

## **A Questionnaire-based survey on depression and anxiety among rheumatology patients during Covid-19 Pandemic: Patient's Perspective**

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### **Abstract**

**Objectives** Coronavirus Disease-2019 (Covid-19) outbreak is a global pandemic which 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 as well as as depression and anxiety symptoms among patients with rheumatic disease(RD) during Covid-19 pandemic.

**Methods** A cross-sectional study was conducted via phone interview using a structured questionnaire in patients with RD aged more than 18 years old, who were scheduled for clinic appointment from 4<sup>th</sup> to 28<sup>th</sup> May 2020, which coincided with second wave of Covid-19 cases in Malaysia. The questionnaire included demographic, Covid-19 screening questions, depression and anxiety symptoms screening using questions derived from Patient Health Questionnaire-2(PHQ-2) and Generalised Anxiety Disorder-2(GAD-2).

**Results** Among 361 patients enrolled, majority were females (83.1%), ethnic Malays (54.3%), mean age of 48.2 years (range:16-80 years), 41.5% with rheumatoid arthritis, 34.6% with

systemic lupus erythematosus, 12.2% with spondyloarthropathy and only 1 patient (0.3%) had Covid-19 infection. Frequency of patients with depression and anxiety symptoms was 8.6% and 6.9%. Married patients were feeling more anxious( $p=0.013$ ) while patients with tertiary education level were feeling more depressed( $p=0.012$ ).

**Conclusion** The incidence of Covid-19 infection is low probably due to low rate of Covid-19 testing. Depression and anxiety symptoms reported by patients in our cohort is modest. Our findings suggest that Covid-19 pandemic has greater impact in patients who are married and higher education level.

**Keywords:** Rheumatic Disease; Covid-19; Incidence; Depression; Anxiety

## **Introduction**

A novel coronavirus was first detected during local outbreak in Wuhan, China on 31<sup>st</sup> December 2019. It is now known as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and was given the name of Coronavirus Disease 2019 (Covid-19).(1) On 11<sup>th</sup> March 2020, World Health Organization (WHO) declared Covid-19 as a global pandemic.(2) This alarming Covid-19 infection has infected 81,294,343 patients and killed 1,774,931 patients worldwide as reported on 28<sup>th</sup> December 2020.(3) In Malaysia, the first Covid-19 case was detected on 25<sup>th</sup> January 2020 with only 22 cases reported till 16<sup>th</sup> February 2020. The second wave started on 27 February 2020 and ended on 7<sup>th</sup> July 2020.(4) Currently, Malaysia is facing third wave since 20<sup>th</sup> September 2020 and confirmed cases has rose to 106,690 patients with 455 reported deaths as reported on 28<sup>th</sup> December 2020.(5)

The current outbreak of Covid-19 has not only caught the attention of the medical community but also the rheumatology fraternity, raising concern of a potential increased risk of infection among rheumatology patients who are on immunosuppressants. Since the declaration of Covid-

19 as a global pandemic, “social distancing” and “lock-down” has 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. Qiu J *et al.* reported that Covid-19 has caused serious threats to people’s physical and psychological health (e.g anxiety, depression, loss of social function and post-traumatic stress disorder) in their survey of 52,730 Chinese people.(6) Many researches have demonstrated negative psychological impact among general population and health care workers. (7 – 9). Higher psychological distress related to Covid-19 pandemic were reported among patients with autoimmune arthritis in Italy.(10) However, studies examining psychological impact in patient with rheumatic diseases are limited globally and none in Malaysia.

The purpose of this research was to study the incidence of Covid-19 infection as well as depression and anxiety symptoms among patients with RD in Hospital Selayang during the Covid-19 pandemic.

## **Methods**

A phone interview was conducted in cross-sectional design using a structured questionnaire. Eligible participants were all patients with RD aged more than 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 Rheumatology clinic appointment from 4<sup>th</sup> May 2020 to 28<sup>th</sup> May 2020 in Rheumatology Unit Hospital Selayang. The study duration coincided with the mid 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, co-morbidities, 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”. Patient was perceived to have depression symptom if patient 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 Generalised Anxiety Disorder-2(GAD-2) as a brief anxiety screening measure.(12) Answers were “yes” or “no”. Patient was perceived to have anxiety symptom if patient responded “yes” to either of these statements:-

- Feeling nervous and anxious?
- Not being able to stop or control worrying?

