



# COVID-19 Screening in Rheumatologic Diseases Cases; Special Look at Chloroquine Derivate Use

Soraya Shadmanfar<sup>1</sup>, Gholamhosein Alishiri<sup>2</sup>, Noushin Bayat<sup>3</sup>, Morteza Izadi<sup>1</sup>, Ahmad Salimzadeh<sup>4</sup>, Abdolrahman Rostamian<sup>5</sup>, Shahla Abolghasemi<sup>6</sup>, Mohammad Hossein Azimzadeh Ardebili<sup>7</sup>, Zeynab Rastgar Moqaddam<sup>8</sup>, Marjan Hasani<sup>7</sup>, Ehsan Rahmanian<sup>7</sup>, Helia Iranpanah<sup>9</sup>, Ghodrat Allah Islami<sup>7</sup>, Amin Saburi<sup>2\*</sup>

<sup>1</sup>Health Research Center, Life Style Institute, Baqiyatallah University of Medical Sciences, Tehran, Iran

<sup>2</sup>Chemical Injuries Research Center, Systems Biology and Poisonings Institute, Baqiyatallah University of Medical Sciences, Tehran, Iran

<sup>3</sup>Exercise Physiology Research Center, Life Style Institute, Baqiyatallah University of Medical Sciences, Tehran, Iran

<sup>4</sup>Sina Hospital, Rheumatology Research Center, Tehran University of Medical Sciences, Tehran, Iran

<sup>5</sup>Department of Rheumatology, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran

<sup>6</sup>Department of Rheumatology, Tehran Medical Sciences, Islamic Azad University, Tehran, Iran

<sup>7</sup>Student Research Committee, Baqiyatallah University of Medical Sciences, Tehran, Iran

<sup>8</sup>Iran University of Medical Science, Tehran, Iran

<sup>9</sup>Shahid Beheshti University of Medical Sciences, Tehran, Iran

\***Corresponding Author:** Amin Saburi, M.D., Chemical Injuries Research Center, Systems Biology and Poisonings Institute, Baqiyatallah University of Medical Sciences, Mollasadra St, Vanak Sq, Tehran, Iran. Tel: +98- 9127376851, Email: aminsaburi@yahoo.com

Received September 29, 2021; Accepted November 27, 2021; Online Published December 15, 2021

## Abstract

**Background:** Among suggested medications for the treatment of COVID-19, chloroquine derivatives and angiotensin-converting-enzyme inhibitors (ACEIs)/angiotensin II type 1 receptor blockers (ARBs) are the two medications with conflicting effects on the development of the disease.

**Objectives:** The present study aimed to evaluate COVID-19 in patients with rheumatic diseases receiving chloroquine derivate.

**Methods:** Every patient with proven rheumatologic diseases registered in two referral centers in Tehran and Alborz, Iran was enrolled in the present descriptive cross-sectional study between May and June 2020. At first, the symptoms of COVID-19 were assessed, and if a case had suspicious symptoms, reverse transcription-polymerase chain reaction (RT-PCR) COVID-19 tests were done. Demographic and clinical data are documented for every patient. Then, the patients were grouped once according to their COVID-19 infection status and another time according to their hydroxychloroquine use.

**Results:** 1159 patients enrolled in the study with a mean age of 49.39 years. Frequency of hypertension was 22.17 %, diabetics (9.49%) and 20 (1.7%) patients were positive for COVID-19 testing. The most common symptoms of the COVID-19 positive cases were cough (5.2%) and fever (4%). There was no significant difference in receiving ACEIs/ARBs or other medications between COVID-19 positive or negative patients. Among the patients receiving hydroxychloroquine, 15 patients (1.7%) had proved COVID-19 versus 5 patients (1.7%) who were not receiving these medications ( $P>0.999$ ).

