

SARS CoV-2 Re Infection after Natural Infection Compared with Previously Sero-negative: Descriptive longitudinal study

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INTRODUCTION

SARS-CoV-2 infection was first observed in December 2019, and later, it spread to different parts of the world. As the spread crossed multiple borders, WHO declared it a pandemic on March 11, 2020. Re-infection is currently a topic of research with very few studies, estimating the re-infection rate in the naturally infected population. Therefore, this study was conducted to find out the same in the previously sero-surveyed population.

Despite more than 250 million people becoming infected worldwide, SARS-CoV-2 re-infections cases have been reported but remain rare.^[1] First case of re-infection was documented in August 2020.^[2] Vitale *et al.* estimated the re-infection rate in Lombardy, Italy, as 0.31%.^[3] A

systematic review by Wang *et al.* of 17 case reports found that 68.8% of re-infected individuals had similar level of severity of infection, while 18.8% had severe infection compared to the previous episode.^[2] Re-infection from different variant of SARS-CoV-2 is very much a possibility seen in the real world.^[4] In India, ICMR found a 4.5% re-infection rate.^[5] The rate of re-infection among healthcare workers has been reported more,^[6] but the rate of re-infection in the general

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ABSTRACT

Background: WHO declared SARS-CoV-2 infection as pandemic on March 11, 2020. As cases recovered, it became important to know the rate of re-infection from the same virus and its severity. Therefore, the study was done to find out re-infection rate among the previously infected individuals.

Aim: To find out re-infection rate among already exposed and nonexposed individuals. **Materials and Methods:** A cohort study was done over 5000 previously serosurveyed individual. They were followed up via telephone. Data was collected using a questionnaire with questions regarding infection post-serosurvey, severity of infection among relatives and vaccination status. Thus information collected was uploaded in Google form. **Results:** Re-infection rate among previously exposed individuals was 1.2%; at the same time period, 6% of nonexposed individuals got infected. All the re-infection cases were mild, whereas 80.74% of individuals who got infected for the first time had mild symptoms. Exposure to SARS-CoV-2 in relatives who were staying with participants was found to be 3.23% and 4.22% among previously exposed and non-exposed individuals respectively. 17% of previously nonexposed individuals were fully vaccinated, whereas 0.65% of exposed individual got fully vaccinated. **Conclusion:** Re-infection rate in the study was less and mild on the basis of severity. Infection rate among the nonexposed was at a higher side stating that chances of getting re-infected are much lesser. Previously exposed individuals did not show the same type of interest for vaccination compared to previously nonexposed individuals.

KEYWORDS: COVID-19, re-infection, SARS-CoV-2, serosurvey

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population is less. Another retrospective cohort study found that out of 1278 previously positive individuals who got tested again after 90 days, 62 got re-infected and concluded that prior infection was highly protective against re-infection.^[7]

A seroprevalence study was conducted in October 2020 in 5000 individuals belonging to various strata residing among the Pimpri Chinchwad Municipal Corporation (PCMC) area Pune, Maharashtra.^[8] Same group of individuals were followed up after 8 months of sero-survey study, to find out re-infection rate and severity of infection. The study also brings out the effect of presence of SARS-CoV-2 positive individuals on previously infected individuals and also highlighted long lasting immunity against the virus. The risk of re-infection in the population, recovered from COVID-19 is crucial to improve quarantine management and optimize the ongoing vaccination campaign.

MATERIALS AND METHODS

A descriptive longitudinal study was conducted among previously sero-surveyed population in PCMC area. A total of 5000 individuals were to be contacted via telephone and Google form to be filled up after taking consent. Due to lack of phone number and wrong number the sample size reduced to 1081 (out of 1726) sero-positive people and 2253 (out of 3284) sero-negative people.

Methodology

As per the Centers for Disease Control and Prevention (CDC),^[1] re-infection means a person was infected (got sick) once, recovered, and then later became infected again. A structured questionnaire was used for collecting data regarding re-infection. The questions were related to whether individual got infected post-serosurvey or not, the severity of infection, whether immediate family member got infected post-serosurvey or not, the severity of infection, and the vaccination status of the individuals. Telephonic interview was conducted, and data entry was done in Google Excel simultaneously.

Statistical analysis

Data analysis was carried out using Epi Info™ 7.2.3.0 statistical software (developed by CDC in Atlanta, Georgia). Categorical data were presented as numbers and percentages.

RESULTS

5000 individuals blood sample were taken and examined for the presence of IgG SARS-CoV-2 antibody during a serosurvey in PCMC area in October 2020. In the above group of individuals, 1726 (34.52%) people came out to be sero-positive, that is they had antibody against the SARS-CoV-2 and rest of them were sero-negative. Due to missing phone number of many participants, it was not possible to collect data from everyone; only 4198 participants' phone number was available for any sort of communication. 1081 of 1408 (76.78%) previously infected people as well as 2253 out of 2790 (80.75%) previously non-infected people responded [Figure 1].

