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The prevalence of self-quarantine for preventing COVID-19 involvement in patients with rheumatoid arthritis who used classic disease-modifying anti-rheumatic drugs

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Key point

This is a descriptive study that was performed on patients with rheumatoid arthritis (RA) were treated with disease-modifying anti rheumatic drugs (DMARDs) to assess prevalence of self-quarantine for preventing COVID-19 involvement. It was observed that self-quarantine lowered the risk of COVID-19 by around 60%.

Abstract

Introduction: Rheumatoid Arthritis (RA) is an autoimmune disorder that is treated with classic Disease-Modifying Anti Rheumatic Drugs (DMARDs), which impair the immune system. It seems that self-quarantine is a good method for COVID-19 prevention in patients with RA.

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Objectives: The aim of this study was to assess the prevalence of self-quarantine for preventing COVID-19 involvement in patients with rheumatoid arthritis who administered disease-modifying anti-rheumatic drugs

Patients and Methods: This descriptive study was conducted in Loghman-Hakim hospital (Tehran, Iran). Patients with RA who took classic DMARDs and who referred to the hospital were assessed according to the age, gender, medications, smoking, history of COVID-19 in relatives, COVID-19 involvement in the patient, COVID-19 symptoms and observing self-quarantine.

Results: The mean age was 53.84 years old and 27.7% were male of one thousand patients with RA who took classic DMARDs. COVID-19 prevalence among these patients was 10.4%. The prevalence of COVID-19 was 21% among patients who did not observe self-quarantine and 9.2% among patients who observed self-quarantine. Self-quarantine lowered the risk of COVID-19 by around 60%.

Conclusion: Self-quarantine is a good method to reduce the prevalence of COVID-19 among RA patients who used classic DMARDs.

Keywords: self-quarantine, quarantine, COVID-19, Rheumatoid arthritis

Introduction

The Coronavirus disease (COVID-19) epidemic occurred in 2019, starting in Wuhan, China, and then it is spread around the world. The first known case of coronavirus was reported on December 29, 2019. Many countries in the world became infected with this virus, such as China, Iran, Korea, the United States and India, and also other parts of the world (1-3). COVID-19 is a virus that attacks the respiratory system and causes a variety of symptoms, from the common cold or flu to acute respiratory distress syndrome (ARDS). These symptoms include fever, cough, body aches, shortness of breath, and other symptoms, since CT scan (computerized tomography) typically reveals a bilateral ground glass consolidation. It is more dangerous in people with co-morbidities and causes high mortality, including heart disorders, lung diseases, and immunodeficiency conditions such as using drugs that decrease the immune system potency, organ transplants and diabetes. Additionally, the age over 65 years have been detected as a risk factor for COVID-19. There are some complications that may occur following this disease such as ARDS, anemia, and secondary infection. People with rheumatic disorders, such as rheumatoid arthritis, need special attention for severe acute respiratory syndrome coronavirus 2 (SARS-COV-2), especially for inflammatory agents following coronavirus. Many of these people are at risk for serious infections due to their immune status and the drugs that act as the modulator of the immune system (4-9).

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The rapid and uncontrolled spread of this epidemic can clearly cause more concern in rheumatic patients because these patients are inherently at increased risk of infection due to their disease and the iatrogenic effects of immunosuppressive agents such as corticosteroids and classic disease modifying anti-rheumatic drug (DMARD) or biological DMARDs (10). Self-quarantine in these patients are very important (11). Since, patients with rheumatoid arthritis are exposed to COVID-19 involvement and they should respect to self-quarantine when their relatives become infected with COVID-19.

Based on our knowledge, there are few studies about the prevalence of self-quarantine on the prevention of COVID-19 in patients with RA.

Objectives

The aim of this study was evaluation of the prevalence of self-quarantine in patients with rheumatoid arthritis who administered “disease modifying anti-rheumatic drugs” to prevent patients from COVID-19 involvement.

Patients and Methods

Study design

This is a descriptive analytical study that was carried out on patients with RA who took classic DMARD and referred to loghman-hakim hospital (Tehran- Iran) from start of 2011 to the end of 2020. Of 1264 patients who referred to the rheumatology department of Loghman hospital, one thousand patients were entered to the study. Inclusion criteria were RA involvement, using classic disease-modifying anti rheumatic drugs including hydroxychloroquine, methotrexate, leflunomide, and sulfasalazine, , patients who referred to the hospital from the start of 2011 to the end of 2020, and age greater than 18 years old. Exclusion criteria were taking biological DMARDs, having other rheumatologic diseases, death due to any reasons except COVID-19.

