RECURRENT COVID-19 INFECTION IN RECOVERED PATIENTS (A CRITICAL REVIEW)

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ABSTRACT

The pandemic of Coronavirus Disease 2019 (COVID-19) is still grooming throughout the world. However, the number of recovered patients with COVID-19 is also increasing day by day. Some discharged patients from hospitals had shown fever and radiological abnormalities again along with positive real-time reverse transcriptase-polymerase chain reaction (RT-PCR). This might be due to relapse of COVID-19 in recovered patients, secondary bacterial infection, the false-positive result after discharging, or a false negative at discharging yet to determine. In this review, a total of seven studies retrieved, in which 1052 COVID-19 infected patients were studied and followed them for one to six weeks. Among 1,052 patients, 12.1% (n=127) patients were found re-infected having positive RT-PCR with different clinical samples including nasopharyngeal swab, an anal swab, throat swab, and sputum samples. All re-infected patients were found with mild to moderate clinical symptoms. These findings suggest that recurrence of COVID-19 is exist. It is important to develop diagnostic tools further to avoid the false negative or positive results. Moreover, followup studies are required to determine the reason behind the recurrence of COVID-19 in recovered. Besides, we suggest because of the current review, further management of discharged patients is crucial especially for immunocompromised patients, old age patients, or patients with comorbidities. The discharge criteria should be ensured for a recovered patient to prevent the relapse of COVID-19.

Keywords: COVID-19, Discharge, Recurrence, Recovered Patients, RT-PCR
INTRODUCTION

The Coronavirus disease 2019 (COVID-19) is caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), which emerged in China and spread throughout the world by traveling and trade. Approximately, three million individuals are diagnosed with COVID-19, whereas 0.2 million are reported deaths. China controlled the COVID-19 epidemic in their country by western and traditional Chinese medicine. From many countries, recently it is reported that patients are recovering with COVID-19 after having a positive real-time reverse transcriptase-polymerase chain reaction (RT-PCR) report. Only a few follow up studies conducted for patients recovered with COVID-19. This review focus on clinical manifestation and prevalence of recovered patients having recurrent positive RT-PCR.

DISCHARGE CRITERIA FOR COVID-19 INFECTED PATIENTS

The discharge criteria were afebrile for three days, disappearance of respiratory symptoms, betterment in radiological imaging by chest computed tomography scanning (CT Scan) and at least two consecutive negative RT-PCR for SARS-CoV-2 from respiratory specimen in 24 hours interval.

The discharge patient should be isolated for at least 8-14 days in-home or safe place, depend on the case status including the severity (mild to severe) of COVID-19 infection and immunity (immunocompromised or immunocompetent) of patients.

LITERATURE OF PREVIOUS STUDIES

Luo Anming reported a case study of women having positive RT-PCR and antibody test after discharging from hospital. Lan et al., also reported recurrence of COVID-19 infection in four medical professional patients, who were exposed to COVID-19 during their duties. Zheng et al., also revealed that 15% of patients were found positive by RT-PCR after discharged from hospital. An et al., also described relapsed of COVID-19 in recovered patients having age less than 14 years. Xing et al. also reported positive RT-PCR in two medical staff recently recovered from COVID-19. Similarly, Xiao et al., also revealed that recurrence of COVID-19 was observed in 21.5% patients after discharged from hospital-based on recovery. Deng et al., also reported 23.5% recurrence of COVID-19 in patients recovered from the disease. Li et al., also reported positive results of SARS-CoV-2 in five patients after discharged from hospital-based on meeting the discharge criteria. Yuon et al., also reported recurrence of SARS-CoV-2 in 11% recovered patients. Li et al., also revealed a case of recurrence of patients, who recently recovered from COVID-19. Zhang et al., revealed 8.3% relapsed of COVID-19 among discharged patients.

A study conducted by Bao et al., on Rhesus monkeys shows that recurrence of COVID-19 infection could not be observed if the antibody produces in early infection. Similarly, the recovered patients would not be able to transmit infection if enough antibodies developed against SARS-CoV-2.