Around 45% of the participants were males and rests were females [Table 1].

Most of the infected participants were from the age group 18 – 59 year.

Mean period between the two positive results for SARS CoV 2 was 144 days (105–195 days).

Re-infection rate was around 1.2%, whereas during the same period, 6% of the previously seronegative people got infected. All the re-infected cases encountered mild symptoms, whereas 80% of seronegative group had similar outcome. Three of the seronegative individuals required ventilation, of which one died. Around 40% of the infected individuals had gone to hospital for treatment [Table 2].

Thirty five previously sero-positive participants had one or more family member infected by SARS-CoV-2 post serosurvey. Among the above group of participants seven admitted that, they got re-infected along with their family members.

Table 1: Demographic variable of re-infected and newly infected participants

Demographic components	Seropositive participants, n (%)	Seronegative participants, n (%)
Gender		
Male	487 (45.05)	1023 (45.41)
Female	594 (54.95)	1230 (54.59)
Age (years)		
Below 18	99 (9.16)	169 (7.50)
18-44	622 (57.54)	1462 (64.89)
45-59	213 (19.70)	372 (16.50)
60 and above	147 (13.60)	250 (11.11)
Total	1081 (100)	2253 (100)

Out of 2253 sero-negative individuals, 95 participants reported that their nearby family members suffered from COVID-19 post sero-survey. Forty four of ninety five sero-negative participants got infected along with their family members [Table 3].

One of the previously seropositive individuals got infected postvaccination, whereas three of seronegative people got mild symptoms after vaccination [Table 4].

DISCUSSION

Understanding the re-infection trend among the previously infected individuals is important for optimizing the quarantine and vaccination strategies for Controlling the spread of SARS-CoV-2.

This study answers many questions related to re-infection among the previously infected individuals and confirms that the re-infection rate is very less and also the severity of re-infection is mild. After a detail analysis of data, it was established that out of 1081 previously infected individuals, only 13 got re-infected; the rate comes out to be 1.2%. Researchers from

University of Missouri School of Medicine found re-infection rate to be 0.7% in their study. A study done in India by ICMR found re-infection rate to be around 4.5%.^[6,9,10] During the same period 135 previously non-exposed individual got infected and therefore infection rate comes out to be 6%. Therefore, the infection rate of 1.2% among previously seropositive individuals was significantly lower than the infection rate of 6% among seronegative individuals.

Most of the infected as well as re infected cases were from the age group 18–59 years. Another research paper highlighted the fact that re infection was mostly seen in 24–89 years of age.^[2]

Predominantly, people who had the virus for first time preferred to stay home rather than going to hospital for treatment, especially when it was a mild one, there was no significant difference between the groups in this aspect. The data related to severity of re infected cases revealed that all were having mild symptoms and majority of them opted to stay in their residence, whereas people who got infected for the first time had

Table 2: Number of participants who got infected by SARS CoV 2 post-serosurvey (October 20)

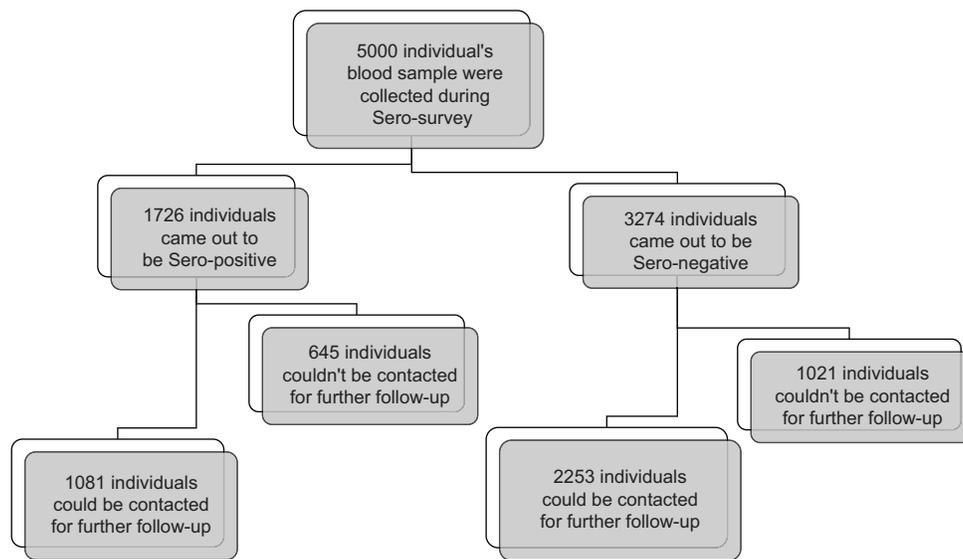
	Previously seropositive participants, n (%)	Previously seronegative participants, n (%)
Number of-19 positive COVID	13 (1.2)	135 (6)
Number of COVID-19 negative	1068 (98.8)	2118 (94)
Total	1081 (100)	2253 (100)
Severity of COVID-19 among the previously serosurveyed individual		
Mild	13 (100)	109 (80.74)
Moderate	0 (0)	23 (17.04)
Severe	0 (0)	3 (2.22)
Total	13 (100)	135 (100)
Place of treatment for infected serosurveyed individual		
Hospital	4 (30.76)	56 (41.48)
Home	9 (69.24)	79 (58.51)
Total	13 (100)	135 (100)

