Knowledge, Attitude and Practice towards COVID-19 among Patients with Musculoskeletal and Rheumatic Diseases in Nepal: A Web-based Cross-Sectional Study

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Abstract
Introduction/objectives: The global health crisis created by Coronavirus Disease (COVID-19) can be a serious concern to rheumatologists. The relationship of rheumatic diseases, their therapies, and COVID-19 with multiple genuine and malicious information available online can influence the knowledge and attitude of rheumatic patients. This web-based google-form study was conducted to understand the knowledge, attitude and practices of rheumatologic patients towards COVID-19 in Nepal.

Methodology: A web based cross-sectional study was conducted among the patients with rheumatic diseases. Modified version of questionnaire prepared by Zhong BL et al was used after consent. It was then translated in Nepali language for comprehensibility. The final questionnaire contained a total of 29 questions; 6 for demographic parameters, 12, 5 and 6 for knowledge, attitude and practice behaviors, respectively. Simple descriptive statistics describing the positive responses in each domain. Multiple linear regression analysis done to observe demographic variables associated with the knowledge, attitude and practice.

Results: Among 380 participants, 63.2% were female. Most of the participants were aware of the clinical features of COVID-19 (91.6 %), 71.5% had positive attitude towards its control, some (31.5 %) thought that they had greater chance of getting COVID-19 than others and 18.9 % believed that the anti-rheumatic medications could increase their susceptibility to infection. Majority (> 94.7%) practiced preventive measures.

Conclusions: Patients with rheumatic diseases were aware of the general clinical features, route of transmission and general preventive measures regarding COVID-19.

Key Points
1. There is a higher chance of infections, including COVID 19 and their complications in patients with rheumatic diseases because of the disease itself and the immunosuppressive drugs used.
2. This survey focused on the knowledge, attitude and practice (KAP) regarding COVID-
19 among patients with rheumatic diseases in Nepal.

3. The patients had acceptable knowledge of general clinical features, route of transmission and general preventive measures regarding COVID-19.

4. Lack of knowledge regarding the susceptibility stratification and recommendations for prevention amongst those using DMARDs has been noted.

Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) belongs to the coronavirus family responsible for the pandemic Coronavirus Disease (COVID-19) which was first identified in Wuhan, China in December 2019.[1, 2] The spectrum of this disease ranges from mild fatigue, myalgia, fever, dry cough, and dyspnea to severe manifestations like acute respiratory distress syndrome (ARDS), septic shock, disseminated intravascular coagulation (DIC), and acute renal failure. SARS-CoV-2 infection has more severe manifestations in elderly adult males with chronic comorbidities like chronic lung diseases, obesity (body mass index >40), liver disease, chronic kidney disease, diabetes mellitus, under immunosuppressant drugs which can weaken the immune functions of these patients. [3, 4] According to the World Health Organization (WHO) recent report (9th April 2020), COVID-19 has been confirmed in 209 countries with total 1,436,198 positive cases; and over 100,000 confirmed deaths by April 11, 2020. [5]

This global health crisis created by COVID-19 can be a serious concern to rheumatologists too. Unlike patients with other co-morbidities, there is no exact clinical evidence from recent and past coronavirus outbreaks that patients with rheumatic diseases fall under the high-risk category.[6, 7] Since rheumatic diseases compromise the patient’s immunity, and the use of immunosuppressant drugs further compounding the effect and leading to a weakened immune system, researchers have started reporting COVID-19 in patients with rheumatic diseases. [8, 9]

This confusing relationship of rheumatic diseases, their therapies, and COVID-19 with multiple genuine and malicious information available online can influence the knowledge and attitude of our patients on treatment thus affecting their practice regarding treatment adherence. This study focuses on the knowledge, attitude and practice (KAP) regarding COVID-19 among patients with rheumatic
Methodology

With the help of a web-based google-form, a cross-sectional study was conducted using a survey questionnaire to understand the knowledge, attitude, and practices of rheumatic patients towards COVID-19 in Nepal during the first week of April 2020.

Study population

Patients with various rheumatologic diseases (Rheumatoid arthritis, RA; Systemic lupus erythematosus, SLE; Fibromyalgia, FMS; Osteoarthritis, OA; Gout et cetera) were selected randomly from the patient registry of National Center for Rheumatic Diseases (NCRD), Kathmandu, Nepal. A computer-generated random number table was used to select the survey participants based on their registration number. A sample size of 384 patients was calculated with an estimated 3 million populations of rheumatic diseases where the margin of error was 5%. Considering a 30% response rate, 1160 patients were invited to participate in the survey.

