



## Re-positive PCR of SARS-CoV-2 in health care persons during COVID-19 pandemic

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### ARTICLE INFO

#### Original paper

#### Article history:

Received: July 18, 2021

Accepted: December 06, 2021

Published: December 15, 2021

#### Keywords:

SARS-CoV-2; Covid-19;

Reinfection; Redetection;

Serology; Health care

personnel; Children's hospital

### ABSTRACT

Reinfection rate with SARS-CoV-2 and degree of protection by the induced antibody after the first episode of the infection is not well known, so it makes a big dilemma for health care personnel (HCP) who work in the front line of combating SARS-CoV-2. In this study, we investigated the frequency of SARS-CoV-2 redetection among HCP after the initial onset of the infection in a children's hospital during one year. Out of 131 seropositive HCP, 13.7% of them were symptomatic and PCR positive during 74-360 days after first sampling. Analysis of demographic data of seropositive HCP showed a correlation between a higher number of family members, higher body mass index, and the existence of underlying diseases with SARS-CoV-2 redetection. In conclusion, reinfection is one of the important problems in the SARS-CoV-2 pandemic. Research on this topic can help us to find answers to questions for estimating the duration of human protection with produced immunity after the infection or vaccination.

DOI: <http://dx.doi.org/10.14715/cmb/2021.67.5.19>

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### Introduction

In December 2019, an outbreak of respiratory infectious disease named Coronavirus Disease 2019, appeared in Wuhan, China and spread rapidly around the world (1-3). The World Health Organization

(WHO) chose the official name of COVID-19 for the new coronavirus disease, and the International Virus Classification Committee (ICTV) announced the name of the virus as SARS-CoV-2, a  $\beta$ -coronavirus, which after SARS (Severe acute respiratory syndrome

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virus) and MERS (Middle East respiratory syndrome-related coronavirus) viruses is considered as the third member of transmitted coronaviruses to humans through animals (4-6). SARS-CoV-2 created a worldwide crisis (7) and has taken victims all over the world about 450,000 within six months since the first reported outbreak in December 2019, according to WHO report (8). Reproduction of SARS-Cov-2 in the upper respiratory tract causes it to spread faster to other people. Symptoms of the infection with the virus appear generally after 2-14 days when its tendency to the lower respiratory tract causes lung lesions. It seems that the risk of infection with the virus is higher in health care persons (HCP) compared with the general population (9). They are prone to infection at least three times greater (10). As the COVID-19 pandemic progresses, HCP will experience repeated exposure to SARS-CoV-2 in hospitals. The exposure rate could be higher in children's hospitals, where HCP are in contact with neonates and children that are asymptomatic for half of the infection and their caregivers (1). Incidence of COVID-19 in children is lower compared to adults (4, 5); however, they can serve as hidden carriers of the virus and transmit it to HCP when referring to hospitals for medical services (11) to SARS-CoV-2 can induce immune responses that persist months after the infection, it is not well known about its induced protection against reinfection. A decrease in the amount of neutralizing antibodies a few weeks after induction following the infection was reported in several studies (9, 12, 13), which show the possibility of reinfection in health care settings and the community. The emergence of new variants, notably B.1.1.7 in the UK, B.1.351 in South Africa, and P.1 in Brazil, which are 75% more transmissible, raised higher concerns about reinfection (10). Insufficient information is available on whether antibodies produced by previous variants of the SARS-COV-2 can prevent reinfection by these new strains. These variants have sequence diversity, mainly in the receptor-binding domain of the spike protein, which able them to escape from the induced immunity in individuals with prior infection history. Reinfection may be defined as clinical recurrence of symptoms compatible with COVID-19, accompanied by positive PCR test ( $Ct < 35$ ), more than 90 days after the onset of the primary infection, supported by

close-contact exposure or outbreak settings, and no evidence of another cause of infection (14).

Although the re-infection/recurrence of Covid-19 following initial infection remains unclear among HCP, the reported cases are mostly related to patients with underlying diseases (15, 16). The rate of reinfection may depend on age, sex, ward of activity, immune status and time of initial exposure. This study was aimed to analyze the frequency of SARS-CoV-2 redetection among HCP in a children's hospital during one year. Correlation of redetection rate with underlying diseases, demographic data and disease severity was also investigated.