**Conclusion:** The present study demonstrated that receiving ARBs or ACEIs was not different among patients with or without COVID-19. Moreover, receiving chloroquine derivate was not related to the development of COVID-19 in patients with rheumatologic disorders.

**Keywords:** Angiotensin-Converting Enzyme Inhibitors, Angiotensin II Type 1 Receptor Blockers, Chloroquine, Hydroxychloroquine, COVID-19

## 1. Background

In late 2019, a novel coronavirus infection was reported from China and spread shortly through the entire world. The World Health Organization (WHO) declared the novel coronavirus diseases (COVID-19) outbreak as a global emergency in mid-March 2020.<sup>1,2</sup> As the number of infected cases began to rise around the globe, every research center dealing with COVID-19 patients started

publishing about the characteristics of their infected cases and their management strategies. Almost every study about the COVID-19 demonstrated that close contact with confirmed cases or traveling history to areas with a high rate of confirmed cases are the main risk factors for becoming infected.<sup>3</sup>

Those who become infected may develop a wide range of symptoms with variable severity ranging from

mild symptomatic presentations to severe or even a lethal disorder.<sup>4,5</sup> The most common symptoms of the COVID-19 patients reported being similar to other viral respiratory tract infections, including fever, dry cough, and dyspnea.<sup>3,6,7</sup> However, some other specific symptoms, including loss of the sense of taste and smell, added to the common respiratory symptoms making the diagnosis more specific.<sup>8-10</sup> Some studies demonstrated specific factors as risk factors of developing COVID-19. These main risk factors include male gender, smoking, age over 65 years, and previous history of respiratory disease, malignancies, and cardiovascular diseases are considered factors that worsen the prognosis of COVID-19.<sup>9,11</sup> Regardless of the clinical presentations and risk factors of COVID-19, the main challenging issue behind the novel coronavirus infection is the treatment strategy.<sup>12</sup>

There are many conflicts in using various medications in COVID-19 cases, and it seems that an effective vaccine may be more helpful than routine medications.<sup>13</sup> During the early stage of the COVID-19 pandemic, some studies suggested that an antimalarial drug might prevent COVID-19 or even treat the patients alone or in combination with other drugs.<sup>14</sup> The chloroquine and hydroxychloroquine are the two antimalarial drugs that have antiviral and immunomodulatory effects.<sup>15</sup> While there are not enough studies with robust clinical methodology available for the effectiveness of these drugs in the treatment of COVID-19, early studies demonstrated that using these drugs in combination with antibiotics including azithromycin might be beneficial in treating COVID-19.<sup>16</sup> Similar to every other pharmaceutical therapy, these drugs also have a specific side effect that is mainly cardiac toxicity.<sup>17</sup> The angiotensin-converting enzyme 2 (ACE2) is a cellular receptor expressed on many cells, including respiratory systems cells.<sup>18</sup> These receptors are used as functional receptors by coronavirus for cellular entrance.<sup>19</sup> Angiotensin-converting-enzyme inhibitors (ACEIs) are considered common antihypertensive drugs used in many diseases, including hypertension, heart failure, and kidney diseases.<sup>20</sup>

## 2. Objectives

Moreover, recent evidence suggested that even using chloroquine or hydroxychloroquine might be harmful to hospitalized COVID-19 patients.<sup>21</sup> While the COVID-19 is still a global concern and also there are some worries about the second waves of the disease soon, studying the effect of chloroquine and hydroxychloroquine in those patients who are receiving these medications as their daily therapeutic regimens for other chronic diseases may provide valuable information within the shortest time.<sup>22,23</sup> There is no general agreement between ACEI use and the development or severity of COVID-19.<sup>20</sup> Recent human studies indicated that using ACEIs or ARBs may not increase ACE2 expression. Therefore, using these drugs during COVID-19 would be safe.<sup>24</sup> While these drugs are considered routine medications in patients with

rheumatologic disorders. Therefore, current study aimed to evaluate the COVID-19 in patients receiving antimalarial drugs as their therapeutic regimen.