Survey instrument

The survey questionnaire constructed by Zhong BL et al was modified and translated in Nepali language for the study.[10] The corresponding author Yi Li was contacted via email and permission to use the same questions with modification in terms of rheumatic patients was obtained. The modified questionnaire was translated into the native language (Nepali) by two independent Nepali speaking translators. A pre-final Nepali questionnaire was developed after sorting out the differences in understanding of common words after a joint meeting with two translators and author BV. This pre-final survey instrument was distributed to randomly selected faculty members to assess its comprehensibility and appropriateness (on a score of 0 to 4), and refinements were made as required to facilitate better comprehension and to organize the questions before the final survey was distributed to the study population. It contained a total of 29 questions; 6 questions pertaining to demographic parameters including the rheumatic disease they were suffering from, 12 to knowledge about the disease, 5 to attitude and 6 to practice behaviors. The responses were classified as true, false or not sure in the knowledge and attitude sections Open-ended questions were not kept to save
the time of the respondents and reduce drop-out rates.[11]

Procedure

A SMS containing objective of the study and invitation for participation was sent to each of the selected participant. It mentioned why they were receiving the SMS and a link to the google form was attached in the SMS itself. It also mentioned about the implied consent for participation on clicking the link. The link provided was applicable for single use only to avoid multiple entries from same user. The responses were collected in an excel sheet.

Statement of human rights

The procedures followed for the study were in accordance with ethical standards.

Statistical Analysis:

All the responses were qualitative in nature. Simple descriptive statistics was used to describe the positive responses in each domain. Multiple linear regression analysis was done to observe demographic variables associated with the knowledge, attitude and practice. Chi square test was done where applicable. SPSS version 21 (SPSS Inc., USA) was used for data analysis and the p-value of $\leq 0.05$ was considered significant.

Results

Questionnaire preparation:

All of the consultants verifying the questionnaire reported good comprehensibility and appropriateness of the final version (score of 2 or 3). The internal consistency between each item of the questionnaire was satisfactory with Cronbach’s alfa of 0.769.

Survey

A total of 380 patients participated in the survey with majority being females (63.2 %) and at least 46.3% had either rheumatoid arthritis or lupus that requires some form of immunosuppressive treatment. Other demographic parameters are mentioned in table no 1.

Knowledge domain:

Most of the participants were aware of the clinical features of COVID-19 (91.6 %) and 70.6 % knew that it can manifest serious outcomes in patients with comorbidities. Patients could differentiate the
symptoms of COVID-19 (48.4 %) from other seasonal flu and 93.7 % were sure that symptomatic and conservative management would help in recovery of the disease. Many were aware (92.6 %) that virus can transmit by droplet infection. Maximum (97.8 %) had idea that avoiding social gathering and maintaining distance would help in prevention of infection and 96.8 % agreed that isolation and treatment of infected would stop the further spread. The results of knowledge of participants regarding COVID-19 infection is given in table no 2.

Attitude domain:
A positive attitude towards the control of COVID-19 was seen in majority (71.5 %). A good proportion of participants (31.5 %) thought that they had greater chance of getting COVID-19 than general population because of their co-morbidity (rheumatic disease) and 18.9 % believed that the anti-rheumatic medications they were receiving could increase their susceptibility to infection. Some (13.6 %) even thought that anti-rheumatic drugs or flu vaccines might have some protective mechanism against COVID-19. The responses for attitude domain are given in table 3.

Practice domain:
Preventive measures like wearing mask (94.7 %) and avoiding public or crowded places (97.9 %) were practiced and 96.9 % did not take flu and pneumonia vaccination as a preventive measure for COVID-19. However, 13.6 % reduced the dose of their anti-rheumatic drugs on their own and few participants admitted to have stopped medication in fear of infection (4.2 %) or unavailability of medicines due to lock down (8.4 %). Details are given in table no 4.

Multiple linear regression analysis did not show significant relationship between demographic variables like gender and education with responses to knowledge, attitude and practice related questions (p-value > 0.312).

Discussion
The dysfunctional immune system along with the use of immunosuppressive drugs with additional comorbidities in patients with musculoskeletal and rheumatic conditions increase their susceptibility to infections. [12] The outbreak of novel coronavirus did not show major evidence that patients with rheumatic diseases are at higher risk for worse outcomes compared to other comorbidities. [6, 7] This
does not mean worse outcomes should not be anticipated as COVID-19 in a rheumatic patient has been reported with a high rate of acute respiratory distress syndrome (ARDS) and high mortality rate. [8] This should alarm rheumatologists to be more alert regarding COVID-19.

