

A Questionnaire-based Survey on Depression and Anxiety among Rheumatology Patients during the COVID-19 Pandemic: Patient's Perspective

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ABSTRACT

Objectives: The Coronavirus Disease 2019 (COVID-19) outbreak is a global pandemic and has caught the attention of the rheumatology fraternity, where patients are thought to be at higher risk of infection. We aimed to study the incidence of COVID-19 infection and depression and anxiety symptoms among patients with rheumatic disease (RD) in Hospital Selayang, Malaysia, during the COVID-19 pandemic. **Methods:** A cross-sectional study was conducted via phone interview using a structured questionnaire in patients with RD aged > 18 years old scheduled for clinic appointments from 4 to 28 May 2020, which coincided with the second wave of COVID-19 cases in Malaysia. The questionnaire included demographics, COVID-19 screening questions, depression and anxiety symptoms screening using questions derived from the Patient Health Questionnaire-2 (PHQ-2) and Generalized Anxiety Disorder-2 (GAD-2). **Results:** Among the 361 patients enrolled, the majority were females (83.1%), and over half (54.3%) were ethnic Malays, 41.6% had rheumatoid arthritis, 34.6% had systemic lupus erythematosus, 12.2% had spondyloarthritis, and only one (0.3%) patient had COVID-19 infection. The mean age of patients was 48.2 years (range: 16–80 years). The frequency of patients with depression and anxiety symptoms was 8.6% and 6.9%, respectively. Married patients reported feeling more anxious ($p = 0.013$), while patients with tertiary education levels reported feeling more depressed ($p = 0.012$). **Conclusions:** The incidence of COVID-19 infection is low, probably due to the low rate of testing. Depression and anxiety symptoms reported by patients in our cohort were modest. Our findings suggest that the COVID-19 pandemic has a greater impact on married patients with RD and those with a higher education level.

A novel coronavirus was first detected following a local outbreak in Wuhan, China, on 31 December 2019. It is now known as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and was given the name Coronavirus Disease 2019 (COVID-19).¹ On 11 March 2020, the World Health Organization (WHO) declared COVID-19 infection a global pandemic.² COVID-19 has infected 81 294 343 people and killed 1 774 931 worldwide as reported on 28 December 2020.³ In Malaysia, the first COVID-19 case was detected on 25 January 2020 with only 22 cases reported on 16 February 2020. The second wave started on 27 February 2020 and ended on 7 July 2020.⁴ Currently, Malaysia is facing a third wave, which started on 20 September 2020, and confirmed cases have risen

to 106 690 patients with 455 reported deaths as reported on 28 December 2020.⁵

The current outbreak of COVID-19 has caught not only the attention of the medical community but also the rheumatology fraternity, raising concern of a potential increased risk of infection among rheumatology patients taking immunosuppressants. Since the declaration of COVID-19 as a global pandemic, social distancing and lockdowns have been implemented to mitigate the spread of the disease. Surveys showed that many people experienced heightened anxiety and fear of becoming unwell since the pandemic struck. COVID-19 has been reported to cause serious threats to people's physical and psychological health (e.g., anxiety, depression, loss of social function, and post-traumatic stress disorder) in a survey of 52 730 Chinese people.⁶

Many pieces of research have demonstrated negative psychological impact among the general population and health care workers.⁷⁻⁹ Higher psychological distress related to the COVID-19 pandemic were reported among patients with autoimmune arthritis in Italy.¹⁰ However, studies examining psychological impact in patients with rheumatic diseases are limited globally and none in Malaysia.

The purpose of this research was to study the incidence of COVID-19 infection and depression and anxiety symptoms among patients with rheumatic disease (RD) in Hospital Selayang, Malaysia, during the COVID-19 pandemic.

METHODS

A phone interview was conducted in a cross-sectional design using a structured questionnaire. Eligible participants were all patients with RD aged > 18 years old on immunosuppressive therapy, including corticosteroids, conventional synthetic disease modifying anti-rheumatic drugs (csDMARDs), biological DMARDs (bDMARDs), and targeted synthetic DMARDs (tsDMARDs) who were scheduled for a rheumatology clinic appointment from 4 to 28 May 2020 in the Rheumatology Unit, Hospital Selayang. The study duration coincided with the middle of the second wave of COVID-19 cases in Malaysia. Patients with severe cognitive, language, or hearing deficits were excluded from the study.

Demographic data such as age, gender, ethnicity, marital status, education level, and occupation were collected. In addition, comorbidities, rheumatological diagnosis, and treatment history were recorded. Supplementary information was also obtained from the hospital electronic medical record system (CERNER Power Chart).