## 3. Methods

### 3.1. Study Design

The descriptive present cross-sectional study took place in two referral centers in Tehran and Alborz, Iran. Data collected was performed during a month starting from 2 May 2020.

### 3.2. Study Subjects

The sampling frame of the current study were patients with documented rheumatologic diseases, including SLE, Rheumatoid arthritis, and other related rheumatic disorders. Patient selection was based on census sampling. As this study aimed to obtain a holistic view of the condition, all patients with the documented diagnosis of rheumatoid diseases were included in the study with no exclusion criteria. Those patients who agreed to participate asked about any flu-like or COVID-19 symptoms, and if everyone had suspicious symptoms, filled an informed consent form and tested for COVID-19 by reverse transcription-polymerase chain reaction (RT-PCR) method.

### 3.3. Measurements

The COVID-19 sampling was performed from the nasopharynx and oropharynx, and the RT-PCR kit (manufactured by Pishtaz Teb, Tehran) was used. Then, every patient received a questionnaire of demographic and medical data. The medical data consisted of any medical comorbidities, medication history, signs and symptoms of COVID-19, and risk factors of developing the disease, including close contact with family members who had COVID-19, using public transport services, and participation in any indoor meeting. Then, patients were grouped once according to COVID-19 infection status, another time according to their chloroquine or hydroxychloroquine use before acquiring the disease of COVID-19 pandemic. Although these two medications are among the routine medications in patients with rheumatoid arthritis, there are cases where these medications have been stopped due to side effects or contraindications. The differences between study groups were analyzed by SPSS software (version 20), and *P* value >0.05 was considered statistically significant.

### 3.4. Statistical Analysis

Descriptive statistics were presented using mean and standard deviation for continuous variables and frequency and percentage for categorical variables. Comparison of the mean values for the continuous variable (age) between groups was performed using the independent student *t*-test. The relationship between categorical variables and the study outcomes (COVID-19 incidence and history for medication usage) was evaluated using the chi-square or Fisher exact tests. Data analysis was performed using

the statistical package for social sciences (SPSS) software version 16 (IBM Inc. Chicago, IL, USA). The level of statistical significance was considered as  $P < 0.05$ .

#### 4. Results

The total number of 1159 subjects enrolled in the present study. Most of the patients were female (81.6%). The mean age of the study subjects was  $49.39 \pm 0.41$  years old. The Demographic, medical history, and clinical characteristics of the study subjects are presented in Table 1.

Twenty (1.7%) out of 1159 patients were positive for COVID-19 testing. The most common symptoms of the study population were cough (5.2%) and fever (4%). The most common medication used among the study population was prednisolone (70.29%) and vitamin D supplementation (57.81%).

A total of 868 (74.9%) of the subjects used hydroxychloroquine. The relationship between study variables and drug usage is presented in Table 1. There was no significant relationship between hydroxychloroquine use and the incidence of COVID-19 ( $P > 0.999$ ).

The relationship between study variables and the incidence of COVID-19 is presented in Table 2. Table 2 showed that none of the study variables were significantly related to the incidence of COVID-19. Therefore, no further adjustment was made for possible confounders.

#### 5. Discussion

The present study demonstrated that among our study population with rheumatologic disorders, only 1.7% had COVID-19. Moreover, our result showed that there is not any significant relation between receiving hydroxychloroquine and the development of COVID-19.

