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Original Article

COVID-19 Reinfection Rate and Related Risk Factors in Fars Province, Iran: A Retrospective Cohort Study

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What's Known

- There are many pieces of evidence that show people are getting reinfected by COVID-19.
- The reinfection rate by COVID-19 may differ based on demographic variables.

What's New

- COVID-19 reinfection happened in 0.97% of the people who were infected by COVID-19 in Fars province, Iran.
- The reinfection rate was higher in the young age group, male patients, inpatients, residents of the urban areas, and healthcare providers.

Abstract

Background: Reinfection with Coronavirus Diseases 2019 (COVID-19) has raised remarkable public health concerns globally. Therefore, the present retrospective cohort study intended to investigate COVID-19 reinfection in registered patients of Fars province in Iran from February 2020 to April 2021.

Methods: The patients' data, including the COVID-19 infection, symptoms, comorbidities, and demographics, were collected using the Health Information Systems (HISs). The patients were divided into three groups in terms of the duration between the initial infection and reinfection, including 28-44, 45-89, and more than 90 days. Following the univariate analysis, logistic regression was used to investigate the factors effective on COVID-19 reinfection.

Results: A total of 213768 patients had a positive Polymerase Chain Reaction (PCR) test. The reinfection rate was 0.97% (2079 patients). Of these re-infected individuals, 14.9%, 18.5%, and 66.6% had their second positive test 28-45, 45-89, and ≥90 days later, respectively. The mean duration between the initial infection and reinfection was 130.56 days (29-370 days). The chance of reinfection was significantly higher in the youths (Odds Ratio (OR)=2.055; P<0.001), men (OR=1.283; P<0.001), urban population (OR=1.313; P<0.001), and healthcare providers (OR=4.453; P<0.001). The patients with chronic pulmonary diseases, chronic kidney diseases, and malignancy were 1.421 (P=0.036), 2.239 (P<0.001), and 3.437 (P<0.001) times, respectively, more likely prone to reinfection.

Conclusion: The results of this study showed that there is a higher risk of reinfection in several vulnerable groups including healthcare providers, young individuals, residents of urban areas, men, and individuals with underlying diseases.

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Keywords ● Coronavirus ● Incidence ● Reinfection ● COVID-19 ● Communicable diseases

Introduction

Until November 06, 2022, Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), as the causative agent of the Coronavirus Diseases 2019 (COVID-19) pandemic, has caused more than 637 million cases of infection and more than 6.6

million deaths globally. Unfortunately,there is a rapid and global spread of the disease due to its extremely high infectivity.[1] It infected almost all global countries in a relatively short time and is currently known as a major threat to global public health.[2, 3] The related global and rapid spread, high infectivity, and significant mortality of COVID-19 made the World Health Organization (WHO) issue a statement on January 30, 2020, announcing the novel coronavirus as the sixth leading cause of global public health emergency.[4]

Besides the primary infection, COVID-19 reinfection has raised further public health concerns.[5, 6] Another vital question and major global public health concern now exists: Is COVID-19 reinfection possible? Moreover, how strong is the body immunity against this disease in individuals with the previous infection?[7, 8] The first case of reinfection with a phylogenetically distinct strain of SARS-CoV-2 was reported in the literature on August 25, 2020,[4] with other 70 cases being reported in the following months, along with more than 30,000 cases of suspected reinfections.[8]

Herd immunity considerations, vaccination strategies, and general epidemic simulations depend on the effectiveness and duration of immunity against COVID-19.[7] Immunity against COVID-19 reinfection or global vaccination can affect the disease severity and spread. It is believed that lack of immunity due to the lack of the previous infection is the main cause of the rapid and global spread of the disease and epidemic continuation.[9] Therefore, a greater understanding of the immunity against COVID-19 reinfection is essential for better management of the disease, greater knowledge for diagnosis, reinfection prevention, and appropriate intervention strategy modifications.[10]

According to the limited evidence available, COVID-19 reinfection is rare and occurs in less than 0.3% of the individuals with previous positive Polymerase Chain Reaction (PCR) for SARS-CoV-2.[11-13] A recent study in Qatar reported that the immunity against reinfection continued for at least seven months in about 95% of the individuals with previous positive PCR.[11] Moreover, another study on healthcare providers in the UK showed that the related immunity could continue for at least 5-6 months post-infection.[14] Despite the evidence showing a high level of immunity against COVID-19 reinfection in healthcare providers, the risk of reinfection in the general population is still unknown.