### **Statistical Analysis**

The data analysis was done using the SPSS version 25. Descriptive data was expressed as mean  $\pm$  standard deviation (SD) for a normally distributed continuous data and relative frequency

and percentages for categorical data. The association of categorical data was analysed using Chi-Squared test of Fisher's Exact test. A p value of < 0.05 is considered statistically significant.

## Ethics

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 prior to data collection.

## Results

### Patient Characteristics

In total, there were 361 patients enrolled into the study and were phone interviewed within the study period. The mean age 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 (18.2%) and others (2%). Majority were married (76.2%) and received secondary education (49.3%). The employment rate was 52.1% and among the unemployed, majority were housewives (66.5%). 49.3% patients had at least one co-morbidity of which 3.8% had chronic lung disease while 0.8% had bronchial asthma. The demographic characteristics are shown in Table 1.

**Table 1:** Demographic Characteristics.

| Characteristics             | n (%)               |
|-----------------------------|---------------------|
| Age, years (mean±SD, range) | 48.2±14.4 (16 - 80) |
| Age Group, years            |                     |
|                             | 18 – 29             |
|                             | 41 (11.3)           |
|                             | 30 – 49             |
|                             | 145 (40.2)          |

|                        |                        |            |
|------------------------|------------------------|------------|
|                        | 50 – 64                | 128 (35.5) |
|                        | ≥ 65                   | 47 (13.0)  |
| <b>Gender</b>          | Male                   | 61 (16.9)  |
|                        | Female                 | 300 (83.1) |
| <b>Ethnic</b>          | Malay                  | 196 (54.3) |
|                        | Chinese                | 92 (25.5)  |
|                        | Indian                 | 66 (18.2)  |
|                        | Punjabi                | 5 (1.4)    |
|                        | <i>Orang Asli</i>      | 1 (0.3)    |
|                        | Filipino               | 1 (0.3)    |
| <b>Marital Status</b>  | Single                 | 65 (18.0)  |
|                        | Married                | 275 (76.2) |
|                        | Divorced               | 11 (3.0)   |
|                        | Widowed                | 10 (2.8)   |
| <b>Education Level</b> | Primary                | 40 (11.1)  |
|                        | Secondary              | 178 (49.3) |
|                        | Tertiary               | 128 (35.4) |
|                        | No formal<br>education | 15 (4.2)   |
| <b>Occupation</b>      | Employed               | 188 (52.1) |
|                        | Unemployed             | 173 (47.9) |
| <b>Co-Morbidities*</b> | Without                | 183 (50.7) |
|                        | With at least<br>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, major depressive disease

### **Rheumatic disease and treatment**

The highest proportion of patients in our study was diagnosed with rheumatoid arthritis (RA; 41.5%), followed by systemic lupus erythematosus (SLE; 34.6%) and spondyloarthropathy (SpA; 12.2%). Consumption of prednisolone was 43.8% with the mean dose of 7.9mg daily

(range: 1 – 40mg). Usage of hydroxychloroquine (44%) was highest, followed by methotrexate (32.4%), leflunomide (23.9%) and sulfasalazine (21.1%). 22/361 (6.1%) patients were taking bDMARD while 3/361 (0.8%) patients were subjected to tsDMARD. The overview of rheumatic disease and its treatment in our studied patients is shown in Table 2.