After the rapid spread of COVID-19 around the world since late 2019, the central management of COVID-19 patients is mainly supportive care. Patients with mild symptoms can be managed by self-isolation and home care, including using analgesics, antipyretics, and adequate hydration.<sup>4</sup> Patients with more severe presentations may require hospital admission and close monitoring of vital signs. These patients are at increased risk of developing respiratory insufficiency and benefit from oxygen support.<sup>5</sup> Alongside the supportive treatment, researchers are searching for a treatment regimen for COVID-19. Antimalarial medication has been among the available treatment regimens among well-known candidate drugs with various beneficial effects in treating diseases since decades ago.<sup>21</sup> Chloroquine or hydroxychloroquine are antimalarial drugs used to treat chronic diseases, especially autoimmune diseases, including lupus and rheumatoid arthritis.<sup>22</sup> These drugs are thought to inhibit virus fusion with host cells and inhibit nucleic acid replication in host cells.<sup>25</sup> During the early days of the outbreak, multicenter clinical trials from China demonstrated the safety of using chloroquine phosphate in managing COVID-19 pneumonia.<sup>26</sup> Earliest reports revealed that more than 100 patients benefited from this drug in managing inhibiting

pneumonia exacerbation and shortening of the disease course without any significant side effects.<sup>26</sup>

Since then, some expert consensus in different countries, including China, Italy, and Germany, suggested using Chloroquine derivatives for patients with different grades of severity.<sup>27</sup> The most recent systematic review on the effectiveness of chloroquine or hydroxychloroquine evaluating seven completed clinical trials demonstrated that using these drugs is superior to supportive care or using Ritonavir/Lopinavir in COVID-19 patients.<sup>26</sup> However, the authors stated that these studies had a considerable risk for bias and methodological shortcomings.<sup>28</sup> Therefore, the authors suggested that considering a therapeutic use of these drugs in daily practice should be made with caution until the ongoing trials become complete.<sup>28</sup> Since then, some studies demonstrated the other side of the coin for using chloroquine or hydroxychloroquine in COVID-19 patients. Boulware et al reported that using hydroxychloroquine after moderate to high-risk exposure with COVID-19 patients might not prevent the illness.<sup>29</sup> Using hydroxychloroquine as a post-exposure medication within the first four days of exposure did not prevent disease development.<sup>29</sup> Another study by Mehra et al evaluated the effect of chloroquine or hydroxychloroquine in hospitalized COVID-19 patients.<sup>30</sup> They demonstrated that using these antimalarial drugs with or without macrolide would not be beneficial.<sup>30</sup>

Their study showed that using these drugs might be associated with cardiac toxicity.<sup>30</sup> The concern about using chloroquine derivate became more evident after this large-scale study demonstrating increased mortality and arrhythmias, and soon, WHO halted testing for hydroxychloroquine in COVID-19 patients.<sup>31</sup> It is noteworthy that according to our results and the studies similar to Mehra et al study, we might conclude that using 4-aminoquinolines may be a double edge sword in COVID-19 patients. It is still unclear that whether the immunomodulatory and antiviral effect of 4-aminoquinolines worsen the severity of COVID-19 in some patients with previous myocardial injuries that thought to be a common problem in COVID-19 patients.<sup>32</sup> Even more, using other drug agents, including azithromycin that has sodium channel blocking effects may worsen the adverse effects of chloroquine or hydroxychloroquine on cardiovascular system.<sup>33,34</sup>

Similar to using chloroquine derivate in COVID-19 patients, using ACEIs during COVID-19 is a conflicting issue. Our study revealed that using ACEI or ARBs is not related to COVID-19. Mancina et al demonstrated that as cardiovascular diseases are more prevalent in COVID-19 patients, these patients are more commonly using ACEI.<sup>20</sup> However, they reported that there is no link between using these antihypertensive agents and development of COVID-19.<sup>20</sup> Later studies demonstrated that using ACEI may increase the T lymphocyte counts and decrease viral load peak in comparison with other antihypertensive drugs.<sup>35</sup> Meng et al demonstrated that using ACEI or

