Original article

Impact of comprehensive rehabilitation on functional capacity, fatigue, and quality of life among long-term COVID-19 survivors in resource limited settings - a randomized controlled trial

Impacto da reabilitação abrangente na capacidade funcional, fadiga e qualidade de vida entre sobreviventes de COVID-19 de longo prazo em ambientes com recursos limitados - um ensaio clínico randomizado

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ABSTRACT | INTRODUCTION: Months or even year after COVID 19 infection, patients suffered from persistent symptoms. The present study aimed to evaluate the impact of comprehensive rehabilitation on functional capacity, fatigue, and quality of life in long-term COVID-19 survivors in resource limited settings. **MATERIALS AND METHODS:** Comprehensive rehabilitation comprising of aerobic, strength, balance, flexibility, breathing exercise and education was administered in low-resource settings to patients aged 25-60 years diagnosed with long COVID in this randomized controlled trial. Functional capacity (assessed by six-minute walk test), fatigue (assessed by fatigue severity scale), and quality of life (assessed by EQ-5D-5L) were documented at the baseline and after six weeks in intervention (n=19) and control (n=19) groups. Categorical variables were reported as percentages and continuous variables as mean and standard deviation (SD). Independent t-test was used for the between group comparison and paired t test for within group comparison to establish the statistical significance. A p-value of < 0.05 was considered as statistically significant. Effect size and post hoc power analysis were performed. Effect sizes were interpreted according to the Cohen's classification. **RESULTS:** Significant improvements were observed in fatigue (p = 0.006, effect size = -1.23), EQ-5D-5L index scores (p = 0.007, effect size = -0.73), EQ-5D visual analog scale scores (p = 0.002, effect size = 1.09), and six-minute walk distance (p < 0.0001, effect size = 1.37) following the rehabilitation program. **CONCLUSION:** Comprehensive rehabilitation in low-resource settings effectively enhances quality of life, reduces fatigue, and improves functional capacity among long-term COVID-19 survivors.

KEYWORDS: Exercise Tolerance. Fatigue. Health Related Quality Of Life. Long COVID.

RESUMO | INTRODUÇÃO: Meses ou mesmo anos após a infecção por COVID 19, pacientes continuaram a relatar sintomas persistentes. O presente estudo teve como objetivo avaliar o impacto da reabilitação abrangente na capacidade funcional, fadiga e qualidade de vida em sobreviventes da COVID-19 longa em ambientes com recursos limitados. **MÉTODOS:** Reabilitação abrangente composta por exercícios aeróbicos, de força, de equilíbrio, de flexibilidade, de exercícios respiratórios e de educação foi administrada em ambientes de poucos recursos em pacientes com idades entre 25 e 60 anos com diagnóstico de COVID longa neste ensaio clínico randomizado. Capacidade funcional (avaliada pelo teste de caminhada de seis minutos), fadiga (avaliada pela escala de gravidade da fadiga) e qualidade de vida (avaliada pelo EQ-5D-5L) foram documentadas no início do estudo e após seis semanas de intervenção (n=19) e grupos controle (n=19). As variáveis categóricas foram relatadas como porcentagens e as variáveis contínuas como média e desvio padrão (DP). O teste t independente foi utilizado para comparação entre grupos e o teste t pareado para comparação dentro do grupo para estabelecer a significância estatística. Um valor de p < 0,05 foi considerado estatisticamente significativo. Foram realizadas análises de tamanho de efeito e poder post hoc. Os tamanhos de efeito foram interpretados de acordo com a classificação de Cohen. **RESULTADOS:** Melhorias significativas foram observadas na fadiga (p = 0,006, tamanho do efeito = -1,23), pontuações do índice EQ-5D-5L (p = 0,007, tamanho do efeito = -0,73), pontuações da escala visual analógica EQ-5D (p = 0,002, tamanho do efeito = 1,09) e distância percorrida no teste de caminhada de seis minutos (p < 0,0001, tamanho do efeito = 1,37) após o programa de reabilitação. **CONCLUSÃO:** A reabilitação abrangente em ambientes com poucos recursos melhora efetivamente a qualidade de vida, reduz a fadiga e melhora a capacidade funcional entre os sobreviventes de longa prazo da COVID-19.

