

# Attitudes and Behaviors of Patients With Rheumatic Diseases During the Early Stages of the COVID-19 Outbreak

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**ABSTRACT.** Objective. To evaluate attitudes and behaviors of patients with rheumatic diseases during the coronavirus disease 2019 (COVID-19) pandemic.

*Methods.* An online survey delivered by text message to 4695 patients on follow-up at a tertiary rheumatology center. Latent class analysis was performed on the survey variables.

**Results.** There were 2239 (47.7%) who responded to the survey and 3 clusters were identified. Cluster 3 (C3) was defined by patients who were most worried about COVID-19, more likely to wear face masks, and more likely to alter or stop their medications. Patients in C3 were more likely to be female, Malay, and unemployed. **Conclusion.** We identified 3 clusters with different healthcare beliefs and distinct sociodemographics.

Key Indexing Terms: COVID-19, immunosuppressants, rheumatic diseases, survey

The novel coronavirus disease 2019 (COVID-19) has become a global pandemic<sup>1</sup>. Whereas increasing age and comorbidities are proven risk factors for poor clinical outcomes<sup>2</sup>, it is unclear<sup>3,4,5,6,7</sup> whether patients with rheumatic diseases should be considered high risk due to both disease and immunosuppressive treatments, especially during the early stages of the pandemic. On the other hand, hydroxychloroquine (HCQ) has been used in the treatment of COVID-19 and anti–interleukin 6 has been used for certain patients with cytokine storm syndrome<sup>8,9</sup>.

COVID-19 has caused increased uncertainty and anxiety among patients, leading to changes in healthcare behaviors<sup>10</sup>. It is important to understand this in the context of rheumatic diseases. As such, we performed a study to explore their attitudes and behaviors, with an aim to identify subgroups of patients with higher needs who may benefit from closer follow-up during this period.

## **MATERIALS AND METHODS**

Patients seen in our tertiary rheumatology clinic in Singapore between March 1, 2019, and February 29, 2020, with Singapore mobile phones were extracted from our data warehouse using a data anonymization solution

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with a unique hashtag key. These patients were sent a 25-question survey (Supplementary Data 1, available with the online version of this article) through SMS on March 28, 2020, with a secure web-based survey tool (Research Database Capture; REDCap)<sup>11</sup>. A further 2 SMS reminders were sent on March 31, 2020, and April 9, 2020, if the survey was not completed. Data points were aggregated with demographics, diagnosis codes, and prescriptions associated with the rheumatology visit; mobile numbers were removed to preserve anonymity. We used an unbiased, multidimensional approach to identify patients with different healthcare attitudes and behaviors and to see if these clusters predict disease characteristics and medication usage. Latent class analysis (LCA) was performed to determine the appropriate number of clusters and the best fitting models were selected using the Akaike information criterion (AIC) and the Bayesian information criterion (BIC)<sup>12</sup>. A 3-cluster solution was obtained after examining the change in the AIC and the BIC values between adjacent clusters. Twenty-two questionnaire responses were selected as input variables for the LCA. Missing data were input as "unknown" to make up a complete dataset. For survey responses, there were no missing data because the questions were all mandated. This analysis places subjects into clusters, suggested by the questionnaire data, not defined a priori. Differences between clusters were explored using the chi-square test and the Kruskal-Wallis test, with the Mann-Whitney U test for pairwise comparisons and the Bonferroni correction for multiple comparisons. Stata v10 (StataCorp) and SPSS v25 (IBM Corp.) were used. This study was approved by the National Health Group Domain Specific Review Board (NHG DSRB Reference: 2020/00248). Informed consent was not required since it was anonymized.

### **RESULTS**

Of the 5085 eligible patients, the survey was sent to 4695 individuals with Singapore mobile numbers: 2239 (47.7%) responded by April 14, 2020 [mean age 53.5 (SD 15.9) yrs, 1567 (70%) females, 1524 (68.1%) Chinese]. Four hundred seventy-seven (26.7%) patients had connective tissue disease (CTD) and 721 (40.3%) patients had inflammatory arthritis (IA). Two hundred fourteen (9.6%) patients were taking HCQ alone, 1032 (46.1%) patients were taking immunosuppressants other than biologics, and 95 (4.2%) patients were taking biologic or targeted synthetic

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disease-modifying antirheumatic drugs. Survey responders tended to be younger, more likely to be female, non-Chinese, more likely to have IA or CTD, and less likely to have comorbid conditions (Table 1). Forty-four (2.03%) patients had been tested for SARS-CoV-2 and only 1 patient was positive. Forty-eight (2.27%) of the patients' coinhabitants tested positive for SARS-CoV-2.

