

Original Article

Six-Week Hospital-Based Pulmonary Rehabilitation in Covid Pneumonia ICU Survivors: Experience from a Tertiary Care Center in Central India

Alkesh Kumar Khurana¹, Aqeel Hussain¹, Abhishek Goyal¹, Sunaina Tejpal Karnal², Saurabh Saigal¹,
Raj Krishnan Soman¹, Mamta Verma³, Sagar Khadanga⁴, Gaurav Sahu¹, Brijendra Singh⁵

¹Department of Pulmonary Medicine, AIIMS, Bhopal, Madhya Pradesh, India

²Anesthesia & Critical Care, AIIMS, Bhopal, Madhya Pradesh, India

³Department of Nursing, AIIMS, Bhopal, Madhya Pradesh, India

⁴Department of General Medicine, AIIMS, Bhopal, Madhya Pradesh, India

⁵Department of Physical Medicine & Rehabilitation, AIIMS, Bhopal, Madhya Pradesh, India

Cite this article as: Kumar Khurana A, Hussain A, Goyal A, et al. Six-week hospital based pulmonary rehabilitation in covid pneumonia ICU survivors: Experience from a tertiary care center in central india. *Turk Thorac J.* 2022;23(2):89-96.

Abstract

OBJECTIVE: There is very limited data on the usefulness of pulmonary rehabilitation in patients with coronavirus pneumonia who have survived intensive care unit care. The primary aim was to explore the feasibility of conducting a pulmonary rehabilitation program in patients with coronavirus disease-19 pneumonia surviving intensive care. The secondary aim was to study the impact of a hospital-based 6-week pulmonary rehabilitation program on exercise capacity, quality of life, and psychological parameters in these patients. This study was conducted at the Center for Pulmonary Rehabilitation, Department of Pulmonary Medicine of the institute.

MATERIAL AND METHODS A total of 27 patients were enrolled. Among them, 14 patients who completed the desired 12 sessions over 6 weeks constituted the pulmonary rehabilitation group and 13 patients who either did not consent or defaulted within the first 2 weeks were considered as controls. Both groups had assessments at 0 and 6 weeks that included a 6-Minute Walk Test, Incremental Shuttle Walk Test, mMRC Dyspnea Scale, Baseline Dyspnea Index, and Transitional Dyspnea Index, Saint George's Respiratory Questionnaire score, and Depression, Anxiety, Stress Scale-21 score.

RESULTS: Significant improvement in dyspnea by mMRC ($P = .01$) and exercise capacity as measured by 6-Minute Walk Test ($P < .001$) and Incremental Shuttle Walk Test ($P = .025$) was seen in the pulmonary rehabilitation group as compared to the control group. There was no significant improvement in quality of life and psychological parameters (Depression, Anxiety, Stress Scale 21 score) after 6 weeks of pulmonary rehabilitation program as measured in our study.

CONCLUSION: Pulmonary rehabilitation is feasible and appears promising in coronavirus disease acute respiratory distress syndrome survivors. However, data from other centers and a larger number of patients are required to imbibe conclusive results.

KEYWORDS: ARDS, COVID, exercise capacity, pulmonary rehabilitation, quality of life

Received: June 10, 2021

Accepted: September 2, 2021

INTRODUCTION

Severe acute respiratory syndrome coronavirus 2 (SARS CoV-2) pandemic is the most critical ongoing global health care problem¹ Globally, as of May 19, 2021, there have been 163 869 893 confirmed cases of coronavirus disease-19 (COVID-19), including 3 398 302 deaths, reported to World Health Organization (WHO).² The course of COVID-19 infection is variable and unpredictable with most patients experiencing mild illness and spontaneous recovery, but a subgroup of individuals require hospitalization for pneumonia that may vary in severity from mild hypoxemic respiratory failure to acute respiratory distress syndrome (ARDS).³ The transmission mechanisms and pathophysiology of COVID-19 have been studied extensively, and strategies to prevent the infection and effectively treat the disease have been devised. As a result, different vaccines have been approved within a year of the pandemic for the prevention of COVID-19 infection and its complications. The progress in the understanding of the treatment strategies has culminated in the formulation of effective treatment guidelines by various organizations like WHO, European Respiratory Society, and Surviving Sepsis Campaign Group.⁴⁻⁶ The most beneficial intervention regarding decreasing mortality has been the use of steroids in appropriate settings.⁷ The follow-up of the patients recovering from COVID-19 deserves equal attention as little is known about the sequelae of the COVID-19 and their management.

As we know that COVID-19 shares characteristics with the SARS including angiotensin-converting enzyme-2 (ACE2)-dependent cellular entry and interleukin-6 (IL-6)-driven hyper-inflammation and ARDS,³ it was anticipated that long-term complications similar to SARS pneumonia could be seen in COVID-19 survivors. The follow-up of SARS survivors months after infection revealed fibrotic features, including airspace opacification and reticular shadowing in up to 36% of the

Corresponding author: Alkesh Kumar Khurana, e-mail: alkesh.pulmed@aiimsbhopal.edu.in



patients.⁸ A 1-year follow-up study of 97 patients recovering from SARS in Hong Kong showed that 27.8% of survivors had decreased lung function and signs of pulmonary fibrosis.⁹ Previous follow-up studies of H1N1-ARDS have revealed that functional impairment persists in some patients even after 6 months of discharge.¹⁰ Anticipating the risk of lung fibrosis in ARDS survivors in general and COVID-related ARDS in particular, different strategies like antifibrotics and pulmonary rehabilitation (PR) have been reviewed in the context of COVID-19.¹¹