There is limited information on the COVID-19 reinfection due to the extremely limited number of reported cases.[15] Therefore, suspected reinfection documentation is essential to illustrate the natural history of the disease and find the risk factors making the individual susceptible to reinfection.[15] Moreover, understanding the COVID-91 reinfection rate, consequences, and determining factors is also essential to gain a proper insight into the pathophysiology of this novel disease, predict the disease course, and guide the ongoing efforts for vaccine development.[11] Therefore, the present study intended to estimate the COVID-19 reinfection rate in all the hospitalized individuals and outpatients recorded in the Fars province, Iran, from early February 2020 to late April 2021. Besides, this study aimed to find the factors that could be related to the reinfection rate.

Patients and Methods

Study Design and Population

This is a retrospective cohort study including the data of all the patients with COVID-19 infection in the Fars province, Iran. With a population of about five million, Fars province is located in southern Iran and is considered a medical hub in the related geographical region. Annually, many patients from neighboring provinces and countries and evens other parts of Iran come to Fars province to receive medical care. The present study population included all the patients with COVID-19 who presented to the healthcare facilities and hospitals under the coverage of the Universities of Medical Sciences of Shiraz, Fasa, Jahrom, and Larestan from early February 2020 to late April 2021. The study was performed using the census method. Thus, no sampling was needed. The inclusion criterion was having a registered positive PCR test, and there were no exclusion criteria. In addition, the study protocol was approved by the Ethics Committee of Shiraz University of Medical Sciences (Ethics Code: IR.SUMS.REC.1400.040).

Variables and Data

The data included COVID-19 infection, patients' symptoms, comorbidities, and demographics and was collected from the Health Information Systems (HISs) of the Universities of Medical Sciences located in Fars province. The variables included the demographic variables of age, sex, admission type (inpatient or outpatient), residence location (rural or urban areas), and job (healthcare providers and those with jobs not related to healthcare). According to the WHO guidelines, the patients were classified into four age groups, including 0-14 years old

(pediatric group), 15-47 years old (young group), 48-63 years old (middle-aged group), and ≥64 years old (elderly group).[16]

The variables related to underlying diseases and conditions included body mass index (BMI), smoking, hypertension, diabetes, cardiovascular diseases, respiratory distress syndrome, mild and severe pneumonia, malignancy, and human immunodeficiency virus (HIV), as well as chronic renal, neurologic, neuromuscular, pulmonary, and hepatic diseases. These variables were described as present or absent.

The clinical presentation variables related to COVID-19 included cough, fever, dyspnea, sputum production, articular, abdominal or chest pain, headache, nausea, diarrhea, rhinorrhea, sore throat, dizziness or irritability, myalgia, fatigue, smell disorder, and taste disorder. These variables were described as present or absent.

The main variable of the present study was reinfection in the study population, which was described as a PCR test positive for SARS-CoV-2 that was taken at least 28 days from the first positive PCR. We considered the cut-off point of 28 days, because previous studies had reported that the related viral load reached its lowest levels after 28 days from the initial infection.[17, 18] Moreover, the patients were divided into three groups in terms of the duration between the primary infection and reinfection, including 28-44 days, 45-89 days,[7] and more than 90 days.[12]

Statistical Analysis

To identify the relation between some categorical risk factors and reinfection, contingency tables were formed. Since the data set included a large number of observations, the Chi squared test was used for preliminary data analysis. Data modeling was performed by logistic regression to estimate the coefficient and effect size of different factors. As the most important and widely used method in categorical response modeling, this method has been increasingly used in a wide variety of applications, especially in biomedical studies, in recent decades.[19]

It should be noted that due to the large number of independent variables that were candidates to enter the model, the variable selection was performed in the way that at first simple logistic regression was fitted for each independent variable; then those variables with coefficient P<0.2 were entered the multiple logistic regression.[20] Obviously, variables with missing observations reduce the number of observations that contribute to the analysis, and also the reduction in the number of observations would lead to a decreased analytical power. It is clear that multiple analysis that involves more variables would lead to more lost observations and consequently less power. Therefore, only the variables having <20% of missing observation entered the multiple logistic regression in the present study. Finally, since two sided-tests are more common than one-sided ones,[19] all tests were performed two-sided and at the significance level of 0.05. Moreover, the data analysis was performed using Excel 2016 and STATA software, version 14 (Stata Corp LLC, 1985-2015, USA).