PALAVRAS-CHAVE: Tolerância ao Exercício. Fadiga. Qualidade de Vida Relacionada à Saúde. COVID Longa.

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1. Introduction

Following the SARS-CoV-2 pandemic, people faced a formidable new wave: long COVID.[1] Months or even year after infection, up to 50% of patients suffered from persistent symptoms, most notably fatigue, which profoundly affected their functionality, quality of life, and work capacity.[1-3] Young adults and non-hospitalized patients were also impacted, leading to significant societal costs.[4]

Long COVID is documented as a major clinical challenge limiting the return to baseline health of a substantial number of people following SARS-CoV-2 infection.[5,6] Few studies on rehabilitation have been published[7,8], however, further studies are needed to determine the optimal protocol, duration, and cost-effectiveness of such rehabilitation efforts.

To the best of our knowledge, there is a scarcity of literature concerning rehabilitation protocols to improve fatigue, functional capacity, and quality of life in such patients, especially in low resource settings.

The aim of the study was to assess the potential changes in functional capacity, fatigue, and quality of life in long term survivors of COVID 19 in resource limited settings. We proposed the hypothesis that comprehensive rehabilitation will have significant difference between groups on fatigue, functional capacity, and quality of life among long term survivors of COVID-19.

2. Methodology

2.1 Ethical clearance

The study was conducted at an OPD of Department of Physiotherapy in India, was approved by the Institutional Ethical committee (CSJMU/IEC/2022/24/06/03) and registered with the Clinical Trials Registry of India (CTRI/2022/07/044517).

2.2 Study Design: Randomised controlled trial

2.2.1 Site, setup and duration

To facilitate cost-effective rehabilitation, minimal equipment's were used. Educational sessions were held in a designated area within the physiotherapy OPD, while an adjacent outdoor corridor was used for walking exercises (Figure 1). Exercises involved body weight, chairs, mats, and paper cones. The study was planned and conducted from March 2022 to August 2023.

2.2.2 Sample size

Assessed by using G*Power software, version 3.1.9.2, with an effect size of 1.61 of quality-of-life scores from a previous study.[7] A type I error of 0.05, and power of 0.90. The required sample size was 14 in each group. Considering 30% drop out, the total sample size required is 38 (19 in each group).

2.2.3 Participants

Participants were recruited via newspaper advertisements and during physiotherapy visits at the OPD. They were informed about the study, and written consent was obtained from all volunteers. A total of 38 participants were recruited.

Figure 1. Site of the study

Corridor used for walking | Area for resting and education session

Source: the authors (2024).

COVID-19 survivors with confirmed real-time polymerase chain rection (RT-PCR) testing aged 25-60 years, diagnosed with long COVID and presenting with persistent or progressive symptoms not requiring hospitalisation or emergency care were recruited for this study. Participants that experienced symptoms lasting at least 2 months within 3 months from the onset of COVID-19 and up to 6 to 12 months post-diagnosis[8], with any of the following symptoms: dyspnoea (assessed by modified MRC dyspnoea scale, score > 2), fatigue (assessed by fatigue severity scale (FSS), score > 36) and rate of perceived exertion (RPE) at rest (assessed by modified Borg scale, score >3). Exclusion criteria encompassed specific medical conditions such as cardiovascular, neurological, diabetes mellitus, hypertension, recent trauma or surgery, pregnancy, lactation, and other respiratory or cognitive impairments that prevented independent functioning.

2.2.4 Randomization and blinding

A computer-generated block randomization method was employed (4x10 block size) using sequentially numbered opaque sealed envelopes. The participants were blinded. Allocation was done 1:1.

2.2.5 Outcome Measures

Outcome measures encompassed the Hindi versions of the Fatigue Severity Scale (FSS)[9] and EQ-5D-5L[10] for fatigue and health-related quality of life, respectively. Secondarily, we assessed dyspnoea at rest and RPE at rest and after 6MWT.

The 6-minute walk test (6MWT)[11] was used for functional capacity assessment. The participants were asked to walk as far down the length of a 30m corridor as they could at their own pace for 6 minutes. Standardised encouragement was provided every 60 seconds during the test, with the following phrases: 'You're doing well' and 'Keep up the good work' in local language.[11,12] We also assessed dyspnoea at rest and rate of RPE at rest and after 6MWT.