Previous studies in COVID-19 have shown that some percentage of post-COVID-19 patients had persisting symptoms and lung function impairment along with pulmonary abnormalities more than 100 days after the diagnosis of COVID-19.¹² The relevance of PR in any respiratory disease depends on the long-term sequelae and associated symptoms of the disease. Dyspnea and fatigue are the symptoms that have shown significant improvement with PR in interstitial lung disease.¹³ Huang et al¹⁴ recently published results from 6 months of follow-up of a large cohort of more than 1700 patients with COVID-19 from China. The most common residual symptoms at 6 months were fatigue/muscle weakness, anxiety/depression, and sleep disturbances.¹⁴ Hence, they suggested that PR could be helpful in these patients. There is promising literature available regarding the benefit of PR in H1N1 ARDS also as mentioned in a study from Taiwan whereby patients received 2 months PR following H1N1 ARDS and resulted in a normal 6-minute walk distance (6MWD > 80% of predicted value) at 6 months post-discharge.¹⁵ Given the potential benefit PR can have in COVID-19 survivors, guidelines recommend that COVID-19 survivors with a need for rehabilitative interventions at 6-8 weeks following hospital discharge (e.g., multiple treatable traits) should receive a comprehensive rehabilitation program.¹⁶ Extrapolating from the above-mentioned data, we tried to explore the feasibility and effect of PR in the patients of COVID-19 pneumonia with respiratory failure discharged from intensive care unit (ICU) with persistent symptoms.

MATERIALS AND METHODS

In this hospital-based longitudinal study, we enrolled patients of COVID pneumonia with respiratory failure managed in ICU and aimed to study the effect of PR program on outcome parameters such as exercise capacity, level of dyspnea, quality of life (QOL), and mental health status.

MAIN POINTS

- There is hardly any literature about pulmonary rehabilitation (PR) in coronavirus disease (COVID) acute respiratory distress syndrome (ARDS) survivors. To the best of our knowledge, this is the first such paper from the Asian subcontinent.
- A hospital-based PR is very much feasible in COVID ARDS survivors.
- Pulmonary rehabilitation significantly improves the dyspnea index and exercise capacity of such patients as measured by mMRC scale and 6-Minute Walk Test and Incremental Shuttle Walk Test, respectively.

For the assessment of exercise capacity, 6MWD and ISWD were evaluated. The assessment of 6MWD is an established method to evaluate functional exercise capacity in patients with respiratory disease.¹⁷ Also, 6MWD has been shown to be a predictor of survival in patients with chronic respiratory disease, especially COPD.¹⁸ Minimal clinically important difference (MCID) in 6MWD in cardiorespiratory diseases has been described as 54-80 m for cardiorespiratory diseases.¹⁹ Also, ISWT was done alongside, the MCID for which has been reported between 35 and 78 m in different studies.^{20,21}

For the assessment of dyspnea severity, mMRC Dyspnea Scale was used, which is a well-known and practiced scale used to stratify dyspnea in patients with chronic respiratory disease.^{22,23} We also measured the Baseline Dyspnea Index (BDI) and Transitional Dyspnea Index (TDI), which have been used previously to assess the change in perception of dyspnea before and after rehabilitation. Baseline Dyspnea Index values range from 0 to 12, and the lower the score, the worse is the severity of dyspnea. Transitional Dyspnea Index values range from -9 to +9, and the negative values measure the worsening of dyspnea and the positive value indicates improvement in dyspnea. Minimal important change in TDI has been mentioned as change of ≥ 1 unit.²⁴

Saint George Respiratory Questionnaire (SGRQ) is a disease-specific instrument designed to measure the impact on overall health, daily life, and perceived well-being in patients with obstructive airway disease. It consists of 50 items and 3 domains. These include symptoms assessment, daily activities that are limited by breathlessness, impact assessment (social functioning, psychological disturbances), and total score. The scores range from 0 to 100 and higher scores indicate more limitations.²⁵ A mean change score of 4 units is associated with slightly efficacious treatment, 8 units for moderately efficacious change, and 12 units for very efficacious treatment for patients with asthma and COPD.²⁶

Depression, Anxiety, Stress Scale-21 is a 3-part instrument used to measure the severity levels of depression, stress, and anxiety. The tool has been accepted and validated for use in PR programs in COPD.²⁷ Depression scores vary from 0 to 28, anxiety scores vary from 0 to 20, and stress scores vary from 0 to 34, with higher score indicating more severe impairment in the item being evaluated. Scores of 0-9 in the depression item, 0-7 in the anxiety item, and score of 0-14 in the stress item are considered to be normal.

The primary objective was (a) to explore the feasibility of a 6-week PR program in COVID ARDS survivors and the secondary objective was (b) to evaluate the impact of PR on functional capacity, QOL, and mental health indices of COVID-19 ARDS survivors.

The study was carried out at the center for PR in the Department of Pulmonary Medicine of the institute. Approval was sought from Institutional Ethics Committee, and written informed consent was obtained from all participants enrolled in the study. The center for PR is equipped with treadmills and cycle ergometers for aerobic exercises and weights for anaerobic/strength training exercises. The

sessions were supervised by a trained staff as well as a resident doctor. Patients with COVID pneumonia after being discharged from ICU were offered a supervised PR program for 6 weeks consisting of 2 sessions per week. All the patients had a P/F ratio ≤ 200 at least for 1 day during their stay in the ICU. Patients who either did not consent to participate in the program or defaulted within the first 2 weeks (≤ 4 sessions) were enrolled as controls for comparative assessment. Out of these 13 controls, 4 had defaulted within 2 weeks of enrollment and 9 refused to participate. There were no exercise-induced side effects in defaulters. Most common reason to default or not to participate was related to logistics and transportation to the hospital. After going through baseline evaluation, they were called only after 6 weeks for the final assessment