**Table 1.** Characteristics of Study Population Based on Receiving Chloroquine Derivate

Item		Hydroxychloroquine (Yes) (n=868)	Hydroxychloroquine (No) (n=291)	Total (n=1159)	P Value
<b>Demographical Variable</b>					
Gender	Male	129 (14.9)	84 (28.9)	213 (18.4)	<0.001 <sup>a</sup>
	Female	739 (85.1)	207 (71.1)	946 (81.6)	
	Age*	49.22 (±0.47)	49.93 (±0.82)	49.39 (±0.41)	0.452 <sup>c</sup>
Marriage	Single	58 (6.7)	22 (7.6)	80 (6.9)	0.595 <sup>a</sup>
	Married	810 (93.3)	269 (92.4)	1079 (93.1)	
Comorbidity	Hypertension	190 (21.89)	67 (23.02)	257 (22.17)	0.684 <sup>a</sup>
	Diabetes	79 (9.1)	31 (10.65)	110 (9.49)	0.421 <sup>a</sup>
	Cardiovascular disease	50 (5.76)	18 (6.19)	68 (5.87)	0.774 <sup>a</sup>
	Angiography	27 (3.11)	6 (2.06)	33 (2.85)	0.420 <sup>a</sup>
	Stenting	10 (1.15)	1 (0.34)	11 (0.95)	0.309 <sup>b</sup>
	CABG	7 (0.81)	3 (1.03)	10 (0.86)	0.718 <sup>b</sup>
	Cerebral infarction	8 (0.92)	1 (0.34)	9 (0.78)	0.464 <sup>b</sup>
	Lung disease	25 (2.88)	3 (1.03)	28 (2.42)	0.080 <sup>b</sup>
	Asthma	17 (1.96)	1 (0.34)	18 (1.55)	0.057 <sup>b</sup>
	COPD	1 (0.12)	0 (0)	1 (0.09)	>0.999 <sup>b</sup>
	Chemical veteran	7 (0.81)	0 (0)	7 (0.6)	0.202 <sup>b</sup>
	kidney disease	27 (3.11)	2 (0.69)	29 (2.5)	0.017 <sup>b</sup>
	Dialysis	1 (0.12)	0 (0)	1 (0.09)	>0.999 <sup>b</sup>
	Kidney transplant	2 (0.23)	0 (0)	2 (0.17)	>0.999 <sup>b</sup>
Risk Factor	Participate in community meetings (yes)	43 (5)	16 (5.5)	59 (5.1)	0.758 <sup>a</sup>
	Use of public transport	34 (3.9)	11 (3.8)	45 (3.9)	>0.999 <sup>a</sup>
	COVID positive in family	9 (1)	2 (0.7)	11 (0.9)	0.740 <sup>b</sup>
	COVID positive (yes)	15 (1.7)	5 (1.7)	20 (1.7)	>0.999 <sup>a</sup>
Outcomes	Fever (yes)	34 (3.9)	12 (4.1)	46 (4)	0.863 <sup>a</sup>
	Cough (yes)	49 (5.6)	11 (3.8)	60 (5.2)	0.284 <sup>a</sup>
	Sputum (yes)	12 (1.4)	3 (1)	15 (1.3)	0.773 <sup>b</sup>
	Shortness of breath (yes)	29 (3.3)	7 (2.4)	36 (3.1)	0.558 <sup>a</sup>
	Chest pain (yes)	16 (1.8)	4 (1.4)	20 (1.7)	0.796 <sup>b</sup>
	Weakness and lethargy (yes)	23 (2.6)	5 (1.7)	28 (2.4)	0.509 <sup>a</sup>
	Muscular pain (yes)	28 (3.2)	5 (1.7)	33 (2.8)	0.224 <sup>a</sup>
	Runny nose (yes)	12 (1.4)	1 (0.3)	13 (1.1)	0.204 <sup>b</sup>
	Sore throat (yes)	27 (3.1)	5 (1.7)	32 (2.8)	0.300 <sup>a</sup>
	Vomiting nausea (yes)	4 (0.5)	4 (1.4)	8 (0.7)	0.115 <sup>b</sup>
Outcomes	Diarrhea (yes)	9 (1)	2 (0.7)	11 (0.9)	0.740 <sup>b</sup>
	Headache (yes)	25 (2.9)	0 (0)	25 (2.2)	0.002 <sup>b</sup>
	Dizziness (yes)	7 (0.8)	0 (0)	7 (0.6)	0.202 <sup>b</sup>
	Weight Loss (yes)	2 (0.2)	2 (0.7)	4 (0.3)	0.263 <sup>b</sup>
	Decreased appetite (yes)	4 (0.5)	1 (0.3)	5 (0.4)	>0.999 <sup>b</sup>
	Decreased olfactory (yes)	11 (1.3)	2 (0.7)	13 (1.1)	0.536 <sup>b</sup>
	Decreased taste (yes)	6 (0.7)	2 (0.7)	8 (0.7)	>0.999 <sup>b</sup>
	Itching (yes)	0 (0)	0 (0)	0 (0)	NC
	Skin rash (yes)	0 (0)	0 (0)	0 (0)	NC
	Itching and eye irritation (yes)	4 (0.5)	0 (0)	4 (0.3)	NC
	Frequent urination (yes)	1 (0.1)	1 (0.3)	2 (0.2)	0.439 <sup>b</sup>
	Burning urine (yes)	4 (0.5)	0 (0)	4 (0.3)	0.557 <sup>b</sup>
	Urinary incontinence (yes)	0 (0)	0 (0)	0 (0)	NC
	Oral plague (yes)	2 (0.2)	0 (0)	2 (0.2)	>0.999 <sup>b</sup>
Drug	Prednisolone	664 (76.59)	150 (51.55)	814 (70.29)	<0.001 <sup>a</sup>
	Biological drug	47 (5.5)	28 (9.82)	75 (6.58)	0.013 <sup>a</sup>
	Vitamin D	544 (62.67)	126 (43.3)	670 (57.81)	<0.001 <sup>a</sup>
	Azathioprine	125 (14.4)	13 (4.47)	138 (11.91)	<0.001 <sup>a</sup>
	Methotrexate	353 (40.67)	122 (41.92)	475 (40.98)	0.731 <sup>a</sup>
	ACEI	23 (2.65)	8 (2.75)	31 (2.67)	>0.999 <sup>a</sup>
	ARB	107 (12.33)	48 (16.49)	155 (13.37)	0.074 <sup>a</sup>