Results

A total of 705,818 PCR tests were performed in Fars province in the study duration. Of all the PCR tests, 218,804 (31%) had positive results, while 487,014 (69%) were negative. The tests were taken from 562,152 individuals, including 56.3% men and 43.7% women. Moreover, each patient had 1.26 PCR tests on average. The duplicated results were omitted, and the number of individuals was calculated using the number of PCR tests. It was found that 213,768 individuals had at least one positive PCR test for SARS-CoV-2.

Table 1 presents the demographics of all the patients with COVID-19 in the Fars province.

Table 1: Demographic characteristics of the population infected with COVID-19 in Fars province

Variable		No. (%)
Age group (Year)	Pediatric (0-14)	6469 (3.03)
	Young group (15-47)	140260 (65.62)
	Middle age (48-63)	42911 (20.08)
	Elderly (≥64 years)	24102 (11.28)
Sex	Male	115318 (53.95)
	Female	98424 (46.05)
Admission type	Outpatient	190530 (89.14)
	Inpatient	23212 (10.86)
Location	Urban	187409 (87.68)
	Rural	26.333 (12.32)
Job	Other jobs	196939 (93.7)
	Health care personnel	13242 (6.3)

According to these data, 54% of the patients were men, while 46% were women. Moreover, 89% and 88% of the patients were outpatients and residents of urban areas, respectively. While 11% and 12% were inpatients and residents of rural areas, respectively. Additionally, 6% of the patients were healthcare providers, wherein 94% had jobs unrelated to healthcare. In terms of age, the least number of COVID-19 patients belonged to the pediatric age group (3%), while the young age group (15-47 years) had the highest number of patients (66%). The middle-aged and elderly groups included 20% and 11% of the patients, respectively.

Regarding the reported cases of reinfection, of a total of 213,768 patients, 2079 had another positive test at least 28 days after the initial infection. Therefore, the overall reinfection rate was calculated to be 0.97% (table 2). Of these patients, 310 (14.9%), 385 (18.5%), and 1384 (66.6%) had their second positive test 28-45, 45-89, and ≥90 days later, respectively (figure 1).

Table 2: COVID-19 reinfection rate in Fars province in terms of demographics and underlying diseases

Variable		Reinfection		P value
		Yes	No	
Overall		2079 (0.97)	211663 (99.03)	
Age group (year)	Pediatric (0-14)	28 (0.43)	6441 (99.57)	<0.001
	Young group (15-47)	1610 (1.15)	138650 (98.85)	
	Middle age (48-63)	288 (0.67)	42623 (99.33)	
	Elderly (≥64)	153 (0.63)	23949 (99.37)	
Sex	Men	1201 (1.04)	114117 (98.96)	<0.001
	Women	878 (0.89)	97546 (99.11)	
Admission type	Outpatient	1709 (0.9)	188821 (99.1)	<0.001
	Inpatient	370 (1.59)	22842 (98.41)	
Location	Urban	1906 (1.02)	185503 (98.98)	<0.001
	Rural	173 (0.66)	26160 (99.34)	
Job	Other jobs	1563 (0.79)	195376 (99.21)	<0.001
	Health care personnel	498 (3.76)	12744 (96.24)	
ICU* hospitalization	Yes	24 (1.54)	1536 (98.46)	0.007
	No	111 (0.84)	13035 (99.16)	
BMI** (Kg/m^2)	Over 40	8 (0.94)	842 (99.06)	0.863
	Below 40	1677 (0.89)	187687 (99.11)	
Smoking	Yes	24 (0.67)	3584 (99.33)	0.153
	No	1661 (0.89)	184945 (99.11)	
Hypertension	Yes	70 (0.61)	11354 (99.39)	0.001
	No	1615 (0.9)	177175 (99.1)	
Diabetes	Yes	67 (0.63)	10591 (99.37)	<0.001
	No	2012 (0.99)	201072 (99.01)	
Cardiovascular	Yes	99 (0.98)	10028 (99.02)	0.959
	No	1980 (0.97)	201635 (99.03)	
HIV***	Yes	4 (2.2)	178 (97.8)	0.514
	No	366 (1.59)	22664 (98.41)	
Chronic kidney diseases	Yes	38 (1.66)	2246 (98.34)	0.001
	No	2017 (0.96)	209125 (99.04)	
Chronic neurologic or neuromuscular disease	Yes	6 (1.52)	389 (98.48)	0.904
	No	364 (1.6)	22453 (98.4)	
Chronic pulmonary disease	Yes	38 (1.23)	3056 (98.77)	0.128
	No	2017 (0.96)	208315 (99.04)	
Hepatic disease	Yes	4 (2.06)	190 (97.94)	0.601
	No	366 (1.59)	22652 (98.41)	
Respiratory distress syndrome	Yes	1 (0.5)	199 (99.5)	0.215
	No	369 (1.6)	22643 (98.4)	
Mild pneumonia	Yes	3 (0.61)	488 (99.39)	0.079
	No	367 (1.62)	22354 (98.38)	
Severe pneumonia	Yes	7 (0.77)	905 (99.23)	0.042
	No	363 (1.63)	21937 (98.37)	
Malignancy	Yes	20 (2.7)	720 (97.3)	<0.001
	No	2059 (0.97)	210943 (99.03)	

