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Original Article

Exploring the Interplay: COVID-19 Vaccination's Influence on Long-term Symptoms and Quality of Life in Post-COVID Recovery

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ABSTRACT

Background: More than the newly diagnosed COVID-19, healthcare systems are increasingly dealing with the complex long-term health consequences of individuals who have not entirely recovered from the SARS-CoV-2 infection. This study aimed to assess the prevalence of long-term COVID and the impact of COVID-19 vaccination on this prevalence and health-related quality of life during recovery. **Materials and Methods:** A prospective cross-sectional study was conducted with 624 individuals who had recovered from COVID-19. Demographic information, vaccination status, Long-COVID symptoms, and health-related quality of life were collected. Follow-up assessments were conducted at 6-month and 12-month intervals. **Results:** The prevalence of ongoing symptomatic COVID-19 manifestations was 87.3%. Cough was the most frequently reported complaint, affecting 64.3% of the participants. The prevalence of post-COVID syndrome decreased to 72.1% at 6 months and remained at 73.9% at 12 months, with fatigue (18.6%) and headaches (20.8%) being the most frequently reported symptoms, respectively. At one month, six months, and twelve months after COVID-19 recovery, the average health-related quality of life for individuals was measured to be 0.90 ± 0.13, 0.93 ± 0.11, and 0.94 ± 0.1, respectively. Long-COVID were more prevalent in vaccinated individuals (74.5%) compared to non-vaccinated (69.6%). The health-related quality of life was significantly lower in those who had received the COVID-19 vaccine compared to unvaccinated individuals (0.94 ± 0.1 vs. 0.96 ± 0.07). **Conclusion:** Long-term COVID symptoms decreased, and health-related quality of life improved during recovery. However, COVID-19 vaccination was associated with increased Long-term COVID prevalence and lower health-related quality of life.

Keywords SARS-CoV-2 infection, Long-term COVID-19, Prevalence, Immunization, Quality of life.

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INTRODUCTION

The pandemic caused by the new SARS-CoV-2 virus has been progressively controlled and has entered the endemic stage. More than the newly diagnosed COVID-19, healthcare systems are increasingly dealing with the complex long-term health consequences of individuals who have not entirely recovered from the SARS-CoV-2 infection.[1] Infected individuals present with persistent acute symptoms of COVID-19, despite the lack of detection of viral DNA by Polymerase Chain Reaction (PCR), which is considered a sign of long-term COVID.[1-3] The signs and symptoms of long-term COVID-19 can appear suddenly, they may linger beyond the initial illness, they may change over time, or they could return back.[4] There is increasing evidence indicating that individuals who have recovered from COVID-19 may experience symptoms affecting multiple organ systems.[5,6]

The prevalence of long-term COVID varies widely across studies, ranging from 4.7% to over 90%.[5-8] A higher risk of developing long-term COVID was observed among older individuals, who had a higher body mass index and were female.[9] The burden of long-term COVID in India has received much less attention.[10] There has been a scarcity of studies conducted on COVID-recovered individuals to ascertain the proportion of individuals who continue to experience symptoms post-recovery. Hence, this study was to evaluate the prevalence of long-term COVID and the health-related quality of life among recovered individuals with varying severity levels of COVID-19 in southern India. Additionally, the study aimed to explore the effect of

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COVID-19 vaccines on long-term COVID-19 and the quality of life in this population.

MATERIALS AND METHODS

Study design

Receiving approval from the Adichunchinagiri Hospital and Research Centre's (AH & RC) Institutional Ethical Committee and with the approval number IEC/AH & RC/AC/005/2021, a prospective cross-sectional study was conducted in the rural area of Mandya, India. Registration number CTRI/2021/08/035758 (dated 18/08/2021) has been assigned to the study by the Clinical Trials Registry of India (CTRI).

Participants

The study comprised participants aged 18 and above who had recovered from COVID-19 at least one month before. The reverse transcriptase polymerase chain reaction (RT-PCR) test was used to confirm the diagnosis of COVID-19. The discharge criteria were based on the standardised revised policy published by the Ministry of Health and Family Welfare, Government of India.[11,12] Individuals with pre-existing mental health disorders or chronic diseases such as arthritis, diabetes, asthma, or COPD were not eligible to participate.