In the PR program, exercise training included a minimum of 2 supervised training sessions per week to all patients. Exercise sessions consisted of 15-30 minutes of both aerobic and anaerobic exercises including a warm-up and cooldown period. Warm-up included a gentle range of motion exercises for both upper and lower limbs with 10-15 repetitions of each exercise. This was followed by endurance training using a treadmill and stationary cycle. Speed of the treadmill was initially set at 70% of the baseline 6MWT speed with a weekly progression of 0.25 km/h in conjunction with the guidance of modified BORG score. Strength training for quadriceps and upper limbs was given using elastic resistance bands, weight cuffs, and dumbbells. Stretching and breathing exercises including diaphragmatic breathing, pursed-lip breathing, and sustained maximal inspiration with a spirometer were also included in each session.

Baseline parameters assessed at the start of the PR program (0 weeks) consisted of a 6MWD, ISWD, spirometry, mMRC score, SGRQ, BDI, and DASS-21 scores. Baseline assessment also comprised echocardiography to rule out any alternative cause of exercise limitation like major cardiac disease, pulmonary hypertension, or pulmonary embolism. The repeat assessment of these parameters along with calculation of TDI was performed after 6 weeks of supervised PR program. All patients were allowed to recover from their illness to an extent where they were able to maintain oxygen saturation above 90% on room air before being enrolled into PR. The

time of enrollment into PR after discharge varied from 1 week to 4 weeks.

Statistical Analysis

We have summarized numerical data using mean and standard deviation and categorical data as count and percentage. For the comparison of numerical parameters across 2 groups, we have used *t*-test or Mann-Whitney *U* test depending upon the distribution of data. Change in scores before and after was calculated and compared between 2 groups. We considered *P* value less than .05 as statistically significant.

RESULTS

A total of 14 patients completed the PR program and 13 patients who either did not give consent or defaulted within 2 weeks of enrollment were taken as controls for this study. Table 1 summarizes the baseline features of both groups. There was a gender difference in PR group with only 1 female and 13 males (*P*-value of .33). Further analysis was not carried out separately for 2 gender groups as only 1 patient in the female group could not be compared with 13 patients in the male group. There was no significant difference in the mean age, mean ICU stays in days, body mass index/fat-free mass index, or proportion of patients on mechanical ventilation/non-invasive ventilation and thus ensuring the homogeneity of the control and PR group.

In our study, significant resolution of the radiologic changes was noted in follow-up computerized tomography (CT) scans of a few patients done in both groups. Figure 1a and b depict pre- and post-intervention CT scans showing significant improvement in a 46-year-old male who underwent PR. Figure 1a shows diffuse ground glass opacities (GGOs) predominantly in lower zones bilaterally, whereas Figure 1b shows complete resolution of these opacities and reveals normal lung parenchyma. Similar improvement is shown in another 36-year-old female who did not opt for enrollment into PR (Figure 1c and d). Figure 1c shows diffusely interspersed GGOs as well as inter and intralobular septal thickening, whereas Figure 1d shows almost complete resolution of these opacities and normal lung parenchyma. The CT findings were almost similar in other patients as well as in both groups. Most of the patients were unable to perform the forced vital capacity (FVC) maneuver as per standards at

Table 1. Baseline Features of Control Group and PR Group

Baseline Feature	Control Group (n = 13)	PR Group (n = 14)	<i>P</i>
Gender			
Male, n (%)	7 (53.8)	13 (92.9)	.33
Female, n (%)	6 (46.2)	1 (7.1)	
Mean (SD) age (years)	56.8 (8.7)	57.6 (10.1)	.7
Mean (SD) BMI (kg/m ²)	26.4 (5.2)	25.0 (2.6)	.6
Mean (SD) FFMI	19.4 (2.7)	19.4 (1.7)	.7
Mean duration of ICU stay in days (SD)	10.76	10.64	>.9
Invasive ventilatory requirement, n (%)	3 (23.1)	4 (28.6)	>.9
NIV/HFNC FiO ₂ requirement, n (%)	10 (76.9)	11(71.4)	>.9

BMI, body mass index; FFMI, fat-free mass index; SD, standard deviation; ICU, intensive care unit.

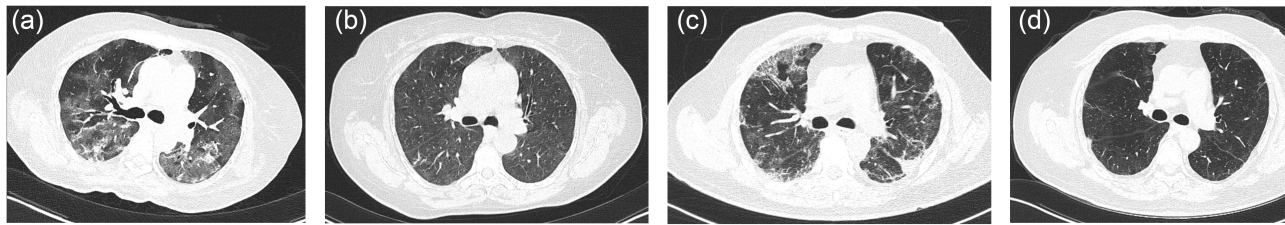


Figure 1. (A) HRCT thorax scan of 46-year-old female after recovery from ICU showing bilateral patchy GGOs predominantly in lower and middle zones (before enrollment into a PR program). (B) HRCT thorax scan of the same patient described in (A) after completion of a 6-week PR program shows marked resolution of the opacities. (C) HRCT thorax scan of 36-year-old male after recovery from ICU showing bilateral patchy GGOs predominantly in lower, middle zones, and subpleural areas. (D) HRCT thorax scan of the same patient described in 2(A) after 6 weeks (without PR intervention) also shows marked resolution of the opacities. ICU, intensive care unit; PR, pulmonary rehabilitation; GGOs, ground glass opacities.

the time of enrollment despite multiple attempts as they had not recovered fully so we could not use pulmonary function tests (PFTs) for comparison on follow-up. Among the patients who were able to perform PFT maneuvers, most of them had moderate restriction on spirometry at the time of enrollment with a mean FEV₁/FVC of 69.3 ± 10.3% in control and 66.3 ± 24.7% in PR group.