**Table 2:** Rheumatic Disease and Treatment.

| <b>Characteristics</b>                     |                       | <b>n (%)</b> |
|--|-----------------------|--------------|
| <b>Rheumatological Diagnosis</b>           | SLE                   | 125 (34.6)   |
|  | RA                    | 150 (41.5)   |
|  | SpA <sup>a</sup>      | 44 (12.2)    |
|  | Others <sup>b</sup>   | 42 (11.7)    |
| <b>Prednisolone usage</b>                  |                       | 158 (43.8)   |
| <b>Prednisolone dose, mg (mean, range)</b> |                       | 7.9 (1 - 40) |
| <b>csDMARDs</b>                            | 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)      |
|  | <b>bDMARDs</b>        | Tocilizumab  |
|  | 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)    |
| <b>tsDMARDs</b>               | Tofacitinib | 2 (0.6)    |
|                               | Filgotinib  | 1 (0.3)    |
| <b>Adherence to treatment</b> |             | 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; <sup>a</sup>Psoriatic arthropathy, Axial & peripheral SpA; <sup>b</sup> Inflammatory Myositis, Undifferentiated Connective Tissue Disease, Overlap Syndrome, Systemic Sclerosis, Vasculitis, Sjogren's Syndrome, Adult Onset Still Disease, Fibromyalgia, Antiphospholipid Syndrome

### Screening for Covid-19 infection

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 seek medical consultation and 12 patients were tested for Covid-19. Among our 361 studied patients, only 1 patient (0.3%) was confirmed positive for Covid-19 infection. (Table 3)

**Table 3:** Covid-19 infection Screening.

|  | n (%)    |
|--|----------|
| <b>Covid-19 Screening Questions for the past 14 days (n=361)</b>   |          |
| <i>1) Have you travelled abroad?</i>   | 10 (2.8) |
| <i>2) Have you attended any mass gathering or wedding ceremony?</i>  | 17 (4.7) |
| <i>3) Are you staying with any of your family members who have attended mass gathering, wedding ceremony or have returned from overseas?</i> | 11 (3.0) |
| <i>4) Have you had close contact with anyone with confirmed Covid-19 infection?</i>  | 1 (0.3)  |
| <b>Covid-19 Symptoms Screening</b>   |          |
| Fever  | 4 (1.1)  |



|  |            |
|--|------------|
| Cough  | 17 (4.7)   |
| Sorethroat   | 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 1 symptom  | 19 (5.3)   |
| No symptoms  | 285 (78.9) |
| <b>Seek medical consultation among symptomatic patients (n=76)</b> | 13 (17.1)  |
| <b>Tested for Covid-19 among symptomatic patients (n=76)</b>       | 12 (15.8)  |
| <b>Covid-19 test</b>   |            |
| Positive   | 1 (0.3)    |
| Negative   | 11 (3.0)   |
| Not done   | 349 (96.7) |

### Depression and Anxiety Symptoms

31/361 (8.6%) and 25/361 (6.9%) patients reported that they were having depression or anxiety symptoms during the Covid-19 pandemic in the country. (Table 4)

**Table 4:** Depression and Anxiety Symptoms - Patient's perspective.

|                       | <b>n (%)</b> |
|-----------------------|--------------|
| Depression symptom(s) | 31 (8.6)     |
| Anxiety symptom(s)    | 25 (6.9)     |

Different parameters affecting depression and anxiety were evaluated. Married patients were found to be feeling more anxious ( $p=0.013$ ) while patients with tertiary education level were found to be feeling more depressed ( $p=0.012$ ). Other parameters such as gender, age, co-

morbidities, rheumatological diagnosis, DMARDs usage did not show significant association.

(Table 5)

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

|                          |                        | Depression (n=31) |              | Anxiety (n=25) |              |
|--------------------------|------------------------|-------------------|--------------|----------------|--------------|
|                          |                        | n (%)             | p value      | n (%)          | p value      |
| <b>Gender</b>            | Male (n =61)           | 4 (6.6)           | 0.802        | 2 (3.3)        | 0.279        |
|                          | Female (n = 300)       | 27 (9.0)          |              | 23 (7.7)       |              |
| <b>Marital status</b>    | Married (n = 275)      | 19 (6.9)          | 0.127        | 16 (5.8)       | <b>0.013</b> |
|                          | 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)          |              |
| <b>Education</b>         | Primary (n = 40)       | 3 (7.5)           | <b>0.012</b> | 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 (n = 15)     | 3 (20)            |              | 2 (13.3)       |              |
| <b>Occupation</b>        | Employed (n =188)      | 19 (10.1)         | 0.283        | 16 (8.5)       | 0.216        |
|                          | Unemployed (n = 173)   | 12 (6.9)          |              | 9 (5.2)        |              |
| <b>Co- Morbidities</b>   | At least one (n = 178) | 16 (9)            | 0.788        | 11 (6.2)       | 0.582        |
|                          | None (n = 183)         | 15 (8.2)          |              | 14 (7.7)       |              |
| <b>Rheumatic disease</b> | 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)        |              |
| <b>DMARDs</b>            | csDMARDs (n = 314)     | 31 (9.9)          | 0.727        | 25 (8)         | 0.707        |
|                          | ts+bDMARDs (n = 25)    | 3 (12)            |              | 1 (4)          |              |