Sample size

The study stratified COVID-19-recovered individuals into two categories based on existing literature: the mild/moderate acute COVID-19 group and the severe/critical acute COVID-19 group. Long-term COVID prevalence was estimated at 20% for the mild/moderate group and 50% for the severe/critical group. To determine the necessary sample size, the formula $n= Z^2p(1-p)/(dp)^2$ was employed, with a relative precision of 20% and a 95% confidence interval. This calculation yielded a sample size of 400 for the mild/moderate group and 100 for the severe/critical group, resulting in a total sample size of 500 for the study.

Study Procedure and data collection

The list of individuals diagnosed and discharged with COVID-19 was obtained from the virology laboratory and COVID ward at AH & RC from July 2021 to December 2021, until the list reached a total of 1000 individuals. Individuals who had been diagnosed with COVID-19 at least one month prior were communicated by telephone, provided with a detailed explanation of the study, and requested to participate. Those who showed interest in participating in the study were requested to visit either the Department of Pharmacy Practice or the Adichunchanagiri Clinical Trial Centre at AH & RC. Upon arrival, they were requested to provide their consent to participate in the study and underwent a screening process to assess their eligibility. A physical examination was performed on all participants, including measurements of Blood Pressure (BP), body weight, Body Mass Index (BMI), and oxygen saturation. Demographic information such as gender, age, height, weight, habits, qualifications, occupation, and vaccination status were obtained through face-to-face interviews using a validated data collection form. Furthermore, the study used the same form to captured a wide range of clinical manifestations, including general symptoms like myalgia, fatigue, and alopecia; respiratory symptoms like cough and dyspnoea; cardiovascular symptoms like chest pain and palpitations; neurological symptoms like headache, cognitive impairment, insomnia, paraesthesia, anxiety, and depression; and gastrointestinal symptoms like anorexia and dyspepsia.

The EQ-5D-5L questionnaire (https://euroqol.org/) was administered to all participants to assess their quality of life.[13,14] Two follow-ups were scheduled every six months from the date of enrolment. The EQ-5D-5L questionnaire, physical examination, and clinical symptoms of the individuals were evaluated at each follow-up. Two chances to reschedule their follow-up were provided to participants.

The severity of COVID-19 disease

Based on the signs and symptoms observed, the disease severity was classified as mild when there was no radiographic evidence of pneumonia, moderate when pneumonia was accompanied by fever and respiratory symptoms, severe when the respiratory rate was ≥ 30 breaths per minute, oxygen saturation was ≤ 93% on room air, or PaO2/FiO2 was ≤ 300mm Hg, and critical when respiratory failure required mechanical ventilation or needed intensive care.[15,16]

EQ-5D-5L questionnaire for quality of life

The EuroQol Group created the EQ-5D-5L in 2011 as a tool to measure Quality of Life (QoL). It assesses five aspects of health: mobility, self-care, activities of daily living, pain/discomfort, and anxiety/depression. There are five response levels for each dimension, ranging from no problems to extreme problems. The sum of the coefficients allotted to the dimensions yields the total score, which represents the participant's overall quality of life.[13,14]

Long-COVID

Long-COVID is an umbrella term that includes two distinct conditions: ongoing symptomatic COVID-19 and post-COVID syndrome. Ongoing symptomatic COVID-19 is characterized by persistent symptoms and signs that persist for 4 to 12 weeks after the initial acute COVID-19 symptoms. Meanwhile, "post-COVID syndrome" refers to symptoms and signs that last for more than 12 weeks and are not explained by any other diagnosis.[3,4]

Statistical analysis

The SPSS version 26 software was utilized to conduct statistical analysis. Frequency and percentage were used to present categorical variables such as gender, habits, qualifications,

occupation, vaccination status, clinical manifestations, and EQ-5D-5L assessment. On the other hand, mean and Standard Deviation (S.D) were used to present numerical variables including age, weight, height, and quality of life.

We assessed the data's normality using the Shapiro-Wilk and Kolmogorov-Smirnov tests. Age, Body Mass Index (BMI), and quality of life were compared between the mild/moderate and severe/critical acute COVID-19 recovery groups using one-way ANOVA, independent samples *t*-test, or Mann-Whitney test, depending on the data distribution. Applying the Chi-square or Fisher's exact test allowed for the examination of the relationship between several parameters and long-term COVID. The prevalence rates of post-COVID syndrome and continued symptomatic COVID-19 were compared using the McNemar test. Statistical significance was defined as a *p*-value of 0.05.