Table 2 shows the details of parameters assessed at 0 and 6 weeks in both the groups.

(a) **Exercise Capacity:** Six-minute walk distance was assessed in all patients at initial assessment (0 weeks) and then at 6 weeks (completion of PR program) as per established ATS guidelines.¹⁷ There was no statistically significant difference in the mean baseline values of 6MWD at 0 week in control and PR groups (320.6 m and 329.3 m, respectively). But, the 6MWD values were statistically

and significantly different at 6 weeks in both groups (360.9 m in control group and 496.4 in PR group). Also, the change between 2 groups (40 m and 167.1 m in control and PR group, respectively) was statistically significant with a *P*-value of less than .001, thus highlighting the effect of PR on functional capacity. Also, it needs to be mentioned again that MCID in 6MWD in cardiorespiratory diseases has been reported as 54-80 m, which in our study could be achieved in the PR group.¹⁹ Exercise capacity was also measured via ISWT. There was a mean improvement of 64.9 m in the control group at 0 and 6 weeks, whereas it was 152.5 m in the PR group with the difference between the 2 being statistically significant with a *P*-value of .02 (Figure 2a). To recapitulate, the MCID for ISWD has been reported between 35 and 78 m in previous studies.^{20,21} The improvement was more than MCID in both PR group and control group for ISWD.

Table 2. Changes in Various Parameters Measured at 0 and 6 Weeks

Parameter	0 Week			6 Weeks			Change		
	Mean (SD)		<i>P</i>	Mean (SD)		<i>P</i>	Controls	PR Group	<i>P</i>
	Controls	PR Group		Controls	PR Group				
mMRC	2.1 (0.9)	2.5 (0.5)	.2	0.8 (0.6)	0.5 (0.5)	.3	-1.3 (0.8)	-2.0 (0.6)	.010
6MWD	320.6 (100.6)	329.3 (86.9)	.6	360.9 (97.0)	496.4 (67.9)	.002	40.3 (44.0)	167.1 (82.2)	<.001
ISWD	243.6 (107.2)	218.2 (52.9)	>.9	308.5 (82.1)	370.7 (74.7)	.080	102.3 (101.5)	199.3 (139.1)	.025
SGRQ S	27.1 (15.5)	28.3 (16.8)	>.9	20.9 (13.1)	33.1 (15.9)	.061	-6.2 (15.9)	4.9 (16.0)	.085
SGRQ A	54.2 (22.2)	56.8 (20.6)	.7	34.6 (18.6)	47.2 (14.4)	.072	-19.6 (13.7)	-9.6 (26.4)	.076
SGRQ I	31.0 (24.8)	32.1 (18.2)	.5	21.7 (19.4)	17.7 (13.4)	.8	-9.3 (15.0)	-14.5 (17.6)	.6
SGRQ T	37.4 (20.2)	39.0 (15.6)	.5	25.0 (16.5)	29.2 (11.8)	.2	-12.4 (10.2)	-9.8 (17.2)	.4
DASS S	7.4 (5.4)	6.9 (4.8)	>.9	2.3 (2.3)	6.7 (7.6)	.081	-5.1 (4.1)	-0.1 (6.4)	.030
DASS A	7.2 (5.4)	8.8 (5.2)	.5	3.4 (2.2)	7.6 (8.0)	.14	-3.8 (4.3)	-1.2 (6.3)	.4
DASS D	4.3 (4.5)	6.9 (4.8)	.2	1.8 (2.6)	4.4 (4.4)	.055	-2.5 (3.0)	-2.4 (4.8)	.7
BDI total score	5.9 (1.1)	5.9 (1.6)	.8						
TDI total score	-	-	-	6.6 (1.9)	7.1 (1.6)	.6			

6MWD, 6-Minute Walk Test; SGRQ, significant improvement in quality of life; DASS, Depression, Anxiety, Stress Scale; BDI, Baseline Dyspnea Index; TDI, Transitional Dyspnea Index.

