+	+			
5 Systemic Lupus Erythematosus (SLE)	+	+	+	+	+	
6 PsA	+	+			+	Weakness
7 SpA	+	+	+	+	+	Anosmia, Chest pain
8 Rheumatoid arthritis (RA), OA knee	+	+	+	+		Anosmia
9 SpA	+		+			
10 RA	+					Headache
11 OA knee	+	+	+	+	+	Weakness
12	+	+	+	+	+	Weakness, anosmia, headache
13 SpA	+	+	+		+	Weakness, anosmia

Laboratory investigations were performed on 10 COVID-19 patients and the remaining 3 declined(table 5). Seven patients had high CRP (mean 45.84), 3 patients had lymphopenia (mean 11.0).

Table-V

Laboratory investigations of COVID-19 cases ofrheumatic patients (n=13)

Investigations	n (%)
High CRP	7 (70%)
Lymphopenia	3 (30%)
Leucopenia	2 (20%)
Raised D- dimer	1 (10%)
High ferritin	2 (20%)

Chest X-ray of all patients had shown bilateral basal ground-glass opacities.HRCT chest performed by six COVID-19 patients- two patients had normal findings while four cases were found to have ground-glass opacities with pulmonary fibrosis.

According tothe COVID-19 severity scoring tool, positive patients were categorized into 9 mild (69.23%), 1 moderate (7.69%), 2 severe (15.38%), and 1 critical (7.69%) patients(figure1).

Five patients with mild symptoms were in the age group of 30-39 years, 4 cases (2 severe, 1 moderate, 1 mild) were the age group of 50-59 years, 2 mild cases were

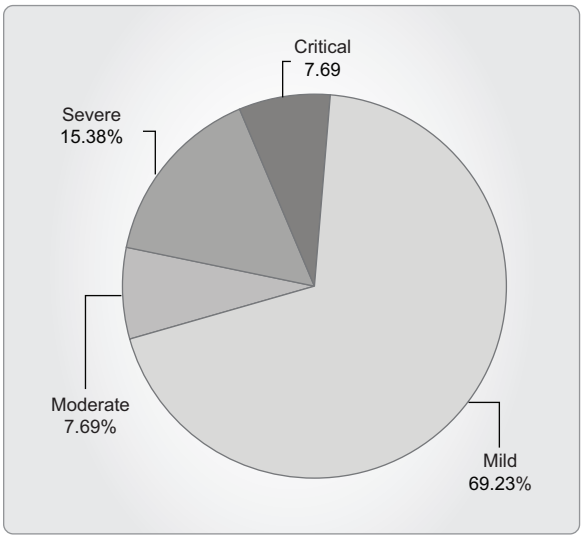

Fig.-1: *Severity of COVID-19 infection among rheumatic patients (n=13)*

between the age group 40-49 years, 1 patient with mild symptoms was the age group of 20-29 years and 1 critical patient was in the age group of e"60 years. Among the COVID-19 positive patients, there were 5DM (2 severe cases, 1 moderate, 1 mild, and 1 critical case), 5 HTN (3 mild cases, 1 severe and 1 critical case), and 4 bronchial asthma (2 severe and 2 mild cases) patients.

The ongoing management of COVID-19 positive patients is shown in Table 2. Among the 13 positive patients, only 10 patients received COVID-19 targeted treatment (table 6).

Table-VI

Management of rheumatic patients in COVID-19 positive patients according to the severity (n=13)

Serial No.	Diagnosis	HRCT (High- Resolution CT) of chest	Category	Ongoing Management
1	PsA	N	Mild	Methotrexate (MTX) 20mg
2	SpA	N	Mild	Sulfasalazine (SSZ) 3g
3	OA knee	Ground glass opacity	Severe	Non-steroidal anti- inflammatory drugs (NSAIDs)
4	SpA		Mild	Tofacitinib
5	SLE	Ground glass opacity	ICU (critical)	HCQ
6	PsA		Mild	a) Secukinumab b) Tofacitinib
7	SpA	Ground glass opacity	Severe	NSAIDs
8	RA, OA knee		Mild	Tofacitinib
9	SpA		Mild	Etanercept
10	RA		Mild	Leflunomide, H/O Rituximab
11	OA Knee	Ground glass opacity	Moderate	
12	Bronchial Asthma		Mild	
13	SpA		Mild	

Discussion:

COVID-19 infection by SARS-CoV-2 in rheumatic patients advocates much interest of rheumatologists nowadays. The rate of COVID-19 infection in rheumatic patients might be higher because of immune suppression. In this study, the ratewas 7.78% higher than the general population which is comparable to another study by Fredi et al, 2020[3]. There might be a diagnostic dilemma due to similirities in symptoms of COVID-19 and flare of rheumatic diseases are often similar such as fever, fatigue, myalgia and also in laboratory tests such as high CRP, high ESR, lymphocytopenia, etc. and often HRCT chest often (GGO is commonly found in rheumatoid lung diseases) can mislead us. That plays a role in the diagnostic delay of COVID-19.Similar symptoms were found in COVID-19 of rheumatic patients and others. In our study subjects, presenting symptoms were fever, dry cough, sore throat, fatigue, shortness of breath and loose motion,etc. which were typical of COVID-19.The most common co-morbidities were diabetes, hypertension, and bronchial asthma similar to previous studies[18-21].Age remains the strongest predictor of hospital admission.In our series,1 patient (>60years) needed ICU support. This finding is also supported by other clinical studies where older age and comorbidities were associated with a higher risk of hospitalization among COVID-19 patients with rheumatic disease[18-21].

Each case either received Azithromycin or Doxycycline and unfortunately, the duration of the treatment was prolonged – Azithromycin for 7-10 days and Doxycycline for 10-14 days. Most of the cases were self-medicated after purchasing the following drugs over the counter – Ivermectin, Montelukast, Doxofylline, and anti-histamine. Despite this predicament, we stuck to our principle of prescribing Enoxaparin and Favipiravir. While on a hydroxychloroquine regimen, only 1 rheumatic patient developed COVID-19. As we have used several drugs concurrently, it is not suitable to conclude which specific drug was effective or therapeutic against COVID-19. We prescribed steroids cautiously in low dose (Dexamethasone 5mg) for 1-2 days to rheumatic patients who had persistent or newly developed fever and profound constitutional features. Based on our findings, we assumed thatthe potential/ effective drugs Enoxaparin, Favipiravir, and steroid. It can be inferred that neither hydroxychloroquine nor any other DMARD protective against COVID-19. Rheumatic patients who were on DMARD and developed severe COVID-19 infection declined hospitalization hence it cannot be concluded DMARD is beneficial.

Monotherapy with biological DMARDs or targeted DMARDs may be associated with lower odds of hospitalization. This is corroborated by other research works where most COVID-19 positive rheumatic patients on biologic or targeted synthetic DMARD (b/ts DMARD) did not require hospitalisation[18]. Three of our patients were on tofacitinib (JAK inhibitor) and 1 patient was on Etanercept (anti-TNF inhibitor), all of them had only mild symptoms supporting this evidence. The lower rate of hospitalization was seen mostly in rheumatic patients taking anti-TNF inhibitors, in comparison to a small proportion of patients on JAK inhibitors[18]. Further studies in a larger sample are required to affirm the potential benefits of the DMARD.Wheather there is a role of hydroxychloroquine in preventing COVID-19 infection or a lower hospitalization rate, but it is not yet clear. Only one patient of our series was on hydroxychloroquine for SLE,but eventually, she had developed severe pneumonia as well as needed ICU support.There is no clear evidence of a bad prognosis of patients taking NSAIDs. Surprisingly, 2 patients of our study subjects were on NSAIDs and both of them had a severe disease of pulmonary involvement, although, both of them were over 50 years of age and had co-morbidities. In contrast, the case series conducted by Gianfrancesco et al revealed no association between NSAID or antimalarial drugs and risk of hospitalization among the COVID-19 positive rheumatic patients[18].Although previously NSAID was assumed to be harmful to COVID-19 patients[22].A recent study showed, in a group of rheumatic patients in an outpatient clinic of Lombardy, Northern Italy, only one patient (25%) was admitted to the hospital and needed oxygen supplementation[3]. Our experience was almost similar. In our series, only one patient needed ICU support and the frequency is 7.69 %.

Conclusion:

In this study, the prevalence of COVID-19 was frequent (7.78%) among the rheumatic patients.Fever was the universal presentation in this study. Patient with SpA and OA of knee were commonly infected with COVID-

19. Among these rheumatic patients, comorbidities like diabetes, hypertension were more likely to be infected with COVID-19.

Limitations of the study

Nonetheless, being an observational cross-sectional study during a pandemic, there are some limitations. Not all rheumatic patients with COVID-19 positive status were included in the study and consecutive sampling of the participants may be subjected to selection bias. There were no specific data on the additional drugs and their duration taken by the patients other than those prescribed during the period of study.

Conflict of interest:
There is no conflict of interest.

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