RESULTS

Out of the initial list of 1000 individuals, we were unable to contact 107 of them, 153 were excluded due to having co-morbidities, and 86 declined to participate in the study. Therefore, a total of 654 individuals were enrolled in the study. During the study, 18 individuals missed the first follow-up and 12 individuals missed the second follow-up. Thus, a total of 624 individuals completed both the first and second follow-ups (Figure 1). Table 1 described the demographic characteristics of the study participants.

Prevalence of ongoing symptomatic COVID-19

In the study, 87.3% (545) of participants who recovered from COVID-19 reported experiencing at least one persistent symptom. The most frequently reported symptom was cough, affecting 64.3% of participants, followed by fatigue at 59.6%, myalgia at 52.6%, and headache at 31.9%. Other symptoms included lack of concentration (24.7%), insomnia (24.2%), hair loss (20.8%), chest pain (18.1%), anxiety (16.5%), indigestion (13%), anorexia (11.7%), depression (11.5%), dyspnoea (10.6%), and palpitations and paraesthesia, each reported by 5.4% of participants. Headaches, lack of concentration, and anorexia were statistically significantly more prevalent in severe to critical COVID-19-recovered individuals ($p<0.001$) (Table 2 and Figure 2).

Prevalence of post-COVID syndrome

After a six-month recovery period from COVID-19, 72.1% (450) of participants reported experiencing one or more long-COVID-19 symptoms. Fatigue was the most frequently reported symptom, affecting 18.6% of participants, followed by headaches at 15.5%, insomnia at 15.1%, hair loss at 14.1%, and cough at 13.6%. Fatigue, myalgia, hair loss, and insomnia were statistically more prevalent in those recovering from severe to critical COVID-19 ($p< 0.05$) (Table 2).

After a twelve-month recovery period from COVID-19, 73.9% (461 individuals) of the participants experienced one or more long-COVID-19 manifestations. Headaches were the most frequently reported ailment, affecting 20.8% of participants. It was followed by fatigue (19.6%), lack of concentration (18.4%), hair loss (16.7%), insomnia (15.7%). Myalgia and hair loss were statistically more prevalent in those recovering from severe to critical COVID-19 ($p< 0.05$) (Table 2 and Figure 2).

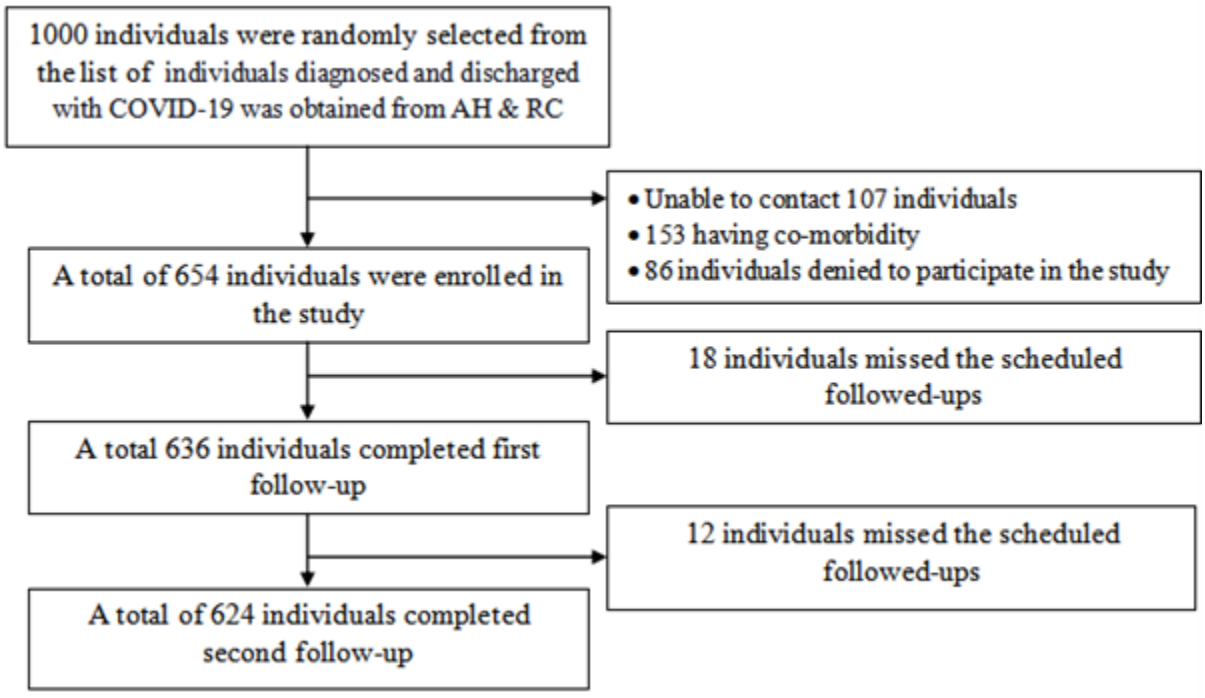

Figure 1: Flow chart of enrolment of study participant.