*ICU: Intensive Care Unit; **BMI: Body Mass Index; ***HIV: Human Immunodeficiency Virus; +Pearson Chi square was used for data analysis.

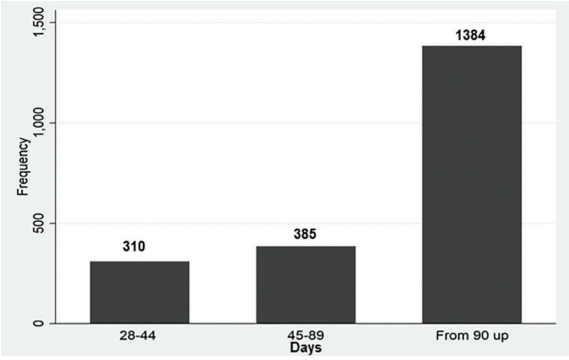

Figure 1: The highest frequency of reinfection interval with COVID-19, according to the interval time between the first and second-time infection, was more than 90 days.

The mean duration between the initial infection and reinfection was 130.56 days, with a range of 29-370 days.

According to univariate analysis (table 2), the reinfection rate was higher in the young age group (1.15%), male patients (1.04%), inpatients (1.59%), residents of the urban areas (1.02%), and healthcare providers (3.76%) than the individuals of other age groups, female patients, outpatients, residents of rural areas, and those with jobs not related to healthcare, respectively.

Regarding the underlying diseases and conditions, the reinfection rate was shown to be significantly higher in the patients who were admitted to the Intensive Care Unit (ICU) (1.54%; P=0.007), those with chronic kidney diseases (1.66%, P=0.001), and patients with malignancy (2.7%, P<0.001). However, the patients with high BMI (P=0.863), cardiovascular diseases (P=0.514), HIV (P=0.863), chronic pulmonary diseases (P=0.904), and hepatic disease (P=0.601) were not different in the reinfection rate. Moreover, it was different for hypertensive and diabetic patients and those with severe pneumonia. Patients without hypertension, diabetes, and severe pneumonia had reinfection rates of 0.9% (P<0.001), 0.99% (P<0.001), and 1.63% (P=0.042), respectively, which were significantly different. Besides, patients who were smokers (P=0.153) or had a chronic neurologic disease (P=0.904), respiratory distress syndrome (P=0.215), or mild pneumonia (P=0.079) had no significant difference.

According to the regression findings (table 3), the chance of reinfection in the young age group was twice the pediatric age group, which was significant; while it was also insignificantly higher in the middle-aged and elderly groups. Moreover, men and residents of the urban areas had 28% and 30% higher chances of reinfection than women and residents of the rural areas, respectively. Eventually, it was found that healthcare providers were four times more likely to have COVID-19 reinfection than people with jobs not related to healthcare.

