

Recurrence of SARS-COV-2: Facts and Myths

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Published on 14th September 2020

The severe acute respiratory syndrome-related coronavirus-2 (SARS-CoV-2) reactivation or reinfection will be an enduring and disquieting problem. SARS-CoV-2 replication in the host reaches its peak in the first week of infection, decreasing rapidly afterwards, due to the development of some levels of immunity. Yet, the infection seems to follow an uncustomary course in some individuals, reactivating after the apparent resolution of symptoms.¹ Reinfection is a major public health concern in terms of global morbidity and possibly mortality.² Several thoughts have been raised due to the “Retest Positive” for SARS-CoV-2 from “recovered” coronavirus disease-19 (COVID-19) patients.³ At the moment, it is difficult to discriminate if the positive nasopharyngeal swab results are due to real recurrence of COVID-19 infection or intermittent shedding of RNA fragments, especially in asymptomatic subjects.⁴ On the other hand, it cannot be excluded that truly negative discharged patients suffered reactivation or were re-infected with another COVID-19 strain, especially in elderly or in subjects with comorbidities.⁵ A report from the largest cohort study confirmed that more than 10% of patients clinically recovered from COVID-19 infection had re-positive RT-PCR at nasopharyngeal swab during post-discharge follow-up, and most of these subjects were asymptomatic at the time of recurrence.⁶ The proportion of re-positive patients among discharged COVID-19 patients varied from 2.4 to 69.2% and lasted from 1 to 38 days after discharge, depending on population size, age of patients, and type of specimens.⁷

The majority of patients who tested re-positive were asymptomatic or had mild symptoms, but some patients progressed critically and died.⁸ Concerningly, it should be noted that the majority of patients were negative for both IgG and IgM antibodies against SARS-CoV-2 virus at the time of the positive PCR re-test. In another study showed that none of the patients who were severely ill at the time of their initial hospitalization had re-positive results. However, serological tests revealed that these patients were positive for antibodies to the SARS-CoV-2 virus and

most of them had turned negative by the time of the later RT-PCR test.

Currently, several causes have been suggested as an explanation for re-positive tests for SARS-CoV-2 in COVID-19 patients during the recovery period, including false RT-PCR results, intermittent virus shedding, viral reactivation or re-infection with another SARS-CoV-2 strain, or exposing to a contaminated environmental surface after discharge. The false-negative rate of RT-PCR varies from 3 to 41%, according to the type of clinical specimen used at the time of discharge is one of the reason for the re-positive result at a later stage. There are many reasons for false-negative RT-PCR results, including the sensitivity/ specificity of the nucleic acid test kit, the sources of samples, and the sampling procedure itself. Respiratory shedding of SARS-CoV-2 may be intermittent. Therefore, a single negative swab could be misleading and may lead to positive result later on. In contrast, PCR tests can also give false-positive results, and patients have been diagnosed as re-positive when they were negative. Other possible reasons for false-positive results are contamination during the laboratory procedures and cross-reactivity with other human coronaviruses. The mean duration of viral RNA positive in stool samples was longer than pharyngeal swabs. This suggests that an anal swab or stool samples must be used to reduce the number of false-negatives.

However, the possibility cannot be excluded that truly negative discharged patients suffered reactivation or were re-infected with another SARS-CoV-2 strain. Genetic characterization of the viruses must be performed to distinguish between re-infection and reactivation of SARS-CoV-2 among re-positive patients. The second episode of COVID-19 infection appeared nearly 5 months after the first. That may be due to wearing out of protective antibody and resulted in reinfection. The result of the SARS-CoV-2 PCR test was positive. Serological tests showed very low levels of antibodies. This suggested a weak humoral immune response to the virus and potential reactivation of SARS-CoV-2. A possible viral reactivation in discharged patients previously diagnosed with

Cite this article as: Benny PV. Recurrence of SARS-COV-2: Facts and Myths. IMA Kerala Medical Journal. 2020 Sep 14;13(3):94–5.

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COVID-19 was also observed in a study in which patients were symptomatic with a fever and biological inflammatory symptoms. Virological factors, host immunity status, and degree of immunosuppression are potential risk factors for the reactivation of the SARS-CoV-2 virus. Repeated infection with the same human common coronavirus HKU1 and OC43 in a period shorter than 1 year has also been described.

The virus remains positive in sputum longer than in nasopharyngeal samples. Therefore, re-positive results in lower respiratory tract samples among discharged patients are more reliable than the upper respiratory tract samples. This means that at the time of discharge from the hospital, the virus exists in small amounts in the lower respiratory tract, so the results of the nasopharyngeal swab test were negative. After a while, the virus multiplied, and the patient turned positive again. The detection of viral RNA in the air samples and environmental surface indicates the important role of environmental transmission. Good ventilation conditions; strict disinfection of environmental facilities, particularly in hospital wards; and strict hand hygiene must be reinforced to reduce the formation of viral aerosols, cut down the aerosol load, and avoid cross-infection in isolation wards. Emphasis should also be placed on toilet sanitation. The high proportion of continuous detection of viral nucleic acids in stool samples despite negative results of RT-PCR test in nasopharyngeal swabs suggests that the virus may be transmitted through the digestive tract or re-transmitted through aerosols containing viruses. The presence of live SARS-CoV-2 in the faeces reinforces the hypothesis of possible faecal-oral contamination by the virus.

In conclusion, the recurrence of COVID-19 infection is a fairly frequent phenomenon. Need more focused research to manage these patients and to avoid impact due to the evolution of the pandemic in the future.

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