## Discussion

In this present study, the incidence of confirmed Covid-19 infection among patients with RD is low. In addition, the patients in our cohort reported low rate of depression and anxiety symptoms. We found significantly that married patients were feeling more anxious while patients with tertiary education level were feeling more depressed.

Patients with RD are more susceptible to infections due to immunological alterations, diseases related factors and drugs related factors. Lung was reported to be the most frequent site of infection.(13) Since the emergence of Covid-19 pandemic, question whether patients with RD especially those receiving DMARDs are at increased risk of Covid-19 infection remains unclear. Prevalence of Covid-19 infection in patients with RD is rather limited. According to the systemic review on 6095 patients from 8 observational cohort studies done by Akhil Sood *et al*, only 2% of patients were found to be Covid-19 positive or highly suspicious for Covid-19 infection based on clinical features.(14). Based on Covid-19 Global Rheumatology Alliance's data on 29<sup>th</sup> December 2020, 847/13363 (6.3%) patients were reported to be infected with Covid-19 infection.(15) Another observational study in Northern Italy reported 65 patients (4.3%) were diagnosed with COVID-19 infection among 1525 patients with rheumatic and musculoskeletal diseases.(16) 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 to our global population. Different strata of society was affected psychologically and socially by this pandemic, including Covid-19 positive patients and quarantined individuals, health care workers, children, old age, marginalised communities and psychiatric patients.(17) Few

published studies demonstrated psychological impact towards patients in RD. In Turkey, there were changes in psychological state and routine of the patients with RD during Covid-19 outbreak.(18) Patients with RA and lupus in Philippines showed moderate to severe anxiety (38.7%), moderate to severe depression (27%), and stress (12.3%) during Covid-19 pandemic.(19) Small number of our patients perceived to have depression and anxiety symptoms. We would expect patients with RD to have higher psychological impact, however it was not shown in our study. Possible explanation to this could be due to rapid response from Government of Malaysia and Ministry of Health to protect the citizens from Covid-19 infection by implementing 'lock down' on 18<sup>th</sup> 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 programmes on basic protective measures (wearing mask, frequent hand washings, social distancing) were easily available via local television and social media. Continuity of care in our patients was maintained via virtual clinic and patient's concerns were addressed via teleconsultation during this pandemic.

Factors affecting psychological impact during Covid-19 pandemic varied from study to study. A study from China in general population reported that uneducated status had more depression, anxiety and stress(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 study done in Pakistan where married people had greater anxiety during quarantine amidst the Covid-19 pandemic.(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 marriage. This was reported in a study in Austria where good relationship quality was a protective factor whereas a poor relationship quality was a risk

factor for anxiety.(22) Interestingly, gender also contributed differently to anxiety where male patients with RD had less anxiety as reported by Tugba *et al.*(23) but study from India reported that males were more likely to be anxious in the general population instead.(24) However, gender did not show any significant association in our sample.

This study has some limitations. First of all, the incidence of Covid-19 infection in this study might not be well represented as a number of patients with Covid-19 – like symptoms were not subjected for Covid-19 test. Secondly, psychological impact assessment pertaining to depression and anxiety was not measured via validated tools and merely based on patient's perception which was a subjective tool of assessment.

### **Conclusion**

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

### **CONFLICT OF INTEREST**

The authors declare no conflict of interest.

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## **ETHICS APPROVAL**

The study has been reviewed and approved by Medical Research and Ethics Committee (MREC), Ministry of Health Malaysia (MOH); ID approval: NMRR-20-839-54731 (IIR). Patient's consent was obtained prior to data collection.

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