Table 1: Demographic details of the study participants.

Parameters		Total (N=624)	COVID-19 severity		*p* value
			Mild/moderate (*n*=509)	Severe/Critical (*n*=115)	
Gender	Male	367 (58.9%)	288 (56.6%)	79 (68.7%)	0.017
	Female	257 (41.2%)	221 (43.4%)	36 (31.3%)	
Age in year	Average age (mean ± S.D)	40.25 ± 17.47	43.14 ± 16.56	52.79 ± 14.99	0.000
	Under 45 years	330 (52.9%)	293 (57.6%)	37 (32.2%)	0.000
	45 to 60 years	180 (28.8%)	137 (26.9%)	43 (37.4%)	
	Above 60 years	114 (18.3%)	79 (15.5%)	35 (30.4%)	
BMI (kg/m^2)	Average (mean ± S.D)	22.59 ± 4.82	22.67 ± 5.3	22.37 ± 5.91	0.225
	Underweight	134 (21.5%)	98 (19.3%)	36 (31.3%)	0.005
	Normal weight	325 (52.1%)	279 (54.8%)	46 (40%)	
	Overweight	165 (26.4%)	132 (25.9%)	33 (28.7%)	
Education	No degree	191 (30.6%)	161 (31.6%)	30 (26.1%)	0.706
	Bachelor	308 (49.4%)	247 (48.5%)	61 (53%)	
	Master	103 (16.5%)	83 (16.3%)	20 (17.4%)	
	Ph.D.	22 (3.5%)	18 (3.5%)	4 (3.5%)	
Occupation	Employed	231 (37%)	183 (36%)	48 (41.7%)	0.560
	House makers	52 (8.3%)	41 (8.1%)	11 (9.6%)	
	Retired	65 (10.40%)	57 (11.2%)	8 (7%)	
	Self employed	38 (6.1%)	32 (6.3%)	6 (5.2%)	
	Student	191 (30.6%)	155 (30.5%)	36 (31.3%)	
	Unemployed	47 (7.5%)	41 (8.1%)	6 (5.2%)	
Personal habit	Alcohol	123 (19.7%)	101 (19.8%)	22 (19.1%)	0.862
	Smoking	121 (19.4%)	99 (19.4%)	22 (19.1%)	0.938
	Both Alcohol and Smoking	87 (13.9%)	72 (14.1%)	15 (13%)	0.758

Comparison of the prevalence of long-term COVID-19 symptoms

The prevalence of at least one long-term COVID-19 symptom decreased from 87.3% during ongoing symptomatic COVID-19 to 72.1% at six months post-recovery ($p < 0.001$). This reduction was statistically significant for several symptoms: fatigue (59.6% to 18.6%), myalgia (52.6% to 13%), hair loss (20.8% to 14.1%), cough (64.3% to 13.6%), dyspnoea (10.6% to 6.1%), chest pain (18.1% to 9.5%), palpitations (5.4% to 2.7%), insomnia (24.2% to 15.1%), headache (31.9% to 15.5%), lack of concentration (24.7% to 9%), paraesthesia (5.4% to 3%), anxiety (16.5% to 8%), and indigestion (13% to 7.7%) ($p < 0.05$). However, there were no statistically significant differences in the prevalence of depression (11.5% to 9.6%) and anorexia (11.7% to 9.3%) from ongoing symptomatic COVID-19 to six months post-recovery ($p > 0.05$) (Table 2).

The prevalence of at least one long-COVID symptom decreased from 87.3% during ongoing symptomatic COVID-19 to 65.7% one-year post-recovery ($p < 0.001$). Significant reductions were observed in symptoms such as fatigue (59.6% to 19.6%), myalgia (52.6% to 12.7%), hair loss (20.8% to 16.7%), cough (64.3% to 15.4%), dyspnoea (10.6% to 9.1%), chest pain (18.1% to 10.6%), palpitations (5.4% to 3.7%), insomnia (24.2% to 15.5%), headache (31.9% to 21%), lack of concentration (24.7% to 18.6%), paraesthesia (5.4% to 2.6%), anxiety (16.5% to 9.6%), anorexia (11.7% to 10.3%), and indigestion (13% to 9.8%) ($p < 0.05$). However, there was a significant increase in the prevalence of depression, rising from 11.5% to 12.5% from ongoing symptomatic COVID-19 to the second follow-up after one year of recovery ($p < 0.05$) (Table 2).