2.2.6 Intervention

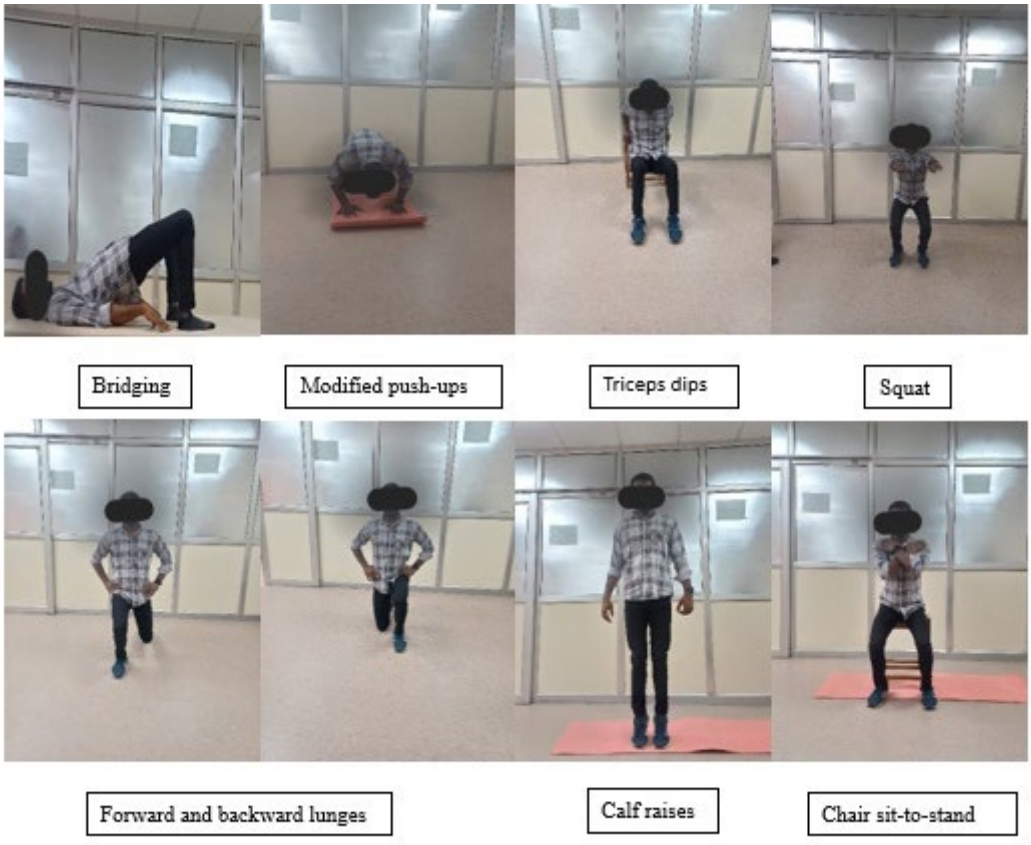
The intervention lasted 6 weeks, with supervised sessions held 3 days a week and self-administered breathing exercises at home on the remaining 2 days, where participants were instructed to maintain a logbook to record their exercises.

The three supervised sessions per week included: the first session focusing on aerobic exercise, breathing exercises, and education; while the second and third sessions incorporated aerobic, strength, flexibility, balance, and breathing exercises.

Participants underwent 30 minutes of supervised ground-based walking, tailored to individual 6MWT results, starting at 80% of their initial 6MWD distance. Walking intensity increased weekly.[13,14] After 3 weeks, a new 6MWT was conducted to adjust intensity with weekly progression. The intensities were calculated and prescribed as per previous reports.[13,14] Participants were educated to cease walking at whatever time they experienced signs such as faintness, blurry vision, or breathing difficulty. Walking intensity was augmented at every week. Initial training distance to be walked in 30 min at 1-week was 80% of 30 m distance, in 2nd week was 90% of 30 m distance, at 3rd week was 100% of 30 m distance. After 3 weeks of walk training, new 6MWT was employed and new 6MWD was sought out. From there, new value was calculated, and walk training for the next week was at 80% of the new distance.[13]

Strength training targeted major muscle groups (shown in figure 2) with initial prescriptions of two sets of 10 repetitions, progressing to three sets in weeks 2-4 and four sets in weeks 4-6.[15]

Figure 2. Strengthening exercise



Source: the authors (2024).