Regarding the underlying diseases, patients with chronic pulmonary disease, chronic renal disease, and malignancy were 1.421, 2.239, and 3.437 times more likely to have reinfection, respectively.

According to table 4, the symptom prevalence rates in the initial infection were as follows: cough=29.12%, myalgia=29.04%, fever=25.86%,

Table 3: Regression estimates of factors affecting reinfection with COVID-19 in Fars province

Variables		Coefficient	Odds Ratio (95% Confidence interval)	P value
Age group (year)	Pediatric (0-14)	Reference		
	Young group (15-47)	0.72	2.055 (1.411-2.9940)	<0.001
	Middle age (48-63)	0.325	1.384 (0.936-2.045)	0.103
	Elderly (≥64)	0.338	1.403 (0.933-2.107)	0.103
Sex	Female	Reference		
	Male		1.283 (1.173-1.403)	<0.001
Admission type	Outpatient	Reference		
	Inpatient	0.07	1.072 (0.941-1.222)	0.292
Location	Rural	Reference		
	Urban	0.272	1.313 (1.121-1.537)	0.001
Job	Other jobs	Reference		
	Health care personnel	1.493	4.453 (3.948-5.021)	<0.001
Diabetes	No	Reference		
	Yes	-0.155	0.855 (0.664-1.102)	0.228
Chronic kidney diseases	No	Reference		
	Yes	0.806	2.239 (1.612-3.110)	<0.001
Severe pneumonia	No	Reference		
	Yes	0.351	1.421 (1.022-1.975)	0.036
Malignancy	No	Reference		
	Yes	1.234	3.437 (2.182-5.416)	<0.001
Model significance		<0.001		

+Logistic regression was used for data analysis.

Table 4: Patients' symptoms in initial COVID-19 infection and reinfection

Symptom	Percentage of patients with the related symptoms	
	Primary infection n (%) N=211663	Reinfection n (%) N=2079
Sputum	190 (0.09)	2 (0.10)
Articular pain	8445 (3.99)	23 (1.11)
Abdominal pain	4191 (1.98)	11 (0.53)
Chest pain	8805 (4.16)	118 (5.72)
Headache	31157 (14.72)	70 (3.37)
Nausea	11133 (5.26)	113 (5.44)
Diarrhea	8170 (3.86)	106 (5.10)
Rhinorrhea	8890 (4.2)	42 (2.02)
Sore throat	45888 (21.68)	533 (25.64)
Confusion or irritability	9631 (4.55)	16 (0.77)
Myalgia	61467 (29.04)	142 (6.83)
Fatigue	33231 (15.7)	353 (16.98)
Dyspnea	24066 (11.37)	268 (12.89)
Cough	61827 (29.21)	611 (29.39)
Fever	54736 (25.86)	471 (22.66)
Smell disorder	14372 (6.79)	83 (3.99)
Taste disorder	7789 (3.68)	47 (2.26)

sore throat=21.68%, fatigue=15.7%, headache=14.72%, dyspnea=11.37%, smell disorders=6.79%, nausea=5.26%, confusion or irritability=4.55%, chest pain=4.16%, rhinorrhea=4.2%, articular pain=3.99%, diarrhea=3.86%, taste disorders=3.68%, abdominal pain=1.98%, and sputum=0.09%.

Moreover, the symptom prevalence rates in the COVID-19 reinfection were as follows: cough=29.39%, sore throat=25.64%, fever=22.66%, fatigue=16.98%, dyspnea=12.89%, myalgia=6.83%, chest pain=5.72%, nausea=5.44%, diarrhea=5.10%, smell disorders=3.99%, headache=3.37%, taste disorders=2.26%, rhinorrhea=2.02%, articular pain=1.11%, confusion or irritability=0.77%, abdominal pain=0.53%, and sputum=0.1%.