Quality of life among individuals recovered from COVID-19

One month after recovering from COVID-19, the average quality of life score for individuals stood at 0.90 ± 0.13. A statistically significant difference was observed between those who had mild to moderate cases and those who experienced severe to critical illness ($p < 0.05$). By the six-month mark, the average quality of life improved to 0.93 ± 0.11, with no significant differences noted

Table 2: Prevalence of long-term COVID at one month, six months, and a year after COVID-19 recovery, and their average health-related quality of life.

Long-COVID		Baseline (V_1)				First follow-up (V_2)				Second follow-up (V_3)				*p* value		
		N (%) (N=624)	Mild/ moderate (*n*=509)	Severe/ critical (*n*=115)	*p* value	N (%) (N=624)	Mild/ moderate (*n*=509)	Severe/ critical (*n*=115)	*p* value	N (%) (N=624)	Mild/ moderate (n=509)	Severe/ critical (*n*=115)	*p* value	V_1 vs V_2	V_1 vs V_3	V_2 vs. V_3
Clinical manifestations	Fatigue	372 (59.6%)	299 (58.7%)	73 (63.5%)	0.350	116 (18.6%)	87 (17.1%)	29 (25.2%)	0.043	122 (19.6%)	100 (19.6%)	22 (19.1%)	0.900	0.000	0.000	0.598
	Myalgia	328 (52.6%)	261 (51.3%)	67 (58.3%)	0.176	81 (13%)	55 (10.8%)	26 (22.6%)	0.001	73 (11.7%)	51 (10%)	22 (19.1)	0.006	0.000	0.000	0.512
	Hair Loss	130 (20.8%)	102 (20%)	28 (24.3%)	0.305	88 (14.1%)	64 (12.6%)	24 (20.9%)	0.021	104 (16.7%)	75 (14.7%)	29 (25.2%)	0.006	0.000	0.014	0.003
	Cough	401 (64.3%)	323 (63.5%)	78 (67.8%)	0.337	85 (13.6%)	75 (14.7%)	10 (8.7%)	0.088	96 (15.4%)	79 (15.5%)	17 (14.8%)	0.843	0.000	0.000	0.145
	Dyspnoea	66 (10.6%)	51 (10%)	15 (13%)	0.341	38 (6.1%)	28 (5.5%)	10 (8.7%)	0.196	37 (5.9%)	29 (5.7%)	8 (7%)	0.606	0.000	0.002	1
	Chest pain	113 (18.1%)	91 (17.9%)	22 (19.1%)	0.753	59 (9.5%)	47 (9.2%)	12 (10.4%)	0.691	61 (9.8%)	54 (10.6%)	7 (6.1%)	0.140	0.000	0.000	0.839
	Palpitation	34 (5.4%)	27 (5.3%)	7 (6.1%)	0.738	17 (2.7%)	13 (2.6%)	4 (3.5%)	0.582	23 (3.7%)	20 (3.9%)	3 (2.6%)	0.497	0.000	0.000	1
	Insomnia	151 (24.2%)	119 (23.4%)	32 (27.8%)	0.315	94 (15.1%)	69 (13.6%)	25 (21.7%)	0.027	98 (15.7%)	79 (15.5%)	19 (16.5%)	0.79	0.000	0.000	0.804
	Headache	199 (31.9%)	133 (26.1%)	66 (57.4%)	0.000	97 (15.5%)	74 (14.5%)	23 (20%)	0.144	130 (20.8%)	105 (20.6%)	25 (21.7%)	0.791	0.000	0.000	0.00
	Lack of concentration	154 (24.7%)	103 (20.2%)	51 (44.3%)	0.000	56 (9%)	43 (8.4%)	13 (11.3%)	0.333	115 (18.4%)	94 (18.5%)	21 (18.3%)	0.959	0.000	0.000	0.000
	Paraesthesia	34 (5.4%)	25 (4.9%)	9 (7.8%)	0.214	19 (3%)	13 (2.6%)	6 (5.2%)	0.133	16 (2.6%)	12 (2.4%)	4 (3.5%)	0.492	0.012	0.005	0.629
	Anxiety	103 (16.5%)	77 (15.1%)	26 (22.6%)	0.051	50 (8%)	40 (7.9%)	10 (8.7%)	0.765	60 (9.6%)	50 (9.8%)	10 (8.7%)	0.711	0.000	0.000	0.134
	Depression	72 (11.5%)	54 (10.6%)	18 (15.7%)	0.126	60 (9.6%)	46 (9%)	14 (12.2%)	0.303	78 (12.5%)	64 (12.6%)	14 (12.2%)	0.907	0.189	0.286	0.057
	Anorexia	73 (11.7%)	44 (8.6%)	29 (25.2%)	0.000	58 (9.3%)	44 (8.6%)	14 (12.2%)	0.239	64 (10.3%)	52 (10.2%)	12 (10.4%)	0.944	0.155	0.456	0.417
	Indigestion	81 (13%)	64 (12.6%)	17 (14.8%)	0.524	48 (7.7%)	35 (6.9%)	13 (11.3%)	0.108	62 (9.9%)	51 (10%)	11 (9.6%)	0.883	0.002	0.088	0.049
	At least one symptom	545 (87.3%)	442 (86.8%)	103 (89.6%)	0.427	450 (72.1%)	363 (71.3%)	87 (75.7%)	0.349	461 (73.9%)	374 (73.5%)	87 (75.7%)	0.632	0.000	0.000	0.278
Quality of life		0.90 ± 0.13	0.91 ± 0.13	0.88 ± 0.15	0.019	0.93 ± 0.11	0.93 ± 0.11	0.91 ± 0.11	0.073	0.94 ± 0.1	0.94 ± 0.1	0.93 ± 0.09	0.48			