The structured questionnaire was designed with closed-ended questions – yes/no questions and multi-choice questions. The questionnaire was composed of:

1. COVID-19 infection screening questionnaires.
2. Patient's adherence to medication.
3. Psychological impact assessment from patient's perspective:
 - a. Depression symptom assessment using questions derived from Patient Health Questionnaire-2 (PHQ-2) as a brief depression screening measure.¹¹ Answers were 'yes' or 'no'. The patient was perceived to have

depression symptoms if they responded 'yes' to either of these statements:

- Little interest and pleasure in doing things?
 - Feeling down, depressed, or hopeless?
- b. Anxiety symptom assessment using questions derived from Generalized Anxiety Disorder-2 (GAD-2) as a brief anxiety screening measure.¹² Answers were 'yes' or 'no'. The patient was perceived to have anxiety symptoms if they responded 'yes' to either of these statements:
 - Feeling nervous and anxious?
 - Not being able to stop or control worrying?

The data analysis was done using SPSS Statistics (IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp.). Descriptive data was expressed as mean±standard deviation (SD) for normally distributed continuous data and relative frequency and percentages for categorical data. The association of categorical data was analyzed using the chi-squared test or Fisher's exact test. A *p*-value < 0.050 was considered statistically significant.

Ethical approval from the Medical Research and Ethics Committee (MREC) was obtained before the initiation of the study (ID approval: NMRR-20-839-54731 (IIR)). The protocol was reviewed and approved by institutional review boards according to local requirements. Verbal consent was obtained from patients before data collection.

RESULTS

A total of 361 patients were enrolled in the study and were phone interviewed within the study period. The mean age of patients was 48.2 years (range: 16–80 years) with female preponderance (83.1% vs. 16.9%). The ethnic distribution in descending order was Malay (54.3%), Chinese (25.5%), Indian (18.3%), and others (2.0%). The majority were married (76.2%) and had a secondary level education (49.3%). The employment rate was 52.1%, and among the unemployed, the majority were housewives (66.5%). Almost half (49.3%) of patients had at least one comorbidity, of which 3.8% had chronic lung disease while 0.8% had bronchial asthma. The demographic characteristics are shown in Table 1.

The highest proportion of patients in our study was diagnosed with rheumatoid arthritis (41.6%),

Table 1: Demographic characteristics of the study patients.

Characteristics	n (%)
Age, mean \pm SD (range), years	48.2 \pm 14.4 (16–80)
Age group, years	
18–29	41 (11.4)
30–49	145 (40.2)
50–64	128 (35.5)
\geq 65	47 (13.0)
Gender	
Male	61 (16.9)
Female	300 (83.1)
Ethnic	
Malay	196 (54.3)
Chinese	92 (25.5)
Indian	66 (18.3)
Punjabi	5 (1.4)
Orang Asli	1 (0.3)
Filipino	1 (0.3)
Marital status	
Single	65 (18.0)
Married	275 (76.2)
Divorced	11 (3.0)
Widowed	10 (2.8)
Education level	
Primary	40 (11.1)
Secondary	178 (49.3)
Tertiary	128 (35.5)
No formal education	15 (4.2)
Occupation	
Employed	188 (52.1)
Unemployed	173 (47.9)
Comorbidities*	
Without	183 (50.7)
With at least one	178 (49.3)

SD: standard deviation.

*Diabetes, hypertension, dyslipidemia, ischemic heart disease, chronic kidney disease, chronic lung disease, bronchial asthma, stroke, thyroid disease, hepatitis B infection, human immunodeficiency virus infection, malignancy, and major depressive disease.

followed by systemic lupus erythematosus (34.6%), and spondyloarthropathy (12.2%). Consumption of prednisolone was 43.8%, with the mean dose of 7.9 mg daily (range: 1–40 mg). Usage of hydroxychloroquine (44.0%) was highest followed by methotrexate (37.4%), leflunomide (13.0%), and sulfasalazine (11.1%). Twenty-two (6.1%, 22/361) patients were taking bDMARD, while three (0.8%, 3/361) patients took tsDMARD. The overview of rheumatic disease and its treatment in our studied patients is shown in Table 2.

Table 2: Rheumatic disease and treatment.