The majority of patients obtained information on COVID-19 through multiple sources, including television (65.8%), social media (62.3%), the Singapore Ministry of Health website and WhatsApp messaging app (61.7%), newspapers (49.5%), or friends and family (50.5%). One hundred sixty-two (7.4%)

patients had contacted healthcare professionals (HCP) for COVID-19 advice and most (90.74%) were reassured by their advice. Patients were worried about COVID-19 [median 73 (IQR 50–89) on a 100-point visual analog scale (VAS), with 100 being the most worried] and worried about going out (median 70, IQR 50–81). Seven hundred thirty-three (33.5%) patients had traveled abroad from December 1, 2019, to the time of the survey and 1020 (47.3%) had canceled travel plans. There were 1012 (46.4%) patients who wore face masks while being in good health, despite this being discouraged by the government at the time of the survey. There were 2088 (96%) patients who sanitized hands more often. During the COVID-19 period,

Table 1. Baseline characteristics.

	Overall Cohort, n = 5085	Survey Responders, n = 2239	Survey Nonresponders, n = 2846
Age, yrs, mean (SD)		53.5 (15.9)	59.2 (16.0)
Sex, female	3450 (67.9)	1567 (70.0)	1883 (66.2)
Race			
Chinese	3596 (70.7)	1524 (68.1)	2072 (72.8)
Malay	483 (9.5)	249 (11.1)	234 (8.2)
Indian	493 (9.7)	233 (10.4)	260 (9.1)
Other	512 (10.1)	233 (10.4)	279 (9.8)
Diagnosis†			
CTD	946 (23.5)	477 (26.7)	469 (21.0)
IA	1599 (39.8)	721 (40.3)	878 (39.3)
Crystal	483 (12.0)	165 (9.2)	318 (14.2)
Noninflammatory	993 (24.7)	426 (23.8)	567 (25.4)
Comorbidities*			
CVD	397 (8.2)	138 (6.4)	259 (9.6)
Hypertension	306 (6.3)	132 (6.1)	174 (6.4)
Diabetes mellitus	337 (6.9)	134 (6.2)	203 (7.5)
CKD	161 (3.3)	60 (2.8)	101 (3.7)
Cancer	218 (4.5)	80 (3.7)	138 (5.1)
Rheumatological medications			
None	1647 (32.4)	699 (31.2)	948 (33.1)
HCQ alone	464 (9.1)	214 (9.6)	250 (8.8)
IS including csDMARD	2212 (43.5)	1032 (46.1)	1180 (41.4)
bDMARD or tsDMARD	189 (3.7)	95 (4.2)	94 (3.3)
Gout medications	573 (11.3)	199 (8.9)	374 (13.1)
Antihypertensives			
None	3496 (68.7)	1604 (71.6)	1892 (66.5)
ACEI/ARB	933 (18.4)	387 (17.3)	546 (19.2)
Other antihypertensives	656 (12.9)	248 (11.1)	408 (14.3)
NSAID or COXIB	1876 (36.9)	855 (38.2)	1021 (35.9)

Values are n (%) unless otherwise specified. †CTD: connective tissue disease, includes systemic lupus erythematosus, immune-mediated inflammatory myositis, systemic sclerosis, systemic vasculitis, Sjögren syndrome, mixed CTD, undifferentiated CTD; IA: inflammatory arthritis, includes rheumatoid arthritis, psoriatic arthritis, axial and peripheral spondyloarthropathy, juvenile idiopathic arthritis, adult-onset Still disease, and undifferentiated IA; noninflammatory: includes primary antiphospholipid syndrome, osteoarthritis, osteoporosis, fibromyalgia, soft tissue rheumatism, and miscellaneous conditions. \*Comorbidities are based on diagnosis codes and are significantly undercoded as seen by proportion taking antihypertensive drugs; diagnosis codes for hypertension, diabetes, CVD, and CKD combined. ACEI: angiotensin-converting enzyme inhibitor; ARB: angiotensin receptor blocker; bDMARD: biologic disease-modifying antirheumatic drug; CKD: chronic kidney disease; COXIB: cycloxygenase-2 inhibitor; csDMARD: conventional synthetic disease-modifying antirheumatic drug; CVD: cardiovascular disease; HCQ: hydroxychloroquine; IS: immunosuppressant; NSAID: nonsteroidal antiinflammatory drug; tsDMARD: targeted synthetic disease-modifying antirheumatic drug.