Balance training incorporated stance exercises: single leg and tandem stance with open (30s) and closed eyes (15 sec), and gait training involving walking over obstacles using paper cones. Flexibility exercises included shoulder, side, and thoracic stretches, held for 30-60 seconds per repetition, with 2-4 repetitions per set and 1-2 sets per day.[16]

Breathing exercises, supervised three days a week, included diaphragmatic and pursed lip breathing, with 3 sets of 5 repetitions each. Patients were instructed to continue these exercises independently at home for two additional days per week.

Weekly education sessions provided detailed information on pathology, energy conservation, pacing strategies, techniques for managing breathlessness and fatigue, and adherence to protocols, with participants receiving printed handouts during their initial visit.

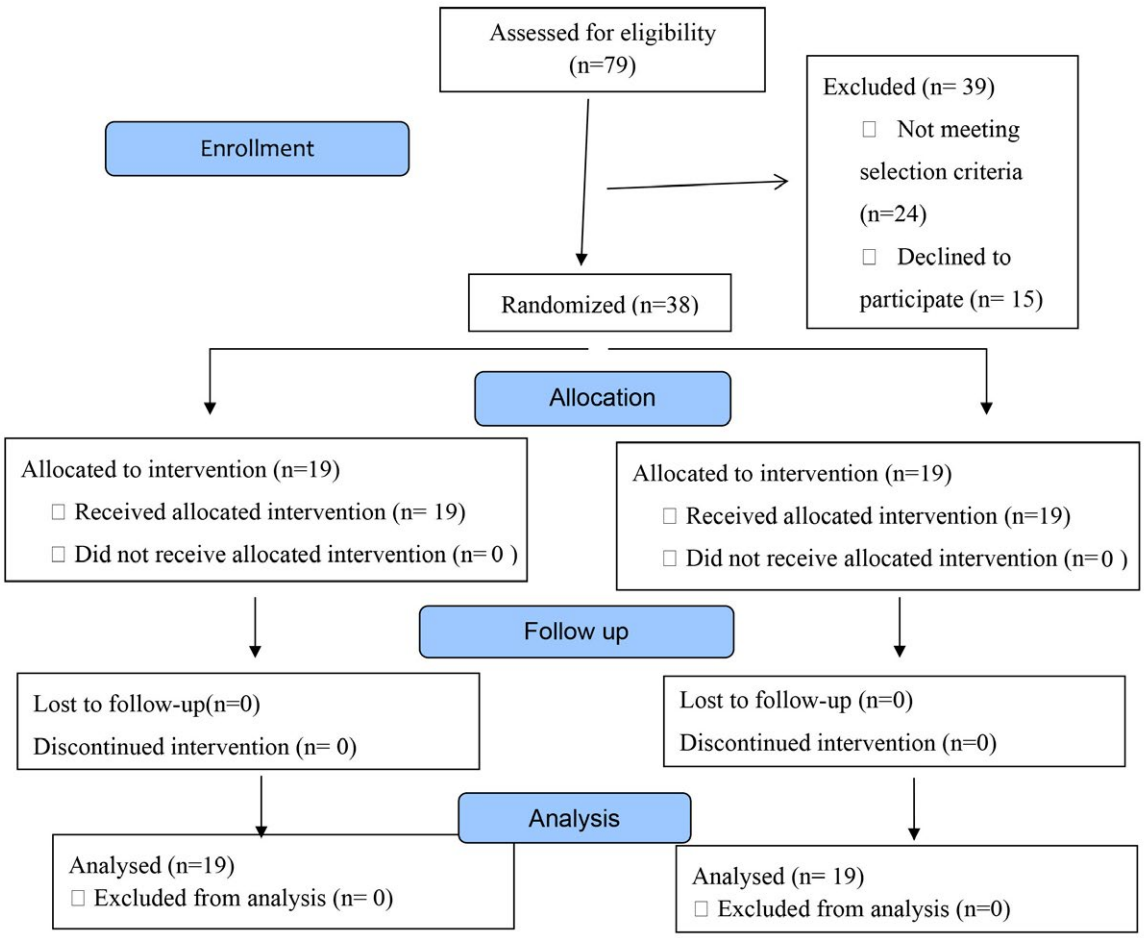
The control group also received instructions and performed breathing exercises in a similar pattern to the intervention group.