Characteristics	n (%)
Rheumatological diagnosis	
SLE	125 (34.6)
RA	150 (41.6)
SpA ^a	44 (12.2)
Others ^b	42 (11.6)
Prednisolone usage	158 (43.8)
Prednisolone dose, mean (range), mg	7.9 (1–40)
csDMARDs	
Hydroxychloroquine	159 (44.0)
Methotrexate	135 (37.4)
Leflunomide	47 (13.0)
Azathioprine	45 (12.5)
Sulfasalazine	40 (11.1)
Mycophenolate Mofetil	21 (5.8)
Cyclosporin	12 (3.3)
Cyclophosphamide	4 (1.1)
Tacrolimus	2 (0.6)
bDMARDs	
Tocilizumab	6 (1.7)
Secukinumab	4 (1.1)
Adalimumab	3 (0.8)
Golimumab	2 (0.6)
Infliximab (Remsima)	2 (0.6)
Rituximab	1 (0.3)
Etanercept	1 (0.3)
Belimumab	1 (0.3)
Ixekizumab	1 (0.3)
Ustekinumab	1 (0.3)
tsDMARDs	
Tofacitinib	2 (0.6)
Filgotinib	1 (0.3)
Adherence to treatment	334 (92.5)

SLE: systemic lupus erythematosus; RA: rheumatoid arthritis; SpA: spondyloarthropathy; csDMARDs: conventional synthetic disease-modifying anti-rheumatic drugs; bDMARDs: biological disease-modifying anti-rheumatic drugs; tsDMARDs: targeted synthetic disease-modifying anti-rheumatic drugs.

^aPsoriatic arthritis, axial, and peripheral SpA; ^binflammatory myositis, undifferentiated connective tissue disease, overlap syndrome, systemic sclerosis, vasculitis, Sjogren's syndrome, adult-onset still disease, fibromyalgia, and antiphospholipid syndrome.

A large proportion of patients had no exposure risk to COVID-19 infection, and 76/361 patients had COVID-19 – like symptoms. However, among the 76 patients, only 13 patients sought medical consultation, and 12 patients were tested for COVID-19. Among our 361 studied patients, only one (0.3%) was confirmed positive for COVID-19 infection [Table 3].

Table 3: COVID-19 infection screening.

Questions	n (%)
Covid-19 screening questions for the past 14 days (n = 361)	
1) Have you traveled abroad?	10 (2.8)
2) Have you attended any mass gatherings or wedding ceremonies?	17 (4.7)
3) Are you staying with any of your family members who have attended mass gatherings, wedding ceremonies, or have returned from overseas?	11 (3.0)
4) Have you had close contact with anyone with confirmed COVID-19 infection?	1 (0.3)
COVID-19 symptoms screening	
Fever	4 (1.1)
Cough	17 (4.7)
Sore throat	7 (1.9)
Runny nose	7 (1.9)
Shortness of breath	2 (0.6)
Diarrhea	2 (0.6)
Arthralgia	13 (3.6)
Fatigue	4 (1.1)
Headache	1 (0.3)
More than one symptom	19 (5.3)
No symptoms	285 (78.9)
Seek medical consultation among symptomatic patients (n = 76)	13 (17.1)
Tested for COVID-19 among symptomatic patients (n = 76)	12 (15.8)
COVID-19 test	
Positive	1 (0.3)
Negative	11 (3.0)
Not done	349 (96.7)

Table 4: Depression and anxiety symptoms as reported by the patients.

Symptoms	n (%)
Depression symptom(s)	31 (8.6)
Anxiety symptom(s)	25 (6.9)

Depression or anxiety symptoms were reported among 31 (8.6%) and 25 (6.9%) patients, respectively [Table 4].

Different parameters affecting depression and anxiety were evaluated. Married patients were found to feel more anxious ($p = 0.013$) while patients with tertiary level education reported feeling more depressed ($p = 0.012$). Other parameters such as gender, age, comorbidities, rheumatological diagnosis, and DMARDs usage did not show significant association [Table 5].

DISCUSSION

The incidence of confirmed COVID-19 infection among patients with RD is low. In addition, the patients in our cohort reported a low rate of depression and anxiety symptoms. We found that married patients were statistically significantly more anxious while patients with tertiary level education felt more depressed.

Patients with RD are more susceptible to infections due to immunological alterations, diseases-related, and drugs-related factors. The lungs were reported to be the most frequent site of infection.¹³ Since the emergence of the COVID-19 pandemic, the question of whether patients with RD, especially those receiving DMARDs are at increased risk of COVID-19 infection, remains unclear. However, the prevalence of COVID-19 infection in patients with RD is limited. According to the systemic review on 6095 patients from eight observational cohort studies, only 2% of patients were found to be COVID-19 positive or highly suspicious for infection based on clinical features.¹⁴ Based on COVID-19 Global Rheumatology Alliance's data on 29 December 2020, 847/13 363 (6.3%) patients were reported to be infected with COVID-19.¹⁵ Another observational study in Northern Italy reported 65 (4.3%) patients were diagnosed with COVID-19 infection among 1525 patients with rheumatic and musculoskeletal diseases.¹⁶ The majority of patients in our cohort with COVID-19-like symptoms were not tested for COVID-19 as they did not seek medical consultation. Hence, this result might not truly reflect the incidence of COVID-19 in our patients.