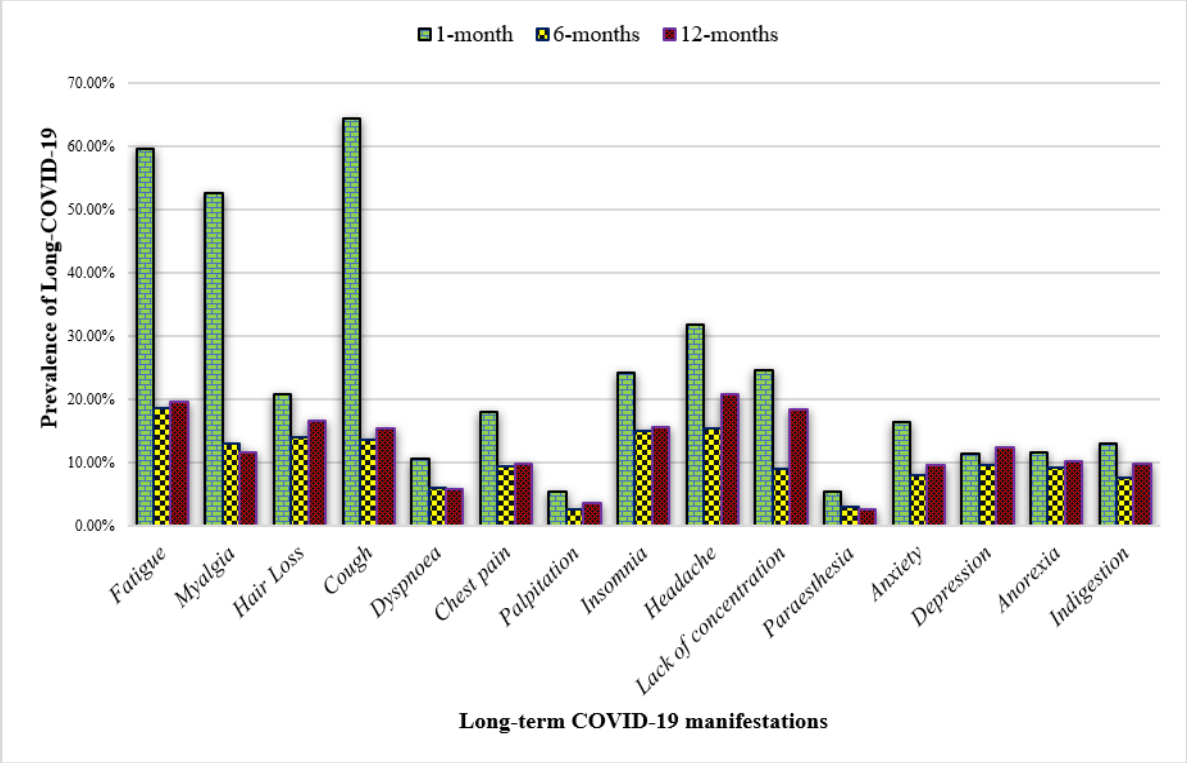

Figure 2: Long-term COVID prevalence at one month, six months, and twelve months after COVID-19 recovery.

between the two groups ($p > 0.05$). After one year of recovery, the quality of life further increased to 0.94 ± 0.10, with no statistically significant differences found between individuals based on the severity of their initial illness ($p > 0.05$) (Table 3).