Table 3: Total household people who got infected post-serosurvey

COVID-19 status of nearby family members	Previously seropositive participants, n (%)	Previously seronegative participants, n (%)
COVID-19 positive	35 (3.23)	95 (4.22)
COVID-19 negative	1046 (96.77)	2158 (95.78)
Total	1081	2253
Severity of COVID-19 among the nearby relative		
Mild	28 (80)	82 (86.31)
Moderate	4 (11.42)	9 (9.47)
Severe	3 (8.58)	4 (4.22)
Total	35 (100)	95 (100)
Place of treatment for nearby relative who had COVID-19		
Home	22 (62.86)	59 (62.11)
Hospital	13 (37.14)	36 (37.89)
Total	35 (100)	95 (100)

Table 4: Vaccination Status of participants

Vaccination status (overall) as on July 2021	Previously seropositive participants, n (%)	Previously seronegative participants, n (%)
Fully vaccinated	7 (0.65)	383 (17)
Partially vaccinated	284 (26.27)	489 (21.70)
Not vaccinated	790 (73.08)	1381 (61.30)
Total	1081 (100)	2253 (100)
Vaccination status of individual who got infected after the serosurvey		
Fully vaccinated	0	18 (13.33)
Partially vaccinated	3 (23.08)	58 (42.96)
Not vaccinated	10 (76.92)	59 (43.71)
Total	13 (100)	135 (100)

**Figure 1:** Number of individuals who participated in the study

higher number of moderate and severe cases. As per the CDC and Wang *et al.*, 88.24% of people had mild infection in the second episode whereas 81% of people who got infection for the first time had experienced mild symptoms.^[2,10]

All the re-infection stated in the study had a mean period of 144 days between the two positive results for SARS-CoV-2, with a range of 105–195 days. Another research paper brought out mean period of the same to be around 60 days with a interquartile range of 51–108 days; second of similar type of paper gave 76 days as a mean interval (range of 19–142 days).^[2,11]

As SARS-CoV-2 spreads by respiratory droplets, it was perceived that common people living in confined area were more vulnerable to the disease. Therefore, as per data given by the participants, it was observed that people who stayed in close contact with previously infected people had lesser chance of getting infected compared to non-infected people. There was hardly any significant difference between

the groups in this aspect. Among 1081 previously sero-positive individual, 35 participants had one or more family member suffering from COVID-19 post serosurvey, within which only seven got re-infected along with their family members and 28 didn't had any infection. This depicts that immunity created in first wave still worked well and waved off the chances of re-infection.

As the study was conducted in July 2021, hence, vaccination status of the participants at the time was taken and it was found out that very few of previously infected, i.e., who got infected during the first wave, went for vaccination (26.92% got one dose or more). However, 38.70% of previously seronegative participants got one dose or more. Predominantly, the data for fully vaccinated convey that 0.65% of people who got infected in first wave were completely vaccinated, whereas 17% of other section of people got fully vaccinated. Therefore, the trend to get vaccinated was more among the previously noninfected people compared to other group of people. Further

studies allied to willingness to get hold of COVID-19 vaccine convey that 71.5% of 13,426 participants from 19 different countries were somewhat or very much interested to take the COVID-19 vaccine, this acceptance rate varies from 90% (China) to less than 55% (Russia), whereas many other studies established the fact that COVID-19 vaccine hesitancy was more than 30%.^[12,13]

Reviewing the vaccination status of both the groups, only 23 sero-positive participants were partially vaccinated before March 2021 (start of the second wave). By the time June arrived, another 268 participant of above group got partially vaccinated. So, majority of above group got protected from the second wave by immunity gained in the first wave. All the sero-negative people who got vaccinated encountered COVID 19 first then later took their first vaccine dose. Post-vaccination break through infection was seen in both the groups; three for sero-negative group and one for sero-positive group. Similarly, another study showed that 16.9% of participants were found to be infected post-vaccination.^[14] One of study stated that people who have taken vaccine had a 13.06 fold increased risk for breakthrough infection with the delta variant compared to those who were previously infected.^[15]

Limitation

The study was conducted by contacting participants via telephone and there was no proof of COVID-19 positivity received from participants' side. Re-infection cases were low in number and therefore, there is need to conduct a study with larger sample size of re-infection cases for a better clarity on severity of re-infection.

CONCLUSION

The finding of the study confirms that the re infection rate in the previously sero-positive individuals was less and it was also mild in nature. The study also found that in spite of immediate family member getting infected, the participants were protected from acquiring infection. Vaccine hesitancy was more in the previously sero-positive.

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Conflicts of interest

There are no conflicts of interest.

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