## Materials and methods

### Study design

In the first part of the study, HCP of Mofid Children's Hospital from different disciplines were included in this cross-sectional study to investigate exposure with SARS-CoV-2 during the early period of the pandemic in March 2020. The study was approved by the Ethical Committee of the Research Institute for Children's Health, Shahid Beheshti University of Medical Sciences, Tehran, Iran. Demographic, laboratory and clinical data from all personnel were initially recorded in a questionnaire during their participation in the first screening serology test by using (COVID-19 IgG/IgM Rapid Test Dipstick, Ref INCP-401, AllTest BiotechCo., China). The sensitivity and specificity of used rapid test in this study compare to PCR was >99.9% and 98%, respectively. All seropositive HCP were followed for presentation of Covid-19 symptoms bases on their request for PCR test for one year until March 2021. Real-time PCR-testing was done using COVID-19 One-Step RT-PCR (Pishtazteb Diagnostics, Iran) with 100% specificity and sensitivity that could identify 200 copy number of the virus in one milliliter on related RNA samples of nasopharyngeal swabs that extracted by RNJia Virus Kit (ROJETECHNOLOGIES, Iran).

### Analysis of reinfection/redetection among seropositive HCP

Analysis of reinfection/redetection was done based on the Pan American Health Organization/World Health Organization (PAHO/WHO) guideline, A symptomatic HCP after  $\geq 45$  days when having

seropositive test which considered as a redetected SARS-CoV-2 cases (ref: Interim guidelines for detecting cases of reinfection by SARS-CoV-2 29 October 2020) Accordingly, HCP with a positive SARS-CoV-2 serology test that was done in March 2020 were followed for one year. A questionnaire was designed and filled by seropositive HCP at the second follow-up time to analyze variables that are linked to SARS-CoV-2 redetection. HCP who don't fill the questionnaire were removed from the study. Sex, age, body mass index, blood group, Number of family members, days after the first infection course (if they were symptomatic in previous), job and ward of activity were analyzed in HCP with redetection of SARS-CoV-2. The diversity of symptoms among seropositive HCP is shown in Table 1.

### Results and discussion

A total of 490 HCP from different disciplines participated in the serology test in March 2020, positive serological results were reported among 131/490 of them (26.7%). Out of the 131 seropositive HCP, 42(31.3%) cases become symptomatic during 74-360 days, until March 2021. For all 42 cases, RT-PCR was done and 18/131 (13.7%) were positive.

According to review files of patients, 63.6% of re-positive HCPs had abnormal BMI and they were overweighting or obese and 72.7% of them with underlying disease (asthma, fatty liver, diabetes, etc.); however, job, ward of activity, blood groups, age didn't show a statistically significant difference ( $p$ -value  $\geq 0.05$ ).

Some of the crucial questions about the COVID-19 pandemic, caused by SARS-CoV-2 associated to what is the rate of reinfection and how long COVID-19 neutralizing antibodies can protect us against reinfection. It was initially assumed that the induced immune response against SARS-CoV-2 could prevent the second infection in the same individuals. Although the development of antibodies against SARS-CoV-2 occurs few weeks after the infection, its involvement in protective immunity and duration of the induced immunity need survey studies (17). Re-infection cases are a major concern for public health and society, and also insufficient information has been obtained about reinfection in health care workers (18).

As yet, various studies around the world (South Korea, Italy, China and Brazil) have reported re-

detectable SARS-CoV-2 infection after the initial onset of the illness (18-24). In this study 31.3% of seropositive HCP was symptomatic and had requested for covid PCR, 13.7 % of them were positive.