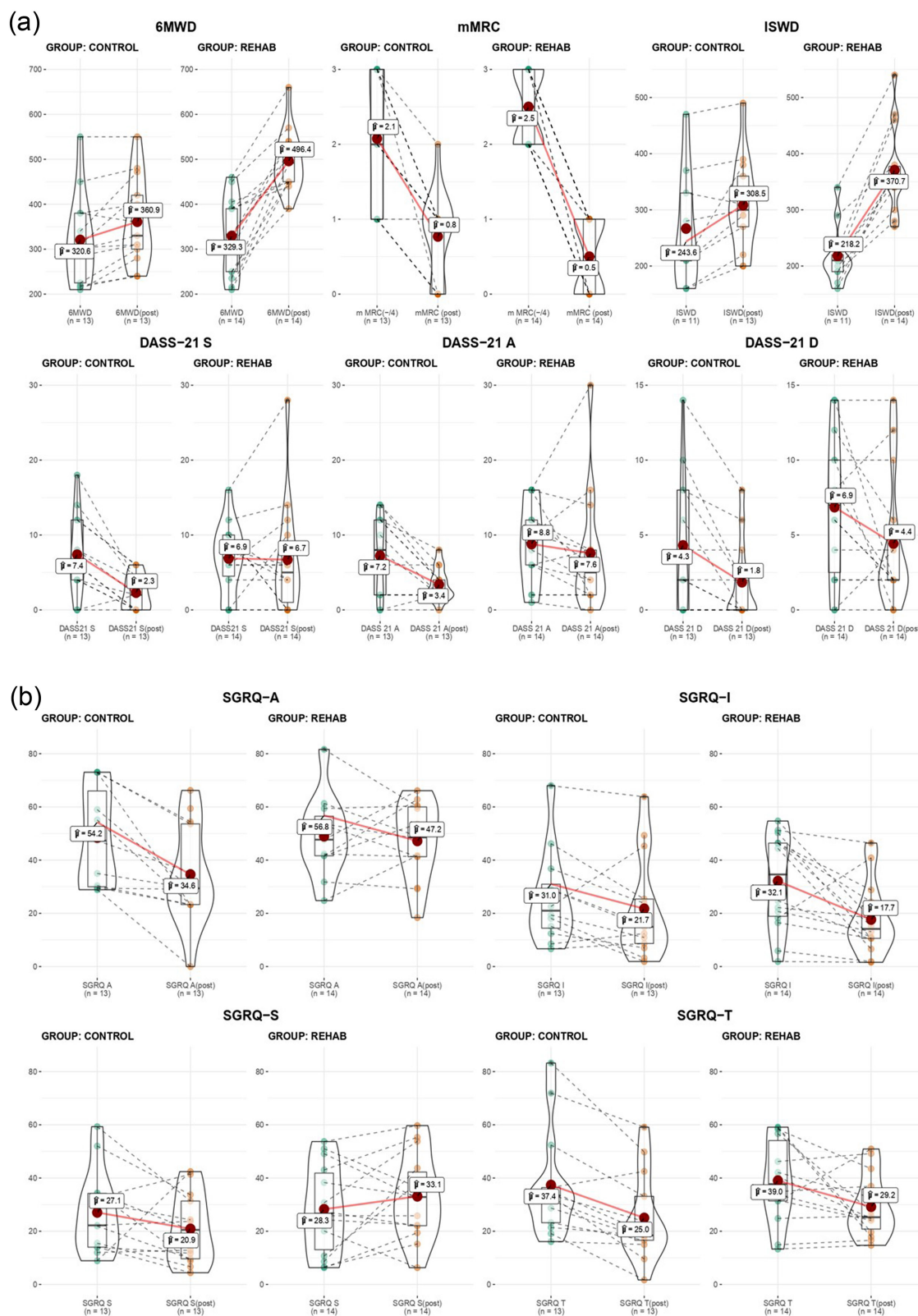


Figure 2. (A) Box violin plot comparing the various parameters namely 6MWD, mMRC, ISWT, DASS-21 stress, DASS-21 anxiety, and DASS-21 depression scores in the control and PR group. The bold line depicts the change in mean values, and the dotted lines reflect the change in individual values in each graph. (B) Box violin plot comparing SGRQ symptom, SGRQ activity, SGRQ impact, and SGRQ total score in the control and PR group. The bold line depicts the change in mean values, and the dotted lines reflect the change in individual values in each graph. 6MWD, 6-Minute Walk Test; DASS, Depression, Anxiety, Stress Scale; ISWT, Incremental Shuttle Walk Test; SGRQ, significant improvement in quality of life.

- (b) *Dyspnea Index*: In our study, mean mMRC score improved from 2.1 to 0.8 in the control group and from 2.5 to 0.5 in the PR group. Mean change in the control group was -1.3 and that in the PR group was -2.0 (Figure 2a). Though dyspnea improved in both groups, the decrease in mMRC score was significantly more in the PR group as compared to the control group with a *P* value of .01. We also measured the BDI and TDI as mentioned in the Methodology section. Change in TDI was 6.6 ± 1.9 in the control group and 7.1 ± 1.6 in the PR group suggesting significant improvement in the perception of dyspnea in both groups. *P* value for change in TDI for PR and control group was .6 suggesting that PR did not confer any additional benefit in this domain if this parameter was used for assessment.
- (c) *Quality of Life*: In the SGRQ symptom assessment, the mean score decreased from 27.1 to 20.9 in the control group but paradoxically and surprisingly increased from 28.3 to 33.1 in the PR group. In the activity and impact domains of SGRQ, there was an improvement in both the control and PR groups, and the difference in improvement between the 2 groups was statically insignificant. The mean score decreased from 54.2 to 34.6 in the control group and 56.8 to 47.2 in the PR group. In the SGRQ impact domain, the mean score decreased from 31.0 to 21.7 in the control group and 32.1 to 17.7 in the PR group. There was no statistically significant difference in the change in the total SGRQ score as well, the change being 37.4 to 25 in the control group and 39 to 29.2 in the PR group. However, the improvement in each component of SGRQ with respect to the baseline values was noticeable in each group individually (Figure 2b).
- (d) *Psychological parameters*: The score in all the 3 items of DASS-21 in our patients was surprisingly normal. The stress score however decreased from 7.4 to 2.3 in the control group and from 6.9 to 6.7 in the PR group. Anxiety score decreased from 7.2 to 3.4 in the control group and from 8.8 to 7.6 in the PR group. Similarly, the change in depression score was from 4.3 to 1.8 in the control group and from 6.9 to 4.4 in the PR group. There was no statistical difference in the change of scores of both depression and anxiety in the 2 groups (Figure 2a). The statistically significant and paradoxical difference in improvement in the stress score of the control group over the PR group is also likely clinically irrelevant, as the 2 groups though having different baseline scores still lied within the normal range of the stress score.