Discussion

The present study found an overall reinfection rate of 0.97%, while previous studies have reported controversial results. For example, some studies in the UK reported different reinfection rates of 0.0%, 0.2%%, 0.057%, and <0.05%,[15, 21] and Abu-Raddad and colleagues in Qatar reported a reinfection incidence of 0.66% per 10,000 individuals per week.[11] Moreover, Pilz and others reported a reinfection rate of <0.3% during two major disease waves in Austria, which has a population of 8.9 million.[13] Moreover, a study by Zare and colleagues in Shahroud, Iran, found 2.5 cases of reinfection per 1000 patients.[18] The results of the mentioned study were different from our results, which can be due to the fact that Fars province is a referral healthcare center in southern Iran and hosts some patients seeking healthcare from neighboring provinces. In general, these controversial results in different studies can be explained by differences in the definition of reinfection, the duration between the initial infection and reinfection, and the specificity and sensitivity of the diagnostic tests.

Regarding the type of occupation, our results showed a higher chance of reinfection (more than four times) in healthcare providers than individuals with other jobs, which is compatible with other studies. According to different studies on healthcare providers in Denmark, the chance of COVID-19 infection in the frontline healthcare providers who worked in COVID-19 wards was 1.38 times higher than the healthcare providers working in other parts of hospitals. Moreover, the overall infection rate was two times higher among the healthcare providers than in the general population.[12, 21] Other studies have also reported a higher chance of reinfection with COVID-19 in healthcare providers.[18, 22] This can be explained by the fact that healthcare providers are at high viral exposure in the healthcare facilities, therefore, they have a higher chance of infection.[12]

Given the effect of age, our findings showed a higher chance of reinfection in the young age group (1.15%) than in other age groups. Moreover, this chance was almost two times higher than the pediatric age group, which was significant. This can be explained by inappropriate behaviors in this age group, such as not following social distancing and other health protocols including frequent handwashing and facemask wearing. These behaviors can increase exposure to the virus and subsequent reinfection.[23] Moreover, this

age group has a higher rate of social relationships in society. Therefore, our findings were compatible with those of Tillett and colleagues and Azam and others regarding the effect of age on reinfection. These studies showed a higher chance of reinfection in this age group as well.[6, 24] Moreover, a 25-year-old individual had severe symptoms in his reinfection.[6] However, the studies by Hansen and others in Denmark and Zhao and colleagues in China reported a higher reinfection rate in the elderly with underlying diseases than in the young age group,[12, 25] which is not compatible with our results.

Regarding the effect of sex on the chance of reinfection, our study showed that men were 28% more likely to have reinfection than women, which is not compatible with other studies. The study by Zare and others in Shahroud showed a higher rate of reinfection in men (2.96 in 1000 individuals) than women (1.98 in 1000 individuals).[18] However, a study by Adrielle and colleagues (2021) in Brazil showed that women included 78.8% of the reinfection cases.[26] Biological differences in the immune systems of women and men can affect their abilities in fighting infections, especially COVID-19.[27] According to studies, women have a more responsible attitude toward the COVID-19 pandemic than men, which can affect their compliance in following the preventive measures, such as frequent handwashing and facemask wearing.[8] Moreover, different lifestyles between the sexes can also affect the reinfection differences. For example, opioid abuse is more frequent in men than women.[28] Another reason can be the prominent role of men as the families' breadwinners. Therefore, men are much more exposed in society than women due to this financial responsibility. This can affect the chance of reinfection.

In terms of residence location, our findings showed a higher reinfection rate (30% higher) in the residents of urban areas than those in rural areas. However, no study investigating this difference was available. Therefore, a comparison of the results was not possible. This can be due to overcrowding in cities, the widespread use of public transport, especially subways, and crowded markets. All these factors can increase the close contact of people, decreasing social distancing.[29]

Regarding the type of admission, our study showed a higher chance of reinfection in the inpatients and ICU-admitted patients than the outpatients. These findings were compatible with those of Yuan and colleagues, who reported a significant positive correlation between hospitalization and the risk of reinfection. This higher risk can be due to the lack of virus clearance from the patients' bodies after the initial infection.[25] Moreover, some COVID-19 patients are more exposed to bacterial and fungal infections due to prolonged hospital stays.[30] This can increase the chance of reinfection.