\*All data are expressed as No. (%) except for age.

<sup>a</sup> The chi-square test was used for the comparison.<sup>b</sup> The Fisher exact test was used for the comparison.<sup>c</sup> The independent t-test was used for the comparison.

**Table 2.** Characteristics of Study Population Based on COVID-19 Status

	Item	COVID (+) (n=20)	COVID (-) (n=1139)	Total (n=1159)	P Value
<b>Demographical Variable</b>					
Gender	Male	5 (25)	208 (18.26)	213 (18.4)	0.393 <sup>a</sup>
	Female	15 (75)	931 (81.74)	946 (81.6)	
	Age* (years)	46.30 (±2.54)	49.45 (±0.41)	49.39 (±0.41)	0.319 <sup>c</sup>
Marriage	Single	1 (5)	79 (6.94)	80 (6.9)	>0.999 <sup>b</sup>
	Married	19 (95)	1060 (93.06)	1079 (93.1)	
Comorbidity	Hypertension	4 (20)	253 (22.21)	257 (22.17)	>0.999 <sup>b</sup>
	Diabetes	1 (5)	109 (9.57)	110 (9.49)	0.713 <sup>b</sup>
	Cardiovascular disease	1 (5)	67 (5.88)	68 (5.87)	>0.999 <sup>b</sup>
	Angiography	1 (5)	32 (2.81)	33 (2.85)	0.422 <sup>b</sup>
	Stenting	0 (0)	11 (0.97)	11 (0.95)	>0.999 <sup>b</sup>
	CABG	0 (0)	10 (0.88)	10 (0.86)	>0.999 <sup>b</sup>
	Cerebral infarction	0 (0)	9 (0.79)	9 (0.78)	>0.999 <sup>b</sup>
	Lung disease	0 (0)	28 (2.46)	28 (2.42)	>0.999 <sup>b</sup>
	Asthma	0 (0)	18 (1.58)	18 (1.55)	>0.999 <sup>b</sup>
	COPD	0 (0)	1 (0.09)	1 (0.09)	>0.999 <sup>b</sup>
	Chemical veteran	0 (0)	7 (0.61)	7 (0.6)	>0.999 <sup>b</sup>
	kidney disease	0 (0)	29 (2.55)	29 (2.5)	>0.999 <sup>b</sup>
	Dialysis	0 (0)	1 (0.09)	1 (0.09)	>0.999 <sup>b</sup>
	Kidney transplant	0 (0)	2 (0.18)	2 (0.17)	>0.999 <sup>b</sup>
Cancer	0 (0)	11 (0.97)	11 (0.94)	>0.999 <sup>b</sup>	
Risk factor	Participate in community meeting (yes)	2 (10)	57 (5)	59 (5.1)	0.758 <sup>b</sup>
	Use of public transport	1 (5)	44 (3.86)	45 (3.9)	>0.999 <sup>b</sup>
	COVID positive in family	3 (15)	8 (0.7)	11 (0.9)	0.740 <sup>b</sup>
Outcomes	Fever (yes)	9 (45)	37 (3.25)	46 (4)	<0.001 <sup>a</sup>