RA was diagnosed based on ACR criteria (1987) for all patients according to clinical data. Data of patients with RA who used classical DMARDs were extracted and the patients were contacted by phone. Study process was explained to the patients and verbal consent to participate in the study was obtained from each patient. Demographic data, drugs, smoking, COVID-19 involvement in the relatives, history of COVID-19 in the patient, Covid-19 symptoms (dry cough, shortness of

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breath, fever, headache, sore throat, dysgeusia, anosmia, headache, muscle pain, fatigue, chest pain, abdominal pain, diarrhea, nausea, and vomiting) were asked and were recorded. We asked about the diagnostic methods for COVID-19 that were conducted for patients including polymerase chain reaction (PCR) of nasal swab specimen, immunoglobulin test (IgG and IgM), and pulmonary CT scan (computerized tomography). If the patient had not performed any diagnostic test, he/she was invited to our hospital for conducting a serological test (IgG and IgM), nasal swab PCR, and lung CT scan. Finally, patients were asked about observing self-quarantine. All data were recorded and analyzed.

Statistical analysis

Quantitative data were displayed using mean and standard deviation. In addition, qualitative data were displayed using frequency and percentage. Independent T-test and chi-square test were employed to analyze the data. If necessary, the p-value of fisher's exact test was reported. Univariate logistic regression was used to estimate the odds ratio of COVID-19. Besides, the upset plot was used to show the symptoms of patients with COVID-19. The significance level was considered 0.05 for statistical tests. SPSS statistical software version 20 and R version 3.6.1 were used for data analysis.

Results

In the current study, 1000 patients with RA who used classic DMARDs were evaluated. The mean and standard deviation of age were 53.84 ± 13.51 years in all patients. The lowest age was 19 years old, and the highest age was 84 years old. Two hundred and twenty-seven patients (27.7%) were male and 723 (72.3%) were female. Forty-two patients (4.2%) were smoker.

In terms of symptoms, 11.3% of patients had at least a symptom of COVID-19 (113 patients). The diagnosis of COVID-19 was confirmed among 104 patients and the diagnostic tests of nine others were negative. COVID-19 prevalence between the patients with RA was 10.4%. The confirmed diagnosis was conducted by blood serology test in forty-eight patients, 31 patients with CT scan, and 25 patients with PCR from nasal swab specimen. About the different types of COVID-19

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symptoms, 63.5% of patients (66 patients) had a fever, 51.9% had a cough (54 patients), 49% had body aches (51 patients), 43.3% had shortness of breath (45 patients), 25% had sore throat (26 patients), 32.7% had headache (34 patients), 19.2% had anorexia (20 patients), 38.5% had diarrhea (40 patients), 25% had vomiting (26 patients), and 25% had dysgeusia and anosmia (26 patients).

The prevalence of COVID-19 symptoms in these patients is seen in Figure 1.

The mean age of RA patients who involved with Covid-19 was 52.64 years with a standard deviation of 12.82 years, and the mean age of RA patients without COVID-19 was 53.98 years with a standard deviation of 13.58 years. There were no statistically significant differences in term of age, gender, and smoke in patients with COVID-19 the prevalence in patients with RA (all P-values > 0.05).

One hundred patients reported that they did not observe self-quarantine and other patients observed self-quarantine. The mean age of patients who did not observe self-quarantine was 51.99 years old and the standard deviation was 16.49 years. The mean age of patients who observed self-quarantine was 54.05 years old and the standard deviation was 13.13 years. There was no significant difference between the mean age of patients about observing self-quarantine ($p = 0.148$). Of patients who did not observe self-quarantine, 9.8% (71 patients) were women and 10.5% (29 patients) were men. The gender proportion of patients who did not observe self-quarantine was not statistically significant ($p = 0.759$).