Regarding the effect of different underlying diseases on the COVID-19 reinfection, our findings indicated a higher chance of reinfection (two times higher) in patients with chronic kidney disease, which was compatible with the study by Krishna and others that reported a higher chance of reinfection in patients undergoing hemodialysis.[31] This can be due to the frequent encountering of these patients with healthcare providers and facilities, as well as their immunosuppression and poor immune responses against SARS-CoV-2.[32]

The present study showed that patients with malignancy were three times more likely to have reinfection, which was compatible with other studies. For example, a study by Kapoor and others in India on patients with hematologic malignancies who developed immunodeficiency after complete recovery from the initial infection, showed that the reinfection in these patients was more severe than the initial infection.[33] Potential reasons include the lack of neutralizing antibodies due to immunosuppression or the phenomenon of virus reactivation, which is observed in immunosuppressive patients and viruses such as the Cytomegalovirus (CMV), herpes viruses, and Epstein Barr Virus (EBV).[33] Additionally, another study by Bellesso and colleagues in Brazil showed a higher chance of reinfection in patients with multiple myeloma.[34] Patients with active multiple myeloma have severe humoral immunodeficiency due to their inability for normal immunoglobulin production and secretion of the monoclonal component. Dysfunctional cellular and innate immune system, as well as high viral exposure due to close contact with healthcare providers, are other possible causes of reinfection in these patients.[35]

The present study results showed a 40% higher rate of reinfection in patients with chronic pulmonary disease. However, no study was available on this topic. Therefore, the comparison of results was not possible. Nevertheless, it is evident that in patients with damaged pulmonary parenchyma due to chronic pulmonary disease, the infectivity of the respiratory viruses is enhanced. Thus, the chance of reinfection with COVID-19 is increased.[36]

Regarding the different clinical symptoms between the initial infection and reinfection, the present study showed that patients with reinfection had fewer symptoms than their initial

infection. The prevalence of most symptoms was decreased in the reinfection, especially the symptoms of confusion, headache, pain, and myalgia that showed significant decreases in the prevalence. This finding is compatible with that of Pan and colleagues (2021), reporting fever (78.6%), cough (71.4%), and fatigue (50.0%) as the most common symptoms in the initial infection, which had a lower prevalence in the reinfection.[37] Some other studies conducted in Hong Kong,[32] Belgium, and the Netherlands[38] had similar results as well. This difference can be due to different immune responses between the initial infection and reinfection.[39] Moreover, the phenomenon of herd immunity can decrease the severity of future infections compared to the initial infection. Moreover, telemedicine can help in alleviating the disease severity and rapid detection of recurrent cases.[32] It is worth noting that the causative agent of the initial infection in the present study was the primary and Chinese variants of the virus, while the reinfection cases were mainly due to Indian and English variants. Additionally, some studies reported several cases of more severe disease in the reinfection. Even some cases of reinfection led to ICU admission and death,[6, 18] which is not compatible with our results.

The present study was the first to comprehensively investigate the COVID-19 reinfection rate and its relationship with demographics, underlying diseases, and clinical presentations in a large population of inpatients and outpatients in southern Iran. This could be the main advantage of the study. However, the study limitations include the potential errors in editing the data, because a large number of data can lead to errors beyond the control of the researchers. Moreover, our diagnostic criteria for reinfection diagnosis are still limited. It is worth noting that some patients might have a recurrence of a reactivated virus, which cannot be diagnosed without gene sequencing. Another limitation was related to explanatory variables, which were included based on the availability of data. Many other factors could affect reinfection such as vaccination, antibody level, and the time to wear a mask. However, this study was limited to the available data. Future studies are suggested for checking the effects of these factors on reinfection.

Conclusion

There is a risk of COVID-19 reinfection. Despite the related risk is limited, it cannot be ignored. The study found the population groups who are vulnerable to being reinfected by COVID-19. Therefore, the policymakers and authorities should emphasize implementing the related health protocols (social distancing, facemask wearing, and so on), especially in the high-risk groups, including healthcare providers, young individuals, residents of urban areas, men, and individuals with underlying diseases.

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Authors' Contribution

A.T: research idea and the data providing; M.L: research idea and acquisition of the data; F.L: the data cleaning and making them ready for analysis. M.B, M.S.E and M.S.A: the data analysis and writing the results section; M.E and S.D: helping in the data cleaning and writing the first draft of the manuscript; K.K: arranging the team and supervising the whole research process. All authors contributed in revising the final version of the manuscript. All authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Conflict of Interest: None declared.

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