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Editorial

Recurrence Possibility of COVID-19 in India

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Editorial

Although nationwide lockdown was imposed in India amid COVID-19 outbreak since March 24, 2020, the COVID-19 infection is increasing day-by-day. India became world's second most affected country. By 13th May, 2021 India recorded 23,703,665 cases with 258,351 deaths and 19,734,823 recovered cases. Here, we described the possibility of COVID-19 reactivation and disease recurrence through horizontal transmission in individuals after recovery from COVID-19 infection, in particularly in India. Additionally, the study will demonstrate how COVID-19 reactivation/reinfection could play a dominant role in disease burden.

WHO (World Health Organization) recommended two times RT-PCR swabs test in discharged patients after clinical recovery from COVID-19 infection to confirm the disease recurrence globally. As per global data, the virus changing the molecular configuration and fluctuating time-by-time mainly because of viral load, occurrence of false-negative results at molecular test, inefficiency of sampling operator, even sampling procedure etc [1]. Recently, Ye et al. [2] mentioned that about 9% reactivation in COVID-19 patients occurred after discharge from the hospital. Further, they demonstrated host status, virologic features and steroid-induced immunosuppression as prime risk factor for the incidence of COVID-19 reactivation. Lombardi et al. [3] recommended domicile quarantine of 14 days after hospital discharge for safety purposes, but clear information about infectiousness time and virus shedding duration is still lacking. Rothe et al. [4] demonstrated that both pre-symptomatic and asymptomatic carriers might be responsible for COVID-19 reactivation, while Chen et al. [1] reported that convalescent might transmit the virus for further re-infection. Therefore, further investigations are needed to define appropriate quarantine period, to avoid transmission.

Recently, COVID-19 reinfection among COVID-19 patients has dazed scientific community, but uncertainty exists whether this second wave is due to reinfection or new virus strain. Till now 64 cases of reinfection has been reported globally in individuals, recovered from COVID-19 with an estimate ranging from 7.35 to 21.4% [5]. Immunological analysis in this regard plays an important role to determine viral reinfection properly as traditional diagnostic methods like RT-qPCR, high through put sequencing, CT scan; blood sample analysis has some limitations. Additionally, different swab sample source, improper sampling, and variable sensitivity/specificity of nucleic acid tests can lead to false negative results implying disease persistence rather than recurrence. Generally, immunoglobulins alone are not enough for long-term immunity. Evidences showed that virus specific $CD4^+$ T cells and $CD8^+$ T cells plays a crucial role in long-term COVID-19 reactivation due to their persistency up to 6 years after SARS-CoV-1 virus infection [6]. Accordingly, Zhang et al. [7] observed lower concentrations of monocyte ACE2 (Angiotensin Converting Enzyme 2) in COVID-19 patients than healthy individuals, which necessitate further study to distinguish between reinfection and new infection. Further, the COVID-19 reactivation duration after first infection may vary between different virus clades of SARS-CoV-2 virus (e.g., A2a, B1), resulting distinct virulence as well. Accordingly, the nature of protective Neutralizing Antibodies (NAbs) varies for different strains and this indicated that NAbs of primary infection are not able to protect re-infection by other strains, resulting lower concentrations of NAbs during reinfection [6].

More recently, virus latency period is considered as potential factor to determine virus reactivation. Wang et al. [8] observed viral latency period 24 days for reinfection. In another study, Ye et al. [2] reported maximum latency period 17 days among 5 patients, but reactivation characteristics were not properly demarcated. They opined that virus is getting reactivated from a latent stage to a lytic stage with similar symptomatic manifestations. Additionally, SARS-CoV-2 virus can survive and replicate in neuronal cell lines [9], which indicated that there is possibility of reactivation through neuro-invasion of virus at later stage. In India, till now, three re-infection cases, one in Ahmedabad and two in Mumbai were brought under ICMR scanner, ICMR Director General Prof. Balram Bhargava said. Tillett et al. [10] demonstrated that individuals recovered from SARS-CoV-2 may not guarantee future immunity and second infection, if happens, was more severe with higher clinical symptoms than the first attack, the report says [10]. Whether the criteria to define a re-infection case is 90 days or 100 days, WHO is still not decided yet the cut-off point, says ICMR Director General Prof. Balram Bharagava. Further, Prof. Balram Bharagava demonstrated that India is considering cut-off about 100 day. But, till now ICMR did not revealed any data regarding those re-infected persons.

Viral shedding is another potentially undetermined factor, which might cause reactivation or disease transmission from an apparently recovered individual or asymptomatic individual to healthy people [11]. Generally, viral shedding begins 2-3 days before symptoms appearance and it happens through non-respiratory or non-classical tract routes such as fecal-oral route, tears and conjunctival secretions etc. Virus remains unrecognized in all these non-respiratory or non-classical routes during patient's discharge, who are tested negative (nasopharyngeal RT-qPCR). But there is possibility of containing highly active viral titers in non-classical transmission sites of recovered patients, indicating that they not only reactivate themselves

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but also have capability to spread further infection.

Accordingly, India should adopt more stringent public health emergency strategy along with exiting practices on urgent basis. Consequently, further research is also required simultaneously to fight the recurrence of COVID-19 symptoms in India. In particularly, infected persons should strictly be discharged after two consecutive RT-qPCR negative results of swab samples from various sources. Further, if possible, they should be monitored during post-discharge domiciliary quarantine period for 14 days followed by one additional RT-qPCR again. Finally, more precious policy should be adopted to stop the further spreading of COVID-19 infection in human population and need regularized monitoring of positive number of COVID-19 cases and death. In conclusion, considering the above-mentioned facts, still there remains some unanswered questions: Are asymptomatic individuals more likely to spread the disease? Is proper treatment removes the virus completely from the system? Are the patients gained immunity for rest of their life? To address these facts, need immediate further study to prevent the COVID-19 infection vis-a-vis its reactivation.

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