255 (11.7%) patients had seen their doctors more often than usual. Three hundred sixteen (14.7%) patients admitted to not taking medications regularly even prior to the pandemic. Since the pandemic, 1991 (94.8%) patients took their medications with the same regularity or more than before. Of the 109 (5.2%) patients who took their medications less regularly, 43.3% did so due to worries about COVID-19. Seven hundred ninety-two (36.8%) patients and 427 (19.9%) patients believed that their rheumatic condition and medications would increase their risk of COVID-19, respectively. Three hundred thirteen (14.7%; 22% of those receiving HCQ) patients believed their medications would protect them from COVID-19. Only 868 (41%) patients were up to date with their influenza and pneumococcal vaccinations (Table 2).

Three clusters were found using the LCA, classifying C1 (295, 13.2%), C2 (703, 31.4%), and C3 (1241, 55.4%). Discriminant analysis showed that 97.7% of the subjects were correctly classified with a cross-validation of 97.3% (Supplementary Figure 1, available with the online version of this article). Group C3 was the most worried about COVID-19 [median VAS 86 (IQR 78–97)] vs Group C2: 52 (IQR 50–63), P < 0.001, and vs Group C1: 20 (IQR 10–29), P < 0.001]. This group had more contact with HCP compared to C1 (9% vs 6%, P = 0.01), with more

patients wearing face masks (53% vs 28%, P < 0.001). They also decreased their social activities (80% vs 68%, P < 0.001). They were most worried that their condition (43% vs 20%, P < 0.001) or medications (22% vs 13%, P < 0.001) would put them at higher risk of being infected. C3 also altered or stopped their medications more during COVID-19 (11% vs 7%, P = 0.002) and took medication less regularly before COVID-19 (20% vs 16%, P = 0.02). C3 obtained less information from newspapers (47% vs 54%, P = 0.03), and fewer were up to date with vaccinations (37% vs 44%, P = 0.006; Table 2).

On examination of the demographic and clinical profiles of the generated clusters, patients in C3 were more likely to be female, of Malay race, and unemployed. Rheumatic conditions and medication type were not different among the 3 clusters (Table 3). In a subset analysis of patients with IA or CTD and/or on immunomodulatory medications, patients with CTD were more likely to belong to C3, although other descriptors of group membership remained the same.

### **DISCUSSION**

To our knowledge, our study is the first to survey a wide spectrum of multiethnic patients with rheumatic diseases about COVID-19. We identified a large subset of patients who were

Table 2. Latent class analysis generation of 3 clusters.

	C1, n = 295	C2, $n = 703$	C3, n = 1241	P
Considered stopping medication, VAS 0–100, median (IQR)	0 (0-9)	2 (0-24)	5 (0-30)	< 0.001
Worried about going out, VAS 0–100, median (IQR)	21 (8-30)	50 (47-61)	80 (72-91)	< 0.001
Worried about COVID-19, VAS 0-100, median (IQR)	20 (10-29)	52 (50-63)	86 (78-97)	< 0.001
Source of information				
MOH website/WhatsApp	194 (66)	438 (62)	749 (60)	0.21
Television	178 (60)	474 (67)	822 (66)	0.89
Newspaper	160 (54)	364 (52)	585 (47)	0.03
Radio	77 (26)	201 (29)	378 (31)	0.30
Friends and family	139 (47)	373 (53)	620 (50)	0.19
Social media	170 (58)	442 (63)	784 (63)	0.20
Has contact with healthcare workers	18 (6)	36 (5)	108 (9)	0.01
Traveled since Dec 1, 2019	89 (30)	247 (35)	397 (32)	0.22
Canceled travel plans	134 (45)	330 (47)	556 (45)	0.68
Participated in social activities				
Same	93 (32)	132 (19)	234 (19)	< 0.001
Less than before	199 (68)	559 (78)	986 (80)	
More than before	3 (1)	12 (2)	21 (2)	
Worn face mask even when well	81 (28)	270 (38)	660 (53)	< 0.001
Washing/sanitizing hands more often	266 (90)	668 (95)	1154 (93)	0.02
Seeing doctor more often	28 (9.5)	74 (10.5)	152 (12.2)	0.29
Taking medication regularly before COVID-19	249 (84)	590 (84)	988 (80)	0.02
Taking medication regularly since COVID-19				
Same	273 (93)	667 (95)	1113 (92)	0.002
Less than before	13 (4)	24(3)	72 (6)	
More than before	9 (3)	12 (2)	56 (5)	
Increased risk of COVID-19 because of rheumatic condition	59 (20)	205 (29)	528 (43)	< 0.001
Belief that medication will protect from COVID-19	39 (13)	90 (13)	184 (15)	0.43
Belief that medication will increase risk of getting COVID-19	39 (13)	110 (16)	278 (22)	< 0.001
Up to date with influenza/pneumococcal vaccinations	129 (44)	279 (40)	460 (37)	0.006