The prevalence of COVID-19 was 21% among patients who did not observe self-quarantine and 9.2% among patients who observed self-quarantine ($p < 0.001$). Quarantine decreased the risk of COVID-19 by 62% in patients with RA (OR = 0.382; 95% CI (0.225 - 0.650)). In all patients with RA, 7.5% had a history of COVID-19 in their relatives. The prevalence of COVID-19 in patients who did not have a positive relatives for COVID-19 was 6.3%. This value was 61.3% in patients who had a positive relative infection for COVID-19. The risk of COVID-19 involvement was 23.71 fold higher in RA patients who had COVID-19 positive relatives (OR = 23.71; 95% CI (13.88 - 40.50); $p < 0.001$; Figure2)

We also evaluated the prevalence of underlying disorders in the patients. The prevalence of Covid-19 among patients with underlying disease was 10.1% and in other patients was 10.9%. Our study showed no statistically significant difference in the prevalence of patients with underlying disease

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(OR = 0.920; 95% CI (0.598 - 1.41); $p = 0.702$). The prevalence of COVID-19 among patients with cardiac disorders (22.6%) was statistically significantly higher than other patients (9.3%) (OR = 2.86; 95% CI (1.64 - 4.99); $p < 0.001$). Underlying diseases (except cardiac disorder) did not increase the risk of developing COVID-19 among patients ($p > 0.05$; Table 1).

Discussion

This study aimed to evaluate the prevalence of self-quarantine for preventing COVID-19 involvement in patients with rheumatoid arthritis who used disease-modifying anti-rheumatic Drugs. This goal is important since, in our experience, these patients believe they are at higher risk than the general population for COVID-19 involvement.

"Quarantine of people" is defined by the World Health Organization as "the limitation of activities or separation of people who are not ill but may have been exposed to an infectious agent or illness, with the primary goal of observing symptoms and detecting cases immediately." Isolation, on the other hand, is the separation of sick or diseased people from others in order to prevent infection or contamination from spreading (12). The term "quarantine" actually refers to selective self-quarantine or quarantine of people suspected of being carriers of the infectious disease; however, a new term "mass quarantine" is gaining traction nowadays, which primarily refers to the government's enforced quarantine of a population to prevent the spread of a disease outbreak (13). The major goal of self-quarantine is to prevent disease spreading between people (14). A previous study mentioned that quarantine makes non-exposed persons are kept with those who are sick for unspecified period of time during an area-wide quarantine (15). In the current study, it was observed that in RA patients who did not observe self-quarantine, the prevalence of COVID-19 was significantly higher. We observed patients who observed self-quarantine had lower rate of COVID-19 involvement. Our finding was in contrast with Petersen et al study while our study showed the self-quarantine reduces the prevalence of COVID-19 in patients with RA (15).

In a study conducted by Almaghrabi et al, detected that general population had a good awareness about quarantine. They also mentioned that quarantine in the current pandemic period should be applied by people and government. This finding can confirm our finding about self-quarantine too. General population in Saudi Arabia believe that quarantine has a good effect on the prevention COVID-19 infection. We also found that self-quarantine by RA patients reduced the prevalence

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of COVID-19 infection (16). It seems that giving training and acceptance of self-quarantine is good method for reducing COVID-19 prevalence in general population and even in at risk population.

Malheiro et al to evaluate the effectiveness of contact tracing and quarantine on reducing COVID-19 transmission, found that quarantine had an positive effect on reducing COVID-19 prevalence (17). The finding of this study was similar to the current study. We found that self-quarantine can significantly reduce the prevalence of COVID-19.

In the present study, we found that the prevalence of COVID-19 was 10.4% in patients who had rheumatoid arthritis. Fredi et al detected that, the prevalence of COVID-19 was about 8% in patients with rheumatic disorder which is similar to our study, approximately. The difference among the two studies was due to the study population. Since Fredi et al study was conducted on patients with rheumatic and musculoskeletal disorders, while we studied patients with RA (18).

In a study on 320 patients with rheumatologic disorders, Monti et al observed that four patients involved with COVID-19 as detected by rhinopharyngeal swabs, while another four patients were highly suggestive for Covid-19 but did not undergo a swab or any other diagnostic test. They found the prevalence of COVID-19 was 2.5 percent of rheumatic patients. As the COVID-19 prevalence in our research was 10.4%, the study patients by Monti et al differs significantly with our findings, whereas the population was one of the differences between the two studies. Individuals with RA were studied in the current study however; Monti et al studied patients with rheumatic disorders. Our study comprised 1000 individuals, whereas the study by Monti et al covered 320 patients. Another difference between the two studies was the drugs administered to participants. In this study, all patients took classic DMARDs, whereas in the other study, patients received biologic, classic, and targeted synthetic DMARDs (19).