There can be a potential chance of serious infections in diseases like connective tissue diseases (CTD), systemic lupus erythematosus (SLE), scleroderma, vasculitis, polymyositis, CTD related interstitial lung disease (ILD), rheumatoid arthritis (RA) related ILD, etc. receiving anti-rheumatic agents like conventional disease-modifying drugs (csDMARDs), mycophenolate mofetil, Janus kinase(JAK) inhibitors, biological agents and glucocorticoids. [9, 13] Majority of our participants have autoimmune rheumatic disease requiring some form of immunosuppression (56.9 %) with others either not sure of their diagnosis; fibromyalgia, gout and degenerative diseases. We did not assess the exact number of patients on immunosuppressive drugs and the degree of immunosuppression as most of the patients from Nepal are unlikely to know the exact names and dosing of the medications. British Society for Rheumatology (BSR) has described risk stratification based on immunosuppressant given to the patients. Patients under immunosuppressive medications excluding hydroxychloroquine and sulphasalazine should self-isolate or maintain social distance.[13] Many patients are on steroids or more than one of these drugs thus increasing the overall risk of contracting COVID-19. They also recommend against withdrawal or dose reduction of ongoing DMARDs because the resulting flare might increase the need for steroid administration further increasing the risk of infection. In our study, maximum patients were not sure if they were at an increased risk for COVID-19 infection due to their disease condition or due to the medication they were taking. Some assumed that the chance of getting infected is more if they are under immunosuppressant due to their ongoing medications and a proportionate number of patients had reduced the dosage by self. Few patients (4.2 %) had stopped their ongoing medications.

Some commonly used drugs in rheumatology like hydroxychloroquine might have some role in inhibition of SARS-CoV-19 by interfering with the glycosylation of cellular receptors and increasing endosomal pH required for viral fusion. [14] Thus, has been recommended for prophylaxis and treatment of COVID-19 infection. This might lead to a false sense of security and irresponsible high-
risk practice amongst patients taking these medications. In contrast to our expectations, only 13.7% of patients considered themselves to have a protective effect with their medications while 86.3% denied or were unsure of this theory. Along with hydroxychloroquine, some studies showed medications like JAK inhibitors, IL-1 inhibitors, IL-6 inhibitors, and some intravenous immunoglobulins might have some protective actions in COVID-19 infection. [15]

Routine vaccination against pneumonia and flu is recommended before initiation of any DMARDs. However, in low-middle income countries like Nepal, this practice is seldom followed. As there was an increasing trend of self-seeking for a flu vaccination during the swine and bird-flu epidemics, we also surveyed a change in this practice in our patients after the COVID-19 pandemic. The majority (96.9%) however denied changing their behavior regarding vaccination practice. The participants, as shown by the results in the knowledge domain of the survey, were aware of the disease. However, results also showed that they were unsure specifically when the relationship between susceptibility to COVID-19 and their disease or anti-rheumatic drugs were considered.

Nepal being in stage 2 of the COVID-19 epidemic, the knowledge regarding the general symptoms, transmission and preventive measures in patients with rheumatic disease should be considered acceptable. This unexpected level of awareness without any formal educational programs could be attributed to the access to information via internet and social-media. This might also translate to a potential participation bias where patients with access to internet would have participated more in the online survey. However, in the current scenario of strict social-distancing, authors believe that this was the best method available to understand the patient perceptions.

Currently, the actual disease manifestations and the outcomes in COVID-19 infected cases remains unclear. Thus, to fill this vacant space with accurate information the rheumatologist, researchers, and patients worldwide came together to form an alliance, the COVID-19 Global Alliance. The alliance in association with Asia Pacific League of Associations for Rheumatology (APLAR) has started a survey for patients to acquire insight about the ways to prevent or treat COVID-19 in the potentially vulnerable population. This survey is one of the first type of KAP conducted in Nepal among rheumatic patients regarding COVID-19. As the relationship between disease susceptibility and severity in
patients on anti-rheumatic drugs become clearer, it seems prudent that the patients are updated by the clinicians and societies regarding the preventive measures frequently to improve the outcomes.

Conclusion
Patients with rheumatic diseases were aware of the general clinical features, route of transmission and general preventive measures regarding COVID-19. However, there was a significant lack of knowledge regarding the susceptibility stratification and recommendations for prevention amongst those using DMARDs.