Impact of vaccination in long-COVID

While vaccinated individuals had a higher incidence of Long-COVID than unvaccinated individuals (74.5% vs. 69.6%), the difference was not statistically significant ($p > 0.05$). Long-COVID incidence was considerably greater among individuals who received a booster dose compared to those who only completed the initial immunisation series or were unvaccinated ($p < 0.05$). Vaccinated individuals had significantly lower quality of life compared to uninfected individuals (0.94 ± 0.10 vs. 0.96 ± 0.07, $p < 0.005$). Those who received a booster dose had an even lower quality of life (0.92 ± 0.11) (Table 4).

DISCUSSION

In this prospective cross-sectional study, our objective is to examine the prevalence and health-related quality of long-term COVID-19 symptoms over a 6- and 12-month period compared to the symptoms experienced within one-month post-COVID-19 recovery and the effect of COVID-19 vaccination on long-term COVID syndrome and health-related quality of life. One month after recovering from COVID-19, the prevalence of long-term symptoms declined from 87.3% (ongoing symptomatic COVID-19) to 72.1% (post-COVID-19 syndrome) and subsequently to 73.9% one-year post-recovery. Huang *et al.*,[17] reported a higher prevalence, and Huang *et al.*[18] reported a lower prevalence of at least one long-term COVID manifestation compared to this study at 6 months from COVID-19 recovery. Similarly, Huang *et al.*,[18] and Fang *et al.*,[19] reported a lower prevalence of at least one long-COVID manifestation than this study in a year from COVID-19 recovery. A potential factor contributing to the decrease in long-term COVID cases could be a reduction in the levels of natural neutralizing antibodies, which may have declined over time. The WHO highlighted the decline in naturally developed neutralizing antibodies after 7 months and urged them to go for COVID-19 vaccination after 6 months of COVID-19 recovery.[14,20,21] The study reveals an increase in the long-term COVID manifestation from six to twelve months after COVID-19 recovery (72.1% vs. 73.9%). All other long-term COVID manifestations significantly decreased, with the exception of depression and anorexia, which persisted from ongoing symptomatic COVID to 6-month post-COVID syndrome and depression, anorexia, and indigestion, which persisted from ongoing symptomatic COVID to 12-month post-COVID syndrome. In the study at 1 year of COVID-19 recovery, 87.33% (545) of the participants were vaccinated with a full or booster dose of the available COVID-19 vaccine. The long-term COVID prevalence appears to be higher in those who received the booster dose (79.4% vs. 69.9% vs. 69.6%) than in those who received the full dosage and were not vaccinated. The increase in neutralizing antibodies following COVID-19 vaccination might be associated with a higher incidence of

Table 3: Assessment of health-related quality of life utilizing EQ-5D-5L questionnaire.