The prevalence of COVID-19 in rheumatic patients was 0.43 percent in the study by Zhong et al, which was significantly lower than the current study. Although Zhong et al, found a relationship between greater age and increased COVID-19 prevalence in rheumatic patients, we were unable to find this relationship in this study. As a result of our study, no significant relationship between age and COVID-19 prevalence in patients with RA was seen (20).

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The study by Michelena et al showed that the prevalence of COVID-19 was approximately 1.5 percent in patients with rheumatic disorders who were using biological DMARDs. Only patients who used biological DMARDs and targeted synthetic DMARDs were studied in this study, since our study evaluated patients who received classic DMARDs. Perhaps the difference in outcomes of these two studies is attributable to the various treatment approaches (21).

Furthermore, Pablos et al evaluated the prevalence of COVID-19 in rheumatic patients who had been hospitalized for their rheumatic diseases. In hospitalized rheumatic patients, the frequency of COVID-19 with positive PCR was found to be greater (1.32-fold). They performed a study on patients who were admitted to hospital since in the hospital the prevalence of COVID-19 is higher than general environment. The current study was conducted on RA patients who observed self-quarantine in their houses. Of these two studies, we can interpret that environment has a great role in prevalence of COVID-19 in patients with RA involvement. When patients are in-hospital, the prevalence of COVID-19 is high and when they observe the self-quarantine, the prevalence of COVID-19 is lower than when they have free relationship with their relatives (22).

Conclusion

The prevalence of COVID-19 in patients with RA who use classic DMARDs was shown to be unrelated to age, gender, or smoking in this study. In RA patients, self-quarantine reduces the risk of COVID-19 to about 62 percent. This data suggests that self-quarantine is an effective method for preventing COVID-19 infection. Patients with positive relatives for COVID-19 had a 10-fold higher prevalence of COVID-19 than those who did not have relatives with a positive COVID-19 infection. This research further demonstrates the need for self-quarantine in the prevention of this infection.

Limitations of the study

The reluctance of patients to participate in the study, as well as the incomplete information provided by some patients to contact them were two of the study's limitations.

Advantages

Of the advantages of this study was the number of studied population and assessment of the effect of self-quarantine in RA patients to reduce COVID-19 involvement.

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Authors' contribution

RA and SB were the principal investigators of the study. RA, SB, ME, FF and AR included in preparing the concept and design. RA and SB revisited the manuscript and critically evaluated the intellectual contents. All authors participated in preparing the final draft of the manuscript, revised the manuscript and critically evaluated the intellectual contents. All authors have read and approved the content of the manuscript and confirmed the accuracy or integrity of any part of the work.

Ethical issues

The research followed the tents of the Declaration of Helsinki. The research procedure was accepted by the ethical committee (IR.SBMU.MSP.REC.1399.329) of the Shahid Beheshti University of Medical Sciences. Verbal consent taken from all participants before completing the questionnaires and participating in the study. This study was extracted from M.D/MSc thesis of xxxxx at this university (Thesis#xxxxxx).

Conflicts of interest

The authors declare that they have no competing interests.