DISCUSSION

The previous literature available about the complications of SARS-related ARDS survivors suggests that these patients do suffer from restrictive lung dysfunction, dyspnea, and impaired QOL as was seen in our study.^{9,28} Similar findings have now been reported in COVID ARDS survivors as well, especially from ICUs. These symptoms have been associated with prolonged bed rest, usage of steroids, and varying degrees of muscle weakness. Persisting symptoms for up to 4-12 weeks after the initial onset have been called as “ongoing symptomatic COVID 19” and those lasting beyond 12

weeks have been now labeled as “Long COVID” or “Post-COVID-19 syndrome.”^{29,30}

Before COVID, PR has been tried in patients of SARS ARDS survivors with promising results. Lau et al³¹ carried out a 6-week PR program in 133 patients of SARS after discharge and noted significant improvement in 6MWD, maximal rate of oxygen consumption, and the strength of some specific muscle groups.³¹ In another small study from China, PR in post-SARS patients helped them attain better dyspnea scores.³² Daynes et al²⁹ very recently not only advocated the feasibility of PR in COVID ARDS survivors based on the 30 patients enrolled in their study but also documented significant improvements above MICDs in exercise capacity and QOL parameters.²⁹ Similar encouraging outcomes have also been published by Gloeckl et al³⁰ who implemented PR in 50 COVID patients, 24 with mild/moderate disease and 26 with severe COVID pneumonia.³⁰

In a recent data on 3 months follow-up of 125 COVID ARDS patients, although abnormal findings were reported in CT scans of 72% patients, fibrotic changes were present in only 21%.³³

In our study, significant improvement with PR was seen in indices measuring dyspnea and exercise capacity as evaluated by mMRC score and 6MWD/ISWD, respectively, though these parameters improved in the control group also. Using mMRC scale, dyspnea improved in both control and PR groups (from 2.1 to 0.8 in the control group and from 2.5 to 0.5 in the PR group), the change in latter being statistically more than the change in the former group. The change was also evident when TDI was used as the measuring index; however, this time the change was insignificant in both control and PR groups (6.6 ± 1.9 and 7.1 ± 1.6 , respectively).

This compels us to mention about a possible component of natural and spontaneous recovery in such patients, which has also been suggested by other authors.²⁹ Similarly, improvements were noted in 6MWD and ISWD in both control and PR groups in our study. The improvement although was more in the PR group, the improvement in the control group nearing MCID also cannot be ignored and again emphasizes at least in part the possibility of spontaneous resolution/recovery in these patients. It needs mentioning that we did not use any antifibrotics in the patients enrolled in this study in either of the 2 groups.

Acute respiratory distress syndrome survivors do demonstrate decrements in QOL after discharge. We assessed QOL by SGRQ that performs better with a 3-month or a 12-month recall as compared to a 1-month recall.^{26,34} However, we need to highlight that we extended the use of this tool within a month after ICU discharge of the patients. The extent of disability in QOL as assessed by the SGRQ total score improved in both our groups with time and PR could not provide any additional benefit. The small number of patients or the inherent nature of the tool designed to use it for a longer recall period is to be considered before interpreting this section of results. In the SGRQ activity and impact domains, there was a minimal and insignificant improvement in both the control

and PR groups. However, in the symptom domain, the mean score decreased in the control group but paradoxically and surprisingly increased in the PR group.

The reason for this paradoxical observation could be that the SGRQ has been traditionally used for chronic respiratory disease and it was extrapolated for the assessment of QOL in a disease of relatively shorter duration. Also, in the symptom domain of SGRQ, more weightage is given to cough and sputum production as compared to functional capacity. Pulmonary rehabilitation offers little benefit in cough and sputum production.³⁵ Exercise-induced bronchoconstriction leading to cough in patients of bronchiectasis can be a cause of this paradoxical observation.³⁶ In a study in patients with bronchiectasis, it was shown that though PR improves dyspnea and fatigue, it does not improve cough-related QOL in patients with bronchiectasis.¹³ Nakazawa et al³⁷ in their review on rehabilitation in interstitial lung disease also mentioned that the efficacy of PR in reducing cough is unclear.³⁷

As with any severe illness, COVID ARDS has its effects on mental health as well. Underlying mechanisms proposed include viral infection, immunological response, corticosteroid therapy, and ICU stay.³⁸ In a study done at Hong Kong in SARS survivors, there was an increase in psychiatric symptoms from 3% to 40% even at 4 years of post-ICU discharge.³⁹ The psychiatric assessment in our patients revealed only mild disturbances, the reason for which we assume to be the positive effect of surviving a severe disease that has caused significant mortality worldwide overshadowing the mild physical and mental impairment associated with it. Also, the significant improvement in dyspnea and exercise capacity with every passing day in most of our patients would have contributed to a positive outlook of our patients toward their disease and a lesser score on the DASS-21 Scale. The further decrease in DASS-21 scores on follow-up in both the groups further endorses the aforementioned assumption. Less number of female participants and small sample size could also have contributed to this paradoxical observation. Another factor to be mentioned is the applicability of this score itself could be questionable because in existing literature this score has been used in COPD patients only, which is a trademark for chronic respiratory disease.

As we now understand, there is still a lack of clarity in the disease outcome patterns of COVID-19. However, since PR is a very cost-effective strategy and has already proven its importance and worth in various other respiratory diseases worldwide, its implementation needs to be extended to a larger needy population in the country including the COVID-19 ARDS survivors.