	Cough (yes)	13 (65)	47 (4.13)	60 (5.2)	<0.001 <sup>a</sup>
	Sputum (yes)	2 (10)	13 (1.14)	15 (1.3)	0.026 <sup>b</sup>
	Shortness of breath (yes)	11 (55)	25 (2.19)	36 (3.1)	<0.001 <sup>a</sup>
	Chest pain (yes)	4 (20)	16 (1.4)	20 (1.7)	<0.001 <sup>b</sup>
	Weakness and lethargy (yes)	4 (20)	24 (2.11)	28 (2.4)	0.001 <sup>b</sup>
	Muscular pain (yes)	7 (35)	26 (2.28)	33 (2.8)	<0.001 <sup>a</sup>
	Runny nose (yes)	0 (0)	13 (1.14)	13 (1.1)	>0.999 <sup>b</sup>
	Sore throat (yes)	6 (30)	26 (2.28)	32 (2.8)	<0.001 <sup>a</sup>
	Vomiting nausea (yes)	2 (10)	6 (0.53)	8 (0.7)	0.007 <sup>b</sup>
	Diarrhea (yes)	3 (15)	8 (0.7)	11 (0.9)	0.001 <sup>b</sup>
	Headache (yes)	6 (30)	19 (1.67)	25 (2.2)	<0.001 <sup>a</sup>
	Dizziness (yes)	1 (5)	6 (0.53)	7 (0.6)	0.115 <sup>b</sup>
	Weight loss (yes)	1 (5)	3 (0.26)	4 (0.3)	0.067 <sup>b</sup>
	Decreased appetite (yes)	0 (0)	5 (0.44)	5 (0.4)	>0.999 <sup>b</sup>
	Decreased olfactory (yes)	2 (10)	11 (0.97)	13 (1.1)	0.02 <sup>b</sup>
	Decreased taste (yes)	2 (10)	6 (0.53)	8 (0.7)	0.007 <sup>b</sup>
	Itching (yes)	0 (0)	0 (0)	0 (0)	NC
	Skin rash (yes)	0 (0)	0 (0)	0 (0)	NC
	Itching and eye irritation (yes)	0 (0)	4 (0.35)	4 (0.3)	>0.999 <sup>b</sup>
Frequent urination (yes)	0 (0)	2 (0.18)	2 (0.2)	>0.999 <sup>b</sup>	
Burning urine (yes)	1 (5)	3 (0.26)	4 (0.3)	0.0162 <sup>b</sup>	
Urinary incontinence (yes)	0 (0)	0 (0)	0 (0)	NC	
Oral plague (yes)	0 (0)	2 (0.18)	2 (0.2)	>0.999 <sup>b</sup>	
Drug	Prednisolone	12 (60)	802 (70.47)	814 (70.29)	0.327 <sup>a</sup>
	Biological drug	1 (5)	74 (6.61)	75 (6.58)	>0.999 <sup>b</sup>
	Vitamin D	13 (65)	657 (57.68)	670 (57.81)	0.649 <sup>a</sup>
	Azathioprine	1 (5)	137 (12.03)	138 (11.91)	0.498 <sup>b</sup>
	Methotrexate	9 (45)	466 (40.91)	475 (40.98)	0.819 <sup>a</sup>
	ACEI	0 (0)	31 (2.72)	31 (2.67)	>0.999 <sup>b</sup>
	ARB	2 (10)	153 (13.43)	155 (13.37)	>0.999 <sup>b</sup>