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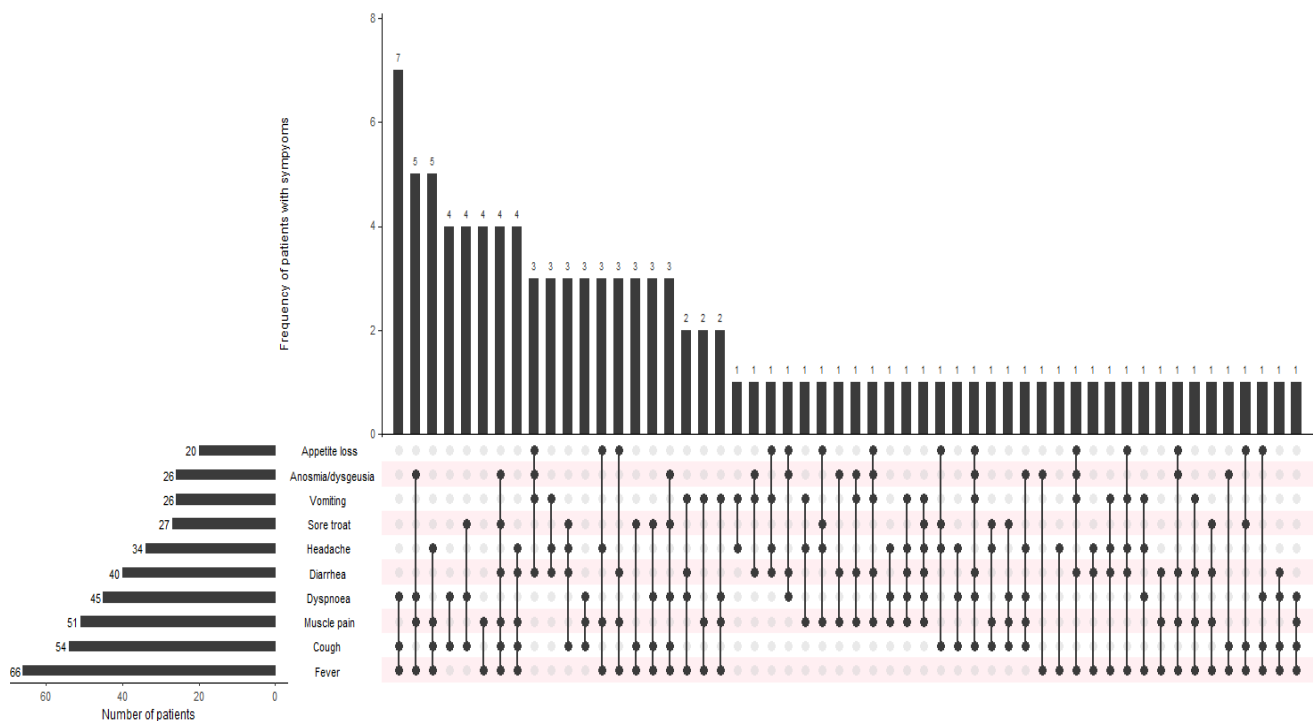


Figure 1. The upset diagram demonstrates symptoms in RA patients with COVID-19. Each vertical line at the end of the graph is related to the combination of observed complications between patients. Each circle on the vertical lines indicates the presence of a symptom in each person. Each vertical bar at the top of the figure shows the frequency of the number of patients

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by combination of the symptoms shown at the bottom. The frequency distribution of each symptom among patients is shown in the lower-left horizontal bars

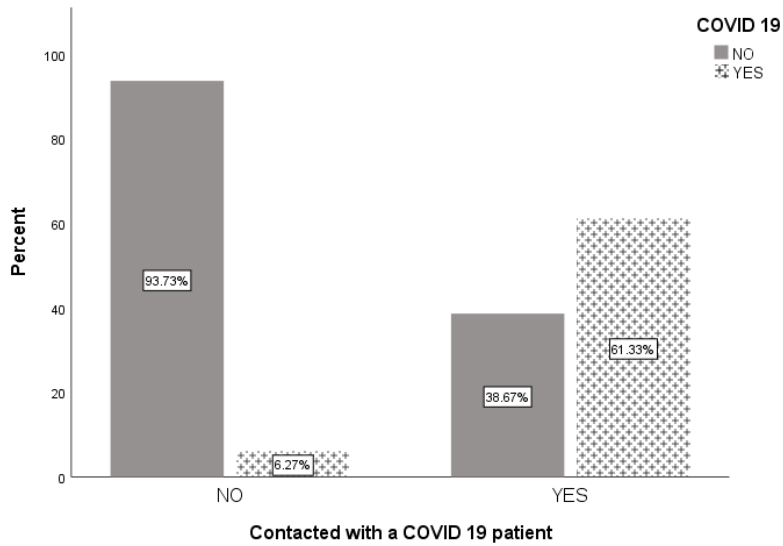


Figure2. Prevalence of COVID-19 in RA patients with a positive relative for COVID-19

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Table1. COVID-19 prevalence according to comorbidities in patients with RA

Comorbidity	total number	COVID-19 patients	COVID-19 prevalence	P-value	Odds ratio (95% confidence interval)
pulmonary disorders	467	56	12	0.123	(0.916-2.07)1.38
Hypertension	232	19	8/2	0.208	(0.426-1.21)0.717
Diabetes	105	9	8/6	0.516	(0.386-1.62)0.789
cardiac disorders	84	19	22/6	<0.001	(1.64-4.99)2.86
Hyperlipidemia	129	8	6/2	0.094	(0.253-1.13)0.534
hypothyroidism	129	9	7	0.172	(0.301-1.25)0.613
psychological disorders	16	0	0	0.397	-
Anemia	21	2	9/5	0.999	(0.208-3.94)0.905
Cancer	5	0	0	0.999	*-
other disorders	32	2	6/3	0.766	(0.133-2.40)0.566