Limitations

The first limitation is the small number of patients and controls in the study. But, since there is minimal literature available on this subject, especially from the Indian subcontinent, this is the initial experience from our center, and we expect to present and share a larger data in the next few months. Also, in the PR group, we could not ensure gender homogeneity as only 1 out of 14 patients was female. Second, certain tools like SGRQ and DASS-21 have been traditionally used

for chronic respiratory diseases in the past. However, since this study was carried mainly as a feasibility study, the use of these tools was extended to COVID ARDS survivors who had a shorter duration of illness.

CONCLUSION

Pulmonary rehabilitation is feasible in COVID ARDS survivors as 15 out of 19 patients who started the PR successfully completed the program. PR significantly improved the dyspnea and exercise capacity of post-COVID ARDS survivors. But the improvement in the control group was also comparable to MCID mentioned in the literature. However, its benefit in improving perceived dyspnea, QOL, and psychological parameters was not found to be significant in this analysis though these parameters improved with time in both the groups. This signifies the possibility of a relatively fast, self-healing process in these COVID ARDS patients, which brings them to their routine within a few weeks after discharge from the hospital. Thus, the PR program is feasible in this population, and the positive results in the improvement of exercise capacity encourage us to continue recruiting more patients and come out with a larger database in the future.

Ethics Committee Approval: This study was approved by Ethics committee of All India Institute of Medical Sciences Bhopal, India University, (Approval No: IHEC-LOP/2021/IM0333).

Informed Consent: Verbal and Written informed consent was obtained from the patients who agreed to take part in the study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – A.K.K., A.H.; Design – A.K.K., A.H., A.G.; Supervision – A.K.K., M.V., A.G., A.H., B.S.; Resources – A.K.K., A.H., S.T.K., S.S., M.V., G.S., .B.S.; Materials – A.K.K., B.S., A.H., S.K.; Data Collection and/or Processing – A.K.K., S.G., A.G., .S.K., G.S.; Analysis and/or Interpretation – A.K.K., .A.H.; Literature Search – A.H., A.K.K., G.S., S.K.; Writing Manuscript – A.K.K., A.H., S.K., S.S.; Critical Review – A.K.K., A.G., A.H., R.S., S.K., S.T.K.

Declaration of Interests: The authors have no conflict of interest to declare.

Funding: The authors declared that this study has received no financial support.

REFERENCES

1. World Health Organization. *Clinical Management of COVID-19*. WHO; Geneva; 2019. WHO/2019-nCoV/clinical/2020.2015.
2. World Health Organization. Available at: <https://covid19.who.int/>.
3. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet*. 2020;395(10223):497-506. [CrossRef]
4. Lamontagne F, Agoritsas T, Siemieniuk R, et al. A living WHO guideline on drugs to prevent covid-19. *BMJ*. 2021;372:n526. [CrossRef]
5. Chalmers JD, Crichton ML, Goeminne PC, et al. Management of hospitalised adults with coronavirus disease 2019 (COVID-19): a European Respiratory Society living guideline. *Eur Respir J*. 2021;57(4):2100048. [CrossRef]