Values are n (%) unless otherwise specified. Cluster groups: C1/C2/C3 used the whole cohort of patients who had responded to questionnaire. Differences between clusters were tested using Kruskal-Wallis test for continuous measures and Pearson chi-square test for categorical measures. MOH: Ministry of Health.

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	All Patients, n = 2239				Patients With IA/CTD or Receiving Immunomodulatory Therapy, n = 1533			
	C1, n = 295	C2, $n = 703$	C3, $n = 1241$	P		IC2, $n = 488$		P
Age, yrs, median (IQR)	55 (41–66)	53 (40-64)	55 (43–66)	0.03	52 (40-65)	51 (38–62)	54 (41-64)	0.008
Male	113 (38.3)	223 (31.7)	336 (27.1)	< 0.001	67 (36.6)	135 (27.7)	194 (22.5)	< 0.001
Race				< 0.001				< 0.001
Chinese	216 (73.2)	493 (70.1)	815 (65.7)		135 (73.8)	320 (65.6)	547 (63.5)	
Malay	17 (5.8)	67 (9.5)	165 (13.3)		8 (4.4)	52 (10.7)	120 (13.9)	
Indian	41 (13.9)	78 (11.1)	114 (9.2)		26 (14.2)	72 (14.8)	89 (10.3)	
Other	21 (7.1)	65 (9.2)	147 (11.8)		14 (7.7)	44 (9.0)	106 (12.3)	
Unemployed	109 (36.9)	269 (38.3)	584 (47.1)	< 0.001	59 (32.2)	175 (35.9)	393 (45.6)	< 0.001
Comorbidities <sup>†</sup>								
Cancer	10 (3.4)	28 (4)	42 (3.4)	0.78	4 (2.2)	11 (2.3)	23 (2.7)	0.86
CVD	20 (6.8)	38 (5.4)	80 (6.4)	0.59	7 (3.8)	18 (3.7)	50 (5.8)	0.17
Diabetes mellitus	14 (4.7)	45 (6.4)	75 (6)	0.60	9 (4.9)	33 (6.8)	45 (5.2)	0.45
Hypertension	14 (4.7)	44 (6.3)	74 (6)	0.64	7 (3.8)	25 (5.1)	44 (5.1)	0.75
Antihypertensive drugs	70 (23.7)	180 (25.6)	385 (31.1)	0.03	41 (22.4)	117 (23.9)	277 (32.2)	0.003
CKD	9 (3.1)	16 (2.3)	35 (2.8)	0.71	5 (2.7)	8 (1.6)	17 (2.0)	0.66
Rheumatological diagnosis*	, ,	, ,	, ,	0.25	, ,	, ,	, ,	0.01
IA	98 (33.2)	243 (34.6)	380 (30.6)		94 (51.4)	245 (50.2)	382 (44.3)	
CTD	51 (17.3)	154 (21.9)	272 (21.9)		49 (26.8)	155 (31.8)	273 (31.7)	
Crystal arthritis	24 (8.1)	51 (7.3)	90 (7.3)		_	_		
Noninflammatory	67 (22.7)	126 (17.9)	233 (18.8)		_	_	_	
Medications	, ,	, ,	, , ,	0.27				0.19
IS none	98 (33.2)	220 (31.3)	381 (30.7)		20 (10.9)	62 (12.7)	102 (11.8)	
HCQ alone	16 (5.4)	69 (9.8)	129 (10.4)		14 (7.7)	71 (14.5)	129 (15.0)	
IS including csDMARD	138 (46.8)	315 (44.8)	579 (46.7)		133 (72.7)	320 (65.6)	579 (67.2)	
bDMARD or tsDMARD	16 (5.4)	34 (4.8)	45 (3.6)		16 (8.7)	32 (6.6)	47 (5.5)	
Gout medications	27 (9.2)	65 (9.2)	107 (8.6)			_ ′	_	