Table No.1: Various reported recurrence of COVID-19 in Recovered patients

<table>
<thead>
<tr>
<th>Author</th>
<th>Total Patient</th>
<th>Re-infection patients</th>
<th>Duration of Followup</th>
<th>Symptoms</th>
<th>RT-PCR Sample</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Luo Anming</td>
<td>01</td>
<td>01</td>
<td>22 days</td>
<td>Normal</td>
<td>Throat Swab</td>
<td>5</td>
</tr>
<tr>
<td>Lan et al.,</td>
<td>04</td>
<td>04</td>
<td>5-23 days</td>
<td>Normal</td>
<td>Throat Swab</td>
<td>6</td>
</tr>
<tr>
<td>Zheng et al.</td>
<td>20</td>
<td>03</td>
<td>7 days</td>
<td>Normal</td>
<td>Feces and Saliva</td>
<td>7</td>
</tr>
<tr>
<td>An et al.,</td>
<td>262</td>
<td>38</td>
<td>14 days</td>
<td>Mild</td>
<td>Anal and Nasal swab</td>
<td>8</td>
</tr>
<tr>
<td>Xing et al.</td>
<td>62</td>
<td>02</td>
<td>14 days</td>
<td>Normal</td>
<td>Throat</td>
<td>9</td>
</tr>
<tr>
<td>Xiao et al.</td>
<td>70</td>
<td>15</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>10</td>
</tr>
<tr>
<td>Deng et al.</td>
<td>17</td>
<td>04</td>
<td>3 days</td>
<td>_</td>
<td>Nasal and pharyngeal swab</td>
<td>11</td>
</tr>
<tr>
<td>Li et al.,</td>
<td>13</td>
<td>04</td>
<td>5-15 days</td>
<td>Normal</td>
<td>Feces and Sputum</td>
<td>12</td>
</tr>
<tr>
<td>Yuan et al.</td>
<td>182</td>
<td>20</td>
<td>7-14 days</td>
<td>Normal</td>
<td>pharyngeal and anal swab</td>
<td>13</td>
</tr>
<tr>
<td>Li et al.,</td>
<td>01</td>
<td>01</td>
<td>18 days</td>
<td>Mild</td>
<td>Nasal swabs, sputum, and stool</td>
<td>14</td>
</tr>
<tr>
<td>Zhang et al.</td>
<td>420</td>
<td>35</td>
<td>-</td>
<td>Mild</td>
<td>Nasal, pharyngeal and anal swab</td>
<td>15</td>
</tr>
</tbody>
</table>

Table No.2: Number of studied patients and no. of re-infected patients

<table>
<thead>
<tr>
<th>Variables</th>
<th>Sample Size n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Patients</td>
<td>1,052</td>
</tr>
<tr>
<td>Re-infected Patients</td>
<td>127 (12.1)</td>
</tr>
</tbody>
</table>

References:

5. Lan et al., also reported recurrence of COVID-19 infection in four medical professional patients, who were exposed to COVID-19 during their duties. BMJ 2020;368:m408. PMID: 32005727.
10. Li et al., also reported positive results of SARS-CoV-2 in five patients after discharged from hospital-based on meeting the discharge criteria. J Med Virol 2020. DOI: 10.1002/jmv.25855.

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RECOMMENDATION AND CONCLUSION

This review highlights the recurrence of COVID-19 infection in recovered patients. In the light of this review, it is unclear that the relapse of COVID-19 infection in recovered patients occurred due to re-infection, false-negative reported at discharge, the false-positive result after discharge or patients discharged without full recovery. The relapse of COVID-19 in recovered is considered a more complicated problem as cases of re-infections are also high. Non-human studies revealed recurrence of COVID-19 are not occurred but human trials are yet to determined. It is necessary to avoid false negative and false positive results by performing the coronavirus antibody tests. Moreover, cohort studies of larger sample size are required for recovered patients to understand the recurrence of COVID-19 infection in recovered patients. Furthermore, the development of advanced diagnostic techniques to detect low viral load, monitoring of antibodies, and the importance of other than respiratory samples are essential for recovered patients.

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