2.3 Statistical Analysis

Categorical variables were presented as percentages and continuous variables were presented as mean and standard deviation (SD). Between group comparison was done using the Independent t test and paired t test for within group comparison to establish the statistical significance. A p-value of < 0.05 was considered as statistically significant. Effect size and post hoc power analysis were performed to determine the level of type-II error. Effect sizes were calculated using Cohens 'd formulae: [(M1-M2) ÷ SD Pooled]. Effect sizes were interpreted according to the Cohen's classification: 0.2 =small effect, 0.5 = moderate and 0.8 = large effect.[17]

3. Results

Figure 3. Consort flow chart



Source: the authors (2024).

All the participants completed the study and there were no drop outs. 60.53% (n=23) of the participants were male and 39.47 % (n=15) were female. Figure 3 shows the consort flow chart. Detailed baseline characteristics of the participants recruited are displayed in Table 1. The data was homogeneous at the baseline.

Table 1. Baseline characteristics of the participants

Demographic Characteristics	Intervention Group (n=19)	Control Group (n=19)
Age (years)	34.36.±8.15	37.42.±10.19
Height (m)	1.58±0.05	1.6±0.06
Weight (Kg)	56.94±4.83	57.47±5.23
Body Mass Index (Kg/m^2)	22.41±2.02	22.48±2.04
Weight circumference (cm)	86.63±10.67	86.47±11.09
Hip circumference (cm)	95.63±6.05	91.89±8.76
Waist Hip ratio	0.89±0.59	0.93±0.04
Gender (males) (%)	57.89 (11)	63.16 (12)
Physiological characteristics		
Resting Heart Rate (bpm)	85.42±5.93	86.47±11.09
Resting Systolic Blood pressure (mmHg)	115.74±5.46	115.63±5.47
Resting Diastolic Blood pressure (mmHg)	82.1±4.36	82.63±3.99
Resting oxyhaemoglobin saturation (%)	97.05±1..08	97.11±1.10
COVID 19 characteristics		
Mild (%)	36.84 (7)	42.10 (8)
Moderate (%)	52.63 (10)	47.36 (9)
Severe (%)	5.26 (1)	5.26 (1)
Critical (%)	5.26 (1)	5.26 (1)
Time to rehabilitation after confirmed COVID-19 (months)#	10.10 ±1.15	9.68 ±1.20
Sign and symptoms of long COVID		
Fatigue (%)	63.16 (12)	68.42 (13)
Dyspnoea (%)	31.58 (6)	36.84 (7)
Rate of perceived exertion (%)	31.58 (6)	26.31 (5)
Difficulty walking long distances (%)	10.53 (2)	10.53 (2)
Difficulty moving around your home (%)	36.84 (7)	31.58 (6)
Other symptoms (%)	21.05 (4)	26.31 (5)

Data are presented as mean ± standard deviation (SD) and percent (frequency) otherwise stated.
Source: the authors (2024).

Significant improvements were observed in functional capacity fatigue, with improvement of quality of life values after six weeks of rehabilitation (Table 2) with large effect (>8) on fatigue, six-minute walk distance (6MWD), EQ-5D-5L VAS, dyspnoea and RPE. The EQ-5D-5L index scores showed medium effect of the intervention. Post-hoc power analysis was performed. From Table 2, it is evident that the study is adequately powered for the outcome measures, fatigue (96%), 6MWT (98%), and EQ 5D EL VAS (90%) and dyspnoea (93%).