6. Alhazzani W, Evans L, Alshamsi F, et al. Surviving sepsis campaign guidelines on the management of adults with coronavirus disease 2019 (COVID-19) in the ICU: first update. *Crit Care Med.* 2021;49(3):e219-e234. [\[CrossRef\]](#)
7. RECOVERY Collaborative Group, Horby P, Lim WS, et al. Dexamethasone in hospitalized patients with Covid-19. *N Engl J Med.* 2021;384(8):693-704. [\[CrossRef\]](#)
8. Hui DS, Joynt GM, Wong KT, et al. Impact of severe acute respiratory syndrome (SARS) on pulmonary function, functional capacity and quality of life in a cohort of survivors. *Thorax.* 2005;60(5):401-409. [\[CrossRef\]](#)
9. Hui DS, Wong KT, Ko FW, et al. The 1-year impact of severe acute respiratory syndrome on pulmonary function, exercise capacity, and quality of life in a cohort of survivors. *Chest.* 2005;128(4):2247-2261. [\[CrossRef\]](#)
10. Toufen C, Costa ELV, Hirota AS, et al. Follow-up after acute respiratory distress syndrome caused by influenza A (H1N1) virus infection. *Clinics.* 2011;66(6):933-937. [\[CrossRef\]](#)
11. George PM, Wells AU, Jenkins RG. Pulmonary fibrosis and COVID-19: the potential role for antifibrotic therapy. *Lancet Respir Med.* 2020;8(8):807-815. [\[CrossRef\]](#)
12. Sonnweber T, Sahanic S, Pizzini A, et al. Cardiopulmonary recovery after COVID-19: an observational prospective multicentre trial. *Eur Respir J.* 2021;57(4):2003481. [\[CrossRef\]](#)
13. Lee AL, Hill CJ, Cecins N, et al. The short and long term effects of exercise training in non-cystic fibrosis bronchiectasis - a randomised controlled trial. *Respir Res.* 2014;15(1):44. [\[CrossRef\]](#)
14. Huang C, Huang L, Wang Y, et al. 6-month consequences of COVID-19 in patients discharged from hospital: a cohort study. *Lancet.* 2021;397(10270):220-232. [\[CrossRef\]](#)
15. Hsieh MJ, Lee WC, Cho HY, et al. Recovery of pulmonary functions, exercise capacity, and quality of life after pulmonary rehabilitation in survivors of ARDS due to severe influenza A (H1N1) pneumonitis. *Influ Other Respir Viruses.* 2018;12(5):643-648. [\[CrossRef\]](#)
16. Spruit MA, Holland AE, Singh SJ, et al. COVID-19: interim guidance on rehabilitation in the hospital and post-hospital phase from a European Respiratory Society and American Thoracic Society-coordinated international task force. *Eur Respir J.* 2020;56(6):2002197. [\[CrossRef\]](#)
17. Brooks D, Solway S, Gibbons WJ. ATS statement on six-minute walk test. *Am J Respir Crit Care Med.* 2003;167(9):1287. [\[CrossRef\]](#)
18. Dajczman E, Wardini R, Kasymjanova G, et al. Six minute walk distance is a predictor of survival in patients with chronic obstructive pulmonary disease undergoing pulmonary rehabilitation. *Can Respir J.* 2015;22(4):225-229. [\[CrossRef\]](#)
19. Wise RA, Brown CD. Minimal clinically important differences in the six-minute walk test and the incremental shuttle walking test. *COPD.* 2005;2(1):125-129. [\[CrossRef\]](#)
20. Singh SJ, Jones PW, Evans R, Morgan MD. Minimum clinically important improvement for the incremental shuttle walking test. *Thorax.* 2008;63(9):775-777. [\[CrossRef\]](#)
21. Evans RA, Singh SJ. Minimum important difference of the incremental shuttle walk test distance in patients with COPD. *Thorax.* 2019;74(10):994-995. [\[CrossRef\]](#)
22. Rajala K, Lehto JT, Sutinen E, et al. mMRC dyspnoea scale indicates impaired quality of life and increased pain in patients with idiopathic pulmonary fibrosis. *ERJ Open Res.* 2017;3(4):00084-2017. [\[CrossRef\]](#)
23. Munari AB, Gulart AA, Dos Santos K, et al. Modified Medical Research Council dyspnea scale in GOLD classification better reflects physical activities of daily living. *Respir Care.* 2018;63(1):77-85. [\[CrossRef\]](#)
24. Witek TJ, Mahler DA. Minimal important difference of the transition dyspnoea index in a multinational clinical trial. *Eur Respir J.* 2003;21(2):267-272. [\[CrossRef\]](#)
25. Jones PW, Quirk FH, Baveystock CM, Littlejohns P. A self-complete measure of health status for chronic airflow limitation. The St. George's Respiratory Questionnaire. *Am Rev Respir Dis.* 1992;145(6):1321-1327. [\[CrossRef\]](#)
26. Jones PW. Interpreting thresholds for a clinically significant change in health status in asthma and COPD. *Eur Respir J.* 2002;19(3):398-404. [\[CrossRef\]](#)
27. Yohannes AM, Dryden S, Hanania NA. Validity and responsiveness of the depression anxiety stress scales-21 (DASS-21) in COPD. *Chest.* 2019;155(6):1166-1177. [\[CrossRef\]](#)
28. Ng CK, Chan JWM, Kwan TL, et al. Six month radiological and physiological outcomes in severe acute respiratory syndrome (SARS) survivors. *Thorax.* 2004;59(10):889-891. [\[CrossRef\]](#)
29. Daynes E, Gerlis C, Chaplin E, Gardiner N, Singh SJ. Early experiences of rehabilitation for individuals post-COVID to improve fatigue, breathlessness exercise capacity and cognition - a cohort study. *Chron Respir Dis.* 2021;18:14799731211015691. [\[CrossRef\]](#)
30. Gloeckl R, Leitl D, Jarosch I, et al. Benefits of pulmonary rehabilitation in COVID-19: a prospective observational cohort study. *ERJ Open Res.* 2021;7(2):00108-2021. [\[CrossRef\]](#)
31. Lau HM-C, Ng GY-F, Jones AY-M, et al. A randomised controlled trial of the effectiveness of an exercise training program in patients recovering from severe acute respiratory syndrome. *Aust J Physiother.* 2005;51(4):213-219. [\[CrossRef\]](#)
32. Huang Z, Wang NH, Lan Y, et al. Rehabilitation for the patients with severe acute respiratory syndrome in remission (in Chinese). *Chin J Rehabil Med.* 2004;10:15-17.
33. González J, Benítez ID, Carmona P, et al. Pulmonary function and radiologic features in survivors of critical COVID-19: a 3-month prospective cohort. *Chest.* 2021;160(1):187-198. [\[CrossRef\]](#)
34. Heyland DK, Groll D, Caeser M. Survivors of acute respiratory distress syndrome: relationship between pulmonary dysfunction and long-term health-related quality of life. *Crit Care Med.* 2005;33(7):1549-1556. [\[CrossRef\]](#)
35. Silverman M, Hobbs FD, Gordon IR, Carswell F. Cystic fibrosis, atopy, and airways lability. *Arch Dis Child.* 1978;53(11):873-877. [\[CrossRef\]](#)
36. Kaplan TA, Moccia G, McKey RM. Unique pattern of pulmonary function after exercise in patients with cystic fibrosis. *Pediatr Exer Sci.* 1994;6(3):275-286. [\[CrossRef\]](#)
37. Nakazawa A, Cox NS, Holland AE. Current best practice in rehabilitation in interstitial lung disease. *Ther Adv Respir Dis.* 2017;11(2):115-128. [\[CrossRef\]](#)
38. Lee AM, Wong JGWS, McAlonan GM, et al. Stress and psychological distress among SARS survivors 1 year after the outbreak. *Can J Psychiatry.* 2007;52(4):233-240. [\[CrossRef\]](#)
39. Leung TYM, Chan AYL, Chan EW, et al. Short- and potential long-term adverse health outcomes of COVID-19: a rapid review. *Emerg Microbes Infect.* 2020;9(1):2190-2199. [\[CrossRef\]](#)