Limitations of the study
This survey was performed on an online web-based platform which might lead to participation bias as patients with no access to internet could not participate in the survey. Also, selection was randomized based on registration number and thus did not only include patients on immunosuppressant.

Declarations
Funding: None
Conflict of interest: None
Ethical consideration: Each participant was informed via SMS that clicking the link would mean implied consent for the study. Ethical clearance was obtained from review board of NCRD.
Consent for publication: All the authors have given the consent for publication of the research article.
Data availability: The corresponding author hold the right to supply data on special request.
Code availability: N/A
Authors’ contribution: The corresponding author Dr Binit Vaidya has significant contribution in conceptualization, methodology, manuscript writing and editing, data interpretation and supervision. All the co-authors have contributed significantly in record keeping, data collection, data analysis and interpretation, manuscript writing and editing.

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Tables
Tables no 1: Demographic status of the participants (n=380)
| Variables        | Sub division | Percentage (%) | Frequency |
|------------------|--------------|----------------|-----------|
| Gender           | Male         | 36.8           | 140       |
|                  | Female       | 63.2           | 240       |
| Age (years)      | 18-29        | 42.1           | 160       |
|                  | 30-39        | 23.2           | 88        |
|                  | 40-49        | 13.7           | 52        |
|                  | 50-59        | 15.8           | 60        |
|                  | 60-69        | 0.2            | 16        |
|                  | 70 or more   | 1.0            | 4         |
| Education        | SEE          | 15.7           | 60        |
|                  | Intermediate | 23.2           | 88        |
|                  | Bachelors    | 35.7           | 136       |
|                  | Masters      | 25.2           | 96        |
| Occupation       | Unemployed   | 4.3            | 16        |
|                  | Housemaker   | 37.8           | 144       |
|                  | Student      | 20.0           | 76        |
|                  | Physical labor| 6.3           | 24        |
|                  | Mental labor | 31.6           | 120       |
| Address          | Urban        | 80.0           | 304       |
|                  | Rural        | 20.0           | 76        |
| Diagnosis        | RA           | 27.4           | 104       |
|                  | SLE          | 18.9           | 72        |
|                  | FMS          | 3.2            | 12        |
|                  | OA           | 7.3            | 28        |
|                  | SPA          | 10.6           | 40        |
|                  | Gout         | 4.3            | 16        |
|                  | Arthritis (name not known) | 11.6 | 44 |
|                  | Not sure     | 7.3            | 28        |
|                  | Others       | 9.4            | 36        |

Abbreviation: SEE: Secondary education examination; RA: Rheumatoid arthritis; SLE: Systemic lupus erythematosus; FMS: Fibromyalgia; OA: Osteoarthritis; SPA: Spondyloarthritis.