Table 2. Comparison of outcome measures between groups

Variable	Time points of outcome assessment	Intervention Group Mean±SD	Control Group Mean±SD	P value	Effect size between the group+	Power
Fatigue severity scale score	Baseline	37.26±8.7	36.63±8.24	0.820		
	Post-test	21.31±6.69	30.63±8.36	0.006*	-1.23#	0.96
EQ-5D-5L index scores	Baseline	0.64±0.15	0.63±0.16	0.759		
	Post-test	0.74±0.09	0.65±0.15	0.007*	0.73@	0.60
EQ-5D-5L visual analogue scale score	Baseline	57.37±5.38	59.58±5.13	0.203		
	Post-test	71. 31±8.63	61.84±4.46	0.002*	1.09#	0.90
Six-minute-walk distance (m)	Baseline	402.73±45.74	400.40±31.06	0.856		
	Post-test	469.00±45.11	414.43±33.97	<0.0001*	1.37#	0.98
Dyspnoea	Baseline	1.89±1.14	2.05±1.22	0.684		
	Post-test	0.53±0.61	1.42±0.90	0.001*	-1.15#	0.93
Rate of perceived exertion at rest	Baseline	2.21±1.03	2.58±0.77	0.220		
	Post-test	0.58±0.51	1.37±0.6	<0.0001*	-1.41#	0.99
Rate of exertion after activity	Baseline	2.79±1.08	2.83±1.05	0.763		
	Post-test	1.05±0.78	1.87±0.89	0.006*	-0.98#	0.84

+ Cohen's d formulae, # large effect, @ medium effect. *P<0.05 is considered significant.
Source: the authors (2024).

The within group effects in intervention and control group are shown in table 3.

Table 3. Comparison of outcome measure within group

Variable	Intervention group Mean Difference Mean±SD	P value	Control group Mean Difference Mean±SD	P value
Fatigue severity scale score	6.74±7.77	0.001*	6.74±7.77	0.001*
EQ-5D-5L index scores	0.14±0.13	<0.0001*	0.017±0.079	0.354
EQ-5D-5L visual analogue scale score	13.52±5.46	<0.0001*	2.26±2.2	0.08
Six-minute-walk distance (m)	66.28±15.17	<0.0001*	14.02±8.56	0.04*
Dyspnoea	1.37±0.76	<0.0001*	0.63±0.49	<0.0001*
Rate of perceived exertion at rest	1.6±0.76	<0.0001*	1.2±0.53	<0.0001*
Rate of exertion after activity	1.74±0.56	<0.0001*	0.85±0.16	0.063

*P<0.05 is considered significant.
Source: the authors (2024).

4. Discussion

This present study is the first study that studied the impact of comprehensive rehabilitation among long term COVID-19 survivors in resource limited settings. Despite the participants of the study being young to middle aged adults with mean age 34.36.+8.15 and 37.42.+10.19 years respectively in experimental and control group experiencing mild to moderate disease, participants reported persistent symptoms such as dyspnoea, reduced exercise capacity, and fatigue (shown in table 1). At baseline, patients reached only approximately 75% of their predicted 6MWD.[18] 65.79% of the participants reported fatigue9 and 28.95% reported dyspnoea.[19] The results of the present study agree with the previous studies identifying long term symptoms in COVID-19 survivors.[1-3] The present study was conducted in India, and there is possibility that declined outdoor activities and physical activity patterns may have been the contributing factors as previous study reported that 57% of the population has failed to comply to the World Health Organization regimen for physical activity.[20,21]

Participants in the intervention group demonstrated significantly reduced fatigue, improved functional capacity, EQ-5D-5L VAS scores, dyspnoea and RPE compared to the control group (Cohen's d effect size >8), indicating a large effect size favouring the intervention.

The improvement in functional capacity and quality of life in the present study was due to the fact that supervised ground-based walking training was tailored to initial 6MWT and supervised by physiotherapists. There is evidence that ground-based walking training is an effective training modality that improves quality of life and endurance exercise capacity in people with pulmonary disease.[22]

The 6MWD had increased from baseline to the end of rehabilitation by 66.27 ±15.17 metres, ($p < 0.0001$) which is larger than the minimal clinically important difference (MCID) of 30.5m.[23] Similar results have been reported in the improvement of functional capacity in a study with three months outpatient rehabilitation among long COVID patients.[7] The exercise capacity has also shown to be improved in a report by authors of a longitudinal quasi-experimental study implementing micro-choice based rehabilitation in long COVID patients.[24]

Patients reported a decrease of 15.05 ± 5.88 points on the FSS ($p < 0.000\ 1$) indicating a clinically significant improvement. These results are in line with the previous reports of rehabilitation on long COVID in normal settings.[7]

Quality of life increased when assessed with the EQ-5D-5L VAS scale by 13.523±5.46 ($p < 0.0001$). The EQ-5D-5L index score increased with 0.14 ±0.13 points ($p < 0.0001$). The improvement in the quality of life in the present study was significant in contrast to a previous study where the results were not significant.[7] The probable reason could be the fact that all our participants filled the EQ-5D-5L questionnaire contrary to the previous report of Nopp et al.[7]

Further, patients improved their level of dyspnoea, RPE at rest and exertion; the values decreased by 1.37 ± 0.76, 1.63 ±0.76 and 1.74±0.56 respectively ($p < 0.0001$).