\*All data are expressed as No. (%) except for age.

<sup>a</sup> The chi-square test was used for the comparison.<sup>b</sup> The Fisher exact test was used for the comparison.<sup>c</sup> The independent t-test was used for the comparison.

angiotensin II type 1 receptor blockers (ARBs) may even help improve the clinical outcomes of hypertensive patients during COVID-19.<sup>35</sup> Also, Mehra et al study demonstrated that using ACEI or ARBs are not related to an increase in-hospital mortality.<sup>36</sup> It should be noted that the duration of usage of these medications may affect their mechanism of action against COVID-19. A limitation of the current study was that data regarding the duration of the consumption of these medications was not available; however, it can be assumed that the majority of the subjects were using these medications for the long term based on the nature of rheumatoid arthritis and the mean age of the subjects. It is suggested that further studies consider the duration of medication use in the evaluation of the association between these medications and the incidence of COVID-19.

## 6. Conclusion

The present study demonstrated that less than 2% of patients with rheumatologic disorders had COVID-19. Receiving ARBs or ACEIs was not different among patients with or without COVID-19. Receiving hydroxychloroquine was not related to the development of COVID-19 in patients with rheumatologic disorders.

### Authors' Contributions

SS, GA, NB, MI, AS, AR, SA: study design, data gathering, data analysis, interpretation, draft preparation. MHAA, ZRM, MH, ER, HI, GAI, AS: data gathering, data analysis, interpretation, draft preparation.

### Conflict of Interest Disclosures

GA serves as an editor in chief of *Hospital Practices and Research*. AS is an assistant editor of *Hospital Practices and Research*. Other authors declare that they have no conflicts of interest.

## Research Highlights

### What Is Already Known?

- Chloroquine derivatives are among the hypothetical medications for COVID-19.
- Due to virus binding to the angiotensin II (ACE) receptors, ACE inhibitors (ACEIs) and angiotensin II type 1 receptor blockers (ARBs) are also hypothesized to prevent COVID-19 progression.
- The findings of previous studies regarding the efficacy of these medications are controversial.

### What Does This Study Add?

- This study showed that the incidence of COVID-19 did not differ between patients who previously used ARB or ACEI and patients who did not take these medications.
- The incidence of COVID-19 did not differ between patients with a history of chloroquine derivative consumption and those without a history of these medications.

## Ethical Approval

The study was approved by Baqiyatallah University of Medical Sciences, Tehran, Iran, with a code of IR.BMSU.REC.1399.020.

## Funding/Support

The study was conducted under the financial supports of Baqiyatallah University of Medical Sciences, Tehran, Iran.

## Acknowledgments

The authors would like to thank the clinical research center of Baqiyatallah Hospital, Tehran, Iran.

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