Table no 2: Knowledge regarding COVID-19 among participants (n=380)
| S.N | Questions                                                                 | Responses | Percentage (%) | Frequency |
|-----|---------------------------------------------------------------------------|-----------|----------------|-----------|
| 1   | The main clinical symptoms of COVID-19 are fever, fatigue, dry cough, and myalgia. | Yes       | 91.6           | 3         |
|     |                                                                           | No        | 2.1            | 8         |
|     |                                                                           | Not sure  | 6.3            | 2         |
| 2   | Unlike the common cold, stuffy nose, runny nose, and sneezing are less common in persons infected with the COVID-19 | Yes       | 48.4           | 1         |
|     |                                                                           | No        | 31.6           | 1         |
|     |                                                                           | Not sure  | 20.0           | 7         |
| 3   | There currently is no effective cure for COVID-19, but early symptomatic and supportive treatment can help most patients recover from the infection | Yes       | 93.7           | 3         |
|     |                                                                           | No        | 1.0            | 4         |
|     |                                                                           | Not sure  | 5.3            | 2         |
| 4   | Not all persons with COVID-19 will develop to severe cases. Only those who are elderly, have chronic illnesses, and are obese are likely to have severe disease | Yes       | 70.6           | 2         |
|     |                                                                           | No        | 15.8           | 6         |
|     |                                                                           | Not sure  | 13.6           | 5         |
| 5   | Eating non-veg or contacting animals would result in the infection by the COVID-19 virus | Yes       | 16.9           | 6         |
|     |                                                                           | No        | 44.2           | 1         |
|     |                                                                           | Not sure  | 38.9           | 1         |
| 6   | Persons with COVID-19 cannot infect the virus to others when a fever is not present | Yes       | 4.2            | 1         |
|     |                                                                           | No        | 84.2           | 3         |
|     |                                                                           | Not sure  | 11.6           | 4         |
| 7   | The COVID-19 virus spreads via respiratory droplets of infected individuals | Yes       | 92.6           | 3         |
|     |                                                                           | No        | 4.2            | 1         |
|     |                                                                           | Not sure  | 3.2            | 1         |
| 8   | Ordinary residents can wear general medical masks to prevent the infection by the COVID-19 virus. | Yes       | 74.8           | 2         |
|     |                                                                           | No        | 15.7           | 6         |
|     |                                                                           | Not sure  | 9.5            | 3         |
| 9   | It is not necessary for children and young adults to take measures to prevent the infection by the COVID-19 virus | Yes       | 9.4            | 3         |
|     |                                                                           | No        | 89.5           | 3         |
|     |                                                                           | Not sure  | 1.1            | 4         |
| 10  | To prevent the infection by COVID-19, individuals should avoid going to crowded places such as gym, theaters and avoid taking public transportations | Yes       | 97.8           | 3         |
|     |                                                                           | No        | 1.1            | 4         |
|     |                                                                           | Not sure  | 1.1            | 4         |
| 11  | Isolation and treatment of people who are infected with the COVID-19 virus are effective ways to reduce the spread of the virus | Yes       | 96.8           | 3         |
|     |                                                                           | No        | 2.1            | 8         |
|     |                                                                           | Not sure  | 1.1            | 4         |
| 12  | Contact persons should isolate for 14 days                                | Yes       | 95.8           | 3         |
|     |                                                                           | No        | 1.1            | 4         |
|     |                                                                           | Not sure  | 3.1            | 1         |

Table no 3: Attitude towards COVID-19 among patients (n=380)
| S.N | Questions                                                                 | Responses | Percentage (%) | Fr |
|-----|---------------------------------------------------------------------------|-----------|----------------|----|
| 1   | Do you agree that COVID-19 will finally be successfully controlled?       | Yes       | 71.5           | 2  |
|     |                                                                           | No        | 6.3            | 2  |
|     |                                                                           | Not sure  | 22.2           | 8  |
| 2   | Do you think that you have more chances of getting the infection because of your rheumatic disease? | Yes       | 31.5           | 1  |
|     |                                                                           | No        | 27.3           | 1  |
|     |                                                                           | Not sure  | 46.3           | 1  |
| 3   | Do you think that you have more chances of getting the infection because of your medicines? | Yes       | 18.9           | 7  |
|     |                                                                           | No        | 41.1           | 1  |
|     |                                                                           | Not sure  | 40.0           | 1  |
| 4   | Do you think that medicines you are taking have protective effect against COVID-19? | Yes       | 13.7           | 5  |
|     |                                                                           | No        | 38.9           | 1  |
|     |                                                                           | Not sure  | 47.4           | 1  |
| 5   | Do you think that vaccination against flu or pneumonia can have protective effect against COVID19 for you? | Yes       | 13.6           | 5  |
|     |                                                                           | No        | 49.5           | 1  |
|     |                                                                           | Not sure  | 36.9           | 1  |

Table no 4: Practice and behaviors of participants towards COVID-19 (n=380)

| S.N | Questions                                                                 | Responses | Percentage (%) | Fr |
|-----|---------------------------------------------------------------------------|-----------|----------------|----|
| 1   | In recent days, have you worn a mask when leaving home?                   | Yes       | 94.7           | 3( |
|     |                                                                           | No        | 5.3            | 2( |
| 2   | In recent days, have you gone to any crowded place?                      | Yes       | 2.1            | 8  |
|     |                                                                           | No        | 97.9           | 3( |
| 3   | Have you reduced the dose of medicine you are taking?                    | Yes       | 13.6           | 5( |
|     |                                                                           | No        | 86.4           | 3( |
| 4   | Have you stopped any medicines you are taking fearing the risk of infection with COVID-19? | Yes       | 4.2            | 1( |
|     |                                                                           | No        | 95.8           | 3( |
| 5   | Have you discontinued any medicine because of lack of availability?      | Yes       | 8.4            | 3( |
|     |                                                                           | No        | 91.6           | 3( |
| 6   | Have you taken vaccination for flu or pneumonia with fear of COVID19?    | Yes       | 3.1            | 1( |
|     |                                                                           | No        | 96.9           | 3( |