The results of the present are in line with the findings of a longitudinal study evaluating safety, changes in functional level and sick leave after a micro-choice based group rehabilitation among long COVID.[24]

The longitudinal study showed that the changes were not spontaneous but gradual. However, in the present study we used a study protocol that was customised and tailored to adapt to each patients' needs. Authors from another study reported that three months of outpatient rehabilitation of Long Covid patients showed improvement in dyspnoea, quality of life, fatigue and functional capacity.[7] The present study agrees with both the previous studies, however, the duration was of moderate length, i.e. six weeks. However, in the present study we used a study protocol that was cost-effective, using minimal equipment for the individualised patients' care. Thus, we concluded that adherence to rehabilitation is important and the choice of rehabilitation protocol depends on the several factors including resources, equipment's, facilities and cost.

There has been emphasis on rehabilitation underlining the importance of a patient-centred holistic approach, tailored to individual needs, with education playing a key role.[25] With a focus on patient-centred care, the rehabilitation program included education to improve participant adherence and intervention uptake. Strength training, utilising the patient's own body weight and supervised for intensity progression, yielded positive outcomes. These exercises, including ground-based walking and self-body weight training, are both easily adaptable and economical for community or home use, promoting sustainable exercise habits among participants in the long term. There were no dropouts, no adverse events and patients reported good compliance with unsupervised home breathing exercises, adding to the feasibility of the study.

The control group also showed significant improvements in fatigue, 6MWT, dyspnoea ta rest and RPE ta rest in within group comparison. There is evidence that intervention of pursed lip breathing combined with diaphragmatic breathing effectively promotes pulmonary function and exercise capacity in patients with respiratory impairment.[26] The possible mechanism could be that the effect of pulmonary function facilitates reduction of symptoms of dyspnoea and RPE along with exercising capacity. Also, educational sessions could have improved the adherence and regular uptake of breathing exercises under supervision and at home.

4.1 Clinical Significance

This research underscores the essential role of customised rehabilitation protocols in alleviating long-term COVID-19 symptoms and improving patient outcomes, particularly in resource-constrained settings, with potential applicability of ground-based walking, self-body weight strength training, balance, flexibility, and breathing exercises in community or home settings.

Physical rehabilitation of long COVID is proposed, but there is scarcity of protocols for low resource settings, also, digital rehabilitation has limitations, such as the linguistic barriers, basic knowledge of the internet, and facilities in rural areas, all of which could be important challenges to overcome.[9,27] The present study also underscores the feasibility of implementing such programs effectively in resource-limited settings, thereby enhancing accessibility. Lessons learned from pandemic may now guide health care strategies including exercise training in settings with limited resources.

The main limitations were that the study were that the study was single centred, the outcome assessor was not blinded, and long term follow up of the participants was not done. The sample size was small, but further research should be conducted to investigate transferability to a larger group of patients with long COVID. However, the study underscores the benefits of comprehensive rehabilitation tailored to individual needs for long COVID-19 survivors.

5. Conclusion

A simple and clinically useful exercise program for patients with long COVID can be efficiently and securely applied in settings with low resources.

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Authors contributions

The authors declared that they have made substantial contributions to the work in terms of the conception or design of the research; the acquisition, analysis or interpretation of data for the work; and the writing or critical review for relevant intellectual content. All authors approved the final version to be published and agreed to take public responsibility for all aspects of the study.

Conflicts of interest

No financial, legal, or political conflicts involving third parties (government, private companies, and foundations, etc.) were declared for any aspect of the submitted work (including but not limited to grants and funding, advisory board participation, study design, manuscript preparation, statistical analysis, etc.).

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