**Table 1.** Diversity of symptoms among seropositive HCP during COVID-19 pandemic

Symptoms	Case <sup>y</sup>		<i>p</i> -value
	1 <sup>st</sup> period	2 <sup>nd</sup> period	
Fever	6/33, 18.1%	12/33, 36.6%	
Cough	8/33, 24.2%	14/33, 42.4%	
Sputum		10/33, 30%	
Dizziness		14/33, 42%	
Headache	15/33, 45%	21/33, 63%	
Nasopharyngeal soreness	10/33, 30%	16/33, 48%	
Shortness of breath	8/33, 24%	13/33, 39%	
Bloating		4/33, 12%	
Diarrhea	5/33, 15%	8/33, 24%	
Fatigue	10/33, 30%	20/33, 60%	0.02
Chest pain	8/33, 24%	14/33, 42%	
Muscle or body aches	5/33, 15%	13/33, 39%	0.05
Chills	9/33, 27%	12/33, 36%	
Nausea and vomiting	8/33, 24%	13/33, 39%	
Rhinorrhoea	3/33, 9%	11/33, 33%	0.03
Anosmia	3/33, 9%	9/33, 27%	
Decreased sense of taste	3/33, 9%	9/33, 27%	
Seizure	3/33, 9%	1/33, 3%	
Pink eye	0	9/33, 27%	0.002
Medication history			
Oseltamivir	1/33, 3%	1/33, 3%	
Arbidol	0	1/33, 3%	
Hydroxychloroquine sulfate	1/33, 3%	3/33, 9%	
Azithromycine	6/33, 18%	18/33, 54%	
Other Antibiotics	0	6/33, 18%	
Hospitalization for COVID-19	2/33, 6%	1/33, 3%	
Yes	31/33, 93%	32/33, 96%	
No			
Traveling			
Yes	2/33, 6%	2/33, 6%	
No	31/33, 93%	31/33, 93%	

<sup>y</sup>Data is presented based on available data at the time of the serological survey and after recall during the second episode of the infection in symptomatic HCP.

Richard L Tillett, et al. published a report of the confirmed case of SARS-CoV-2 reinfection in the

USA with a unique clade on Oct 12, 2020 (19). According to the South Korea Center for Disease Control, up to 19 April 2020, re-detectable SARS-CoV-2 was obtained in 3.3% of patients after discharge after COVID-19 infection (24). Similarly, the first four Chinese patients had a re-positive test in February 2020 (20). Mei et al. worked on recovered COVID-19 patients in Wuhan, China, of these, 3.5% were found to be re-positive by Real-Time PCR (25). In a case series study in China, a 16.7% redetection rate was reported among discharged patients with mild to moderate disease (26). The difference rate with our result can be related to: in some study, redetection was shedding of the original virus from the first episode of the infection, since the time between discharge and the first re-positive test ranged between 1 and 35 days, which is not epidemiologically definition supported for re-infection. A positive PCR test less than a 90-day course probably represents prolonged shedding rather than reinfection; however, in immunocompromised patients detection of replication-competent virus for a longer period after the first positive test, up to 143 days, has been reported (27). In this study, we couldn't confirm reinfection since the sequencing of the virus from the initial sample and its comparison with the second isolate is required for confirmation.

Redetection of SARS-COV-2 in 13.7% of our cases can confirm the fact that they lost their immunity against COVID-19 in 74-360 days and according to results the estimated protection rate was 86.3%.

A similar estimated protection rate, 80% under the age of 65 years, was reported in a Large-scale assessment of reinfection rates in Denmark against reinfection during one year (28). In contrast, a higher protection rate, as high as 99.7%, was reported against reinfection in a one-year cohort study among seropositive individuals in Qatar (27). The difference rate with the current study may be due to our methodology, we checked the point prevalence of serology in the first step and follow them during one year, we don't know the exact interval between of first and second infection. In addition, we did this study on a high-risk population. On the other hand, diverse incidence rate SARS-COV-2 epidemiology in different countries and infectivity of new variants and their ability for immune evasion (14) could be

important reasons for reinfection in different population.

In a meta-analysis, available data of 18 studies showed 16% re-positive cases (95% CI, 12 to 20%) after follow-up; 43% with at least one comorbidity (27). In our study, no correlation was detected between job, ward of activity, blood group, and age with redetection. High body mass index, family member  $\geq 4$ , and underlying diseases were the most prominent finding although the P-value was not significant.

## Conclusion

In this study possibility of SARS-CoV-2 reinfection was investigated among HCP of a children's hospital for one year. Our results showed the redetection in 13.7% of seropositive HCP during 74-360 days. The results of this study show the re-infected by COVID-19 can happen.

## Study limitation

In this study, although most of the redetection of SARS-CoV-2 was observed >90 days after the first course of the serological analysis, some of our cases were not symptomatic, so we just defined suspected re-infection based on the definition. Moreover, the exact time of the first infection was not clear to us, so we could not predict the exact period of protection through induced antibodies at the early infection course. Underestimation of the redetection/reinfection rate should be considered in the current study, since just symptomatic HCP, but not all of the seropositive cases included.

## Acknowledgments

Special thanks to the personnel of the Pediatric Infections Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

## Interest conflict

This study does not have any conflict of interest.

## Funding

This study does not have any financially supported.

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