Values are n (%) unless otherwise specified. Cluster groups: C1/C2/C3 used the whole cohort of patients who had responded to questionnaire. A subgroup analysis was carried out on patients with a diagnosis of connective tissue disease, inflammatory arthritis, and/or on immunosuppressive agents (IC1/IC2/IC3). Differences between clusters were tested using Kruskal-Wallis test for continuous measures and Pearson chi-square test for categorical measures. \* Unknown = 450. † CTD: Connective tissue disease, includes systemic lupus erythematosus, immune mediated inflammatory myositis, systemic sclerosis, systemic vasculitis, Sjögren syndrome, mixed CTD, undifferentiated CTD; IA: inflammatory arthritis, includes rheumatoid arthritis, psoriatic arthritis, axial and peripheral spondyloarthropathy, juvenile idiopathic arthritis, adult-onset Still disease, and undifferentiated IA; noninflammatory: includes primary antiphospholipid syndrome, osteoarthritis, osteoporosis, fibromyalgia, soft tissue rheumatism, and miscellaneous conditions. bDMARD: biologic disease-modifying antirheumatic drug; C1, C2, C3: cluster 1, 2, 3; CKD: chronic kidney disease; csDMARD: conventional synthetic disease-modifying antirheumatic drug; CVD: cardiovas-cular disease; HCQ: hydroxychloroquine; IS: immunosuppressant; tsDMARD: targeted synthetic disease-modifying antirheumatic drug.

more worried about COVID-19 because of their underlying disease and medications. These patients were more likely to contact HCP, modify their social behaviors, and alter/stop medications. This group had a lower proportion of patients reading the newspaper, being adherent to their medications, or being up to date with their vaccinations. This cluster represented a vulnerable sociodemographic group, with significantly higher unemployment, more women, and belonging to an ethnic minority, but who were not different in the distribution of rheumatic diseases or immunosuppressive medications. Patients with such disadvantaged sociodemographic profiles are also similarly seen in other cohorts of rheumatic diseases [e.g., Lupus in Minority: NAture vs Nurture (LUMINA) cohort]<sup>13</sup>. Patients clustered in C3 may benefit from more rheumatology services.

In a US survey (response rate 7.5%), 530 patients with rheumatic diseases were significantly worried about risk of COVID-19, with 14% self-changing their medication or dose<sup>14</sup>. In our study, medication adjustments were observed only in 5%

of the patients, possibly due to the patients' perception that their rheumatic disease itself posed a greater risk. However, increased handwashing, less travel, and fewer social activities among the general US population were similar to our findings<sup>10</sup>.

Our study has several strengths. We were able to distribute the survey link through SMS to 92% of the patients with a high response rate. We used a unique cluster analysis to avoid bias from testing for multiple outcomes. Our patients include a multiethnic population, representative of Singapore, which is predominantly Chinese (74%), followed by Malays (13%) and Indians (9%)<sup>15</sup>, allowing us to study racial and cultural differences in attitudes and behavior. However, while associations exist between sociodemographics and perceived risk of COVID-19, causation cannot be demonstrated due to the study design. We were limited by the cross-sectional nature of our survey, which did not allow us to determine the longitudinal stability of our clusters. Although not included in our survey, patient-perceived disease activity may have influenced their attitudes during and

toward COVID-19 and would be thus informative to include in future studies. This survey was conducted mostly before stricter lockdown measures were implemented in Singapore on April 7, 2020; behavior may since have changed.

The pathological and psychological effect of COVID-19 on patients with rheumatic diseases likely exists as a consequence of their immunosuppressive state and inherently heightened anxiety and depression levels16. While almost 20% of respondents were concerned that their medications would increase their risk for COVID-19, only a small proportion sought advice from their physicians. An effective platform for patients to express their concerns in the context of COVID-19 will be fundamental to prevent unnecessary or even harmful unilateral changes of treatment by patients. Some rheumatological societies have published recommendations to address these issues; however, these societies additionally recommend cancellation of routine visits<sup>17,18,19</sup>. Rheumatologists will need to find novel ways to engage their patients proactively to allay anxiety. We have identified a subgroup of patients where these efforts should be most targeted.

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#### **ONLINE SUPPLEMENT**

Supplementary material accompanies the online version of this article.

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