The COVID-19 pandemic has led to significant psychological and social effects on our global population. Different strata of society were affected psychologically and socially by this pandemic, including COVID-19 positive patients and quarantined individuals, health care workers, children, the elderly, marginalized communities, and psychiatric patients.¹⁷ Few published studies reported the psychological impact in patients with RD. In Turkey, there were changes in the psychological state and routines of patients with RD during the COVID-19 outbreak.¹⁸ Patients with rheumatoid arthritis and lupus in the Philippines showed moderate to severe anxiety (38.7%), moderate to severe depression (27.7%), and stress (12.3%) during the pandemic.¹⁹ A small number of our patients perceived themselves to have depression

Table 5: Relationship between different parameters with depression and anxiety symptoms.

Parameters	Depression (n = 31)		Anxiety (n = 25)	
	n (%)	p-value	n (%)	p-value
Gender				
Male (n = 61)	4 (6.6)	0.802	2 (3.3)	0.279
Female (n = 300)	27 (9.0)		23 (7.7)	
Marital status				
Married (n = 275)	19 (6.9)	0.127	16 (5.8)	0.013
Single (n = 65)	10 (15.4)		5 (7.7)	
Divorced (n = 11)	1 (9.1)		4 (36.4)	
Widowed (n = 10)	1 (10.0)		0 (0.0)	
Education				
Primary (n = 40)	3 (7.5)	0.012	1 (2.5)	0.353
Secondary (n = 178)	8 (4.5)		11 (6.2)	
Tertiary (n = 128)	17 (13.3)		11 (8.6)	
No formal education (n = 15)	3 (20.0)		2 (13.3)	
Occupation				
Employed (n = 188)	19 (10.1)	0.283	16 (8.5)	0.216
Unemployed (n = 173)	12 (6.9)		9 (5.2)	
Comorbidities				
At least one (n = 178)	16 (9.0)	0.788	11 (6.2)	0.582
None (n = 183)	15 (8.2)		14 (7.7)	
Rheumatic disease				
SLE (n = 125)	12 (9.6)	0.882	11 (8.8)	0.499
RA (n = 150)	12 (8.0)		10 (6.7)	
Others (n = 86)	7 (8.1)		4 (4.7)	
DMARDs				
csDMARDs (n = 465)	31 (6.7)	0.727	25 (5.4)	0.707
ts+bDMARDs (n = 25)	3 (12.0)		1 (4.0)	

SLE: systemic lupus erythematosus; RA: rheumatoid arthritis; csDMARDs: conventional synthetic disease-modifying anti-rheumatic drugs; bDMARDs: biological disease-modifying anti-rheumatic drugs; tsDMARDs: targeted synthetic disease-modifying anti-rheumatic drugs.

and anxiety symptoms. We would expect patients with RD to have a higher psychological impact; however, this was not shown in our study. A possible explanation for this could be the rapid response from the Malaysian government and Ministry of Health to protect citizens from infection by implementing a lockdown on 18 March 2020 at the first peak of COVID-19 cases in Malaysia. Transparent up-to-date information about relevant news on COVID-19 infection was delivered to the public through daily press briefings. Additionally, awareness programs on basic protective measures (mask wearing, frequent hand washing, and social distancing) were easily available via local television and social media. Continuity of care in our patients was maintained via virtual clinics and any concerns were addressed via teleconsultation.

Factors affecting psychological impact during the COVID-19 pandemic varied from study to study. A

study from China in the general population reported more depression, anxiety, and stress in uneducated individuals.²⁰ However, this was contradictory to our analysis where patients with tertiary education had more depression symptoms. Married patients were more anxious in our analysis and this was in agreement with a study done in Pakistan.²¹ We would anticipate that married couples had better support in reducing anxiety, yet it was shown differently in our study, probably due to the quality of the marital relationship. This was reported in a study in Austria where good relationship quality was a protective factor, whereas poor relationship quality was a risk factor for anxiety.²² A study from India reported that males in the general population were more likely to be anxious.²³ However, gender did not show any significant association in our sample.

This study has some limitations. First, the incidence of COVID-19 infection in this study

might not be well represented as a number of patients with symptoms were not subjected to testing. Second, psychological impact assessment pertaining to depression and anxiety was not measured via validated tools and merely based on the patient's perception, which was a subjective assessment tool.

CONCLUSION

The incidence of COVID-19 infection in our cohort was low, probably due to the low rate of testing. Depression and anxiety symptoms reported by patients with RD in our cohort was modest. Our findings suggest that the COVID-19 pandemic has a greater impact in patients who are married and had a higher education level. Future studies are necessary to explore and validate the conclusions that can be drawn from this study.

Declaration

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