EQ-5D-5L		Baseline		*P* value	First follow-up		*P* value	Second follow-up		*P* value
		Severe to critical (*n*=115)	Mild to moderate (*n*=509)		Severe to critical (n=115)	Mild to moderate (n=509)		Severe to critical (*n*=115)	Mild to moderate (*n*=509)	
Self-care	60.9% (70)	60.9% (70)	68.8% (340)	0.629	78.3% (90)	84.5% (430)	0.093	67.8% (78)	76.6% (390)	0.079
	20.9% (24)	20.9% (24)	15.7% (80)		18.3% (21)	10% (51)		19.1% (22)	14.7% (75)	
	13.9% (16)	13.9% (16)	12.6% (64)		3.5% (4)	4.7% (24)		13% (15)	6.7% (34)	
	1.7% (2)	1.7% (2)	2.8% (14)		0	0.8% (4)		0	1.2% (6)	
	2.6% (3)	2.6% (3)	2.2% (11)		0	0		0	0.8% (4)	
Usual activities	60% (69)	60% (69)	64.6% (329)	0.603	69.6% (80)	83.9% (427)	0.003	61.7% (71)	75% (382)	0.018
	18.3% (21)	18.3% (21)	16.1% (82)		19.1% (22)	8.8% (45)		16.5% (19)	14.1% (72)	
	11.3% (13)	11.3% (13)	11.4% (58)		9.6% (11)	6.7% (34)		13% (15)	7.5% (38)	
	9.6% (11)	9.6% (11)	6.1% (31)		1.7% (2)	0.6% (3)		7.8% (9)	2.9% (15)	
	0.9% (1)	0.9% (1)	1.8% (9)		0	0		0.9% (1)	0.4% (2)	
Pain/ discomfort	57.4% (66)	57.4% (66)	62.3% (317)	0.598	73.9% (85)	83.1% (423)	0.003	60.9% (70)	72.5% (369)	0.029
	20.9% (24)	20.9% (24)	15.9% (81)		20.9% (24)	8.6% (44)		20.9% (24)	11.6% (59)	
	14.8% (17)	14.8% (17)	16.9% (86)		4.3% (5)	7.5% (38)		13.9% (16)	13.2% (67)	
	5.2% (6)	5.2% (6)	3.5% (18)		0.9% (1)	0.8% (4)		4.3% (5)	2% (10)	
	1.7% (2)	1.7% (2)	1.4% (7)		0	0		0	0.8% (4)	
Anxiety/ depression	79.1% (91)	79.1% (91)	81.7% (416)	0.868	86.1% (99)	88.6% (451)	0.569	81.7% (94)	84.1% (428)	0.779
	13.9% (16)	13.9% (16)	10.4% (53)		10.4% (12)	7.1% (36)		12.2% (14)	9.2% (47)	
	4.3% (5)	4.3% (5)	4.5% (23)		3.5% (4)	3.7% (19)		4.3% (5)	4.1% (21)	
	1.7% (2)	1.7% (2)	2% (10)		0	0.6% (3)		1.7% (2)	1.6% (8)	
	0.9% (1)	0.9% (1)	1.4% (7)		0	0		0	1% (5)	

EQ-5D-5L		Baseline		*P* value	First follow-up		*P* value	Second follow-up		*P* value
		Severe to critical (*n*=115)	Mild to moderate (*n*=509)		Severe to critical (n=115)	Mild to moderate (n=509)		Severe to critical (*n*=115)	Mild to moderate (*n*=509)	
Mobility	73 (63.5%)	73 (63.5%)	68.6% (349)	0.332	73% (84)	82.1% (418)	0.67	67.8% (78)	75.6% (385)	0.041
	16.5% (19)	16.5% (19)	17.5% (89)		16.5% (19)	13.2% (67)		13.9% (16)	15.5% (79)	
	11.3% (13)	11.3% (13)	50 (9.8%)		7.8% (9)	3.3% (17)		13% (15)	6.3% (32)	
	5.2% (6)	5.2% (6)	2.4% (12)		2.6% (3)	1.4% (7)		4.3% (5)	2.4% (12)	
	3.5% (4)	3.5% (4)	1.8% (9)		0	0		0.9% (1)	0.2% (1)	
Quality of life		0.88 ± 0.15	0.91 ± 0.13	0.019	0.91 ± 0.11	0.93 ± 0.11	0.073	0.93 ± 0.09	0.94 ± 0.1	0.48

Table 4: Impact of COVID-19 vaccination on long-term COVID manifestation.

Parameters		Vaccination Status		*p* value	Vaccination Status			*p* value
		Yes	No		Full dose	Booster dose	No	
Severity of COVID-19	Mild to Moderate (N=509)	443 (87%)	66 (13%)	0.628	224 (44%)	219 (43%)	66 (13%)	0.736
	Severe to Critical (N=115)	102 (88.7%)	13 (11.3%)		55 (47.8%)	47 (40.9%)	13 (11.3%)	
Long-COVID syndrome (N=624)	Fatigue	108 (19.8%)	14 (17.7%)	0.661	54 (19.4%)	54 (20.2%)	14 (17.9%)	0.9
	Myalgia	68 (12.5%)	5 (6.3%)	0.112	33 (11.8%)	35 (13.1%)	5 (6.3%)	0.252
	Hair Loss	93 (17.1%)	11 (13.9%)	0.484	44 (15.8%)	49 (18.4%)	11 (13.9%)	0.555
	Cough	84 (15.4%)	12 (15.2%)	0.959	42 (15.1%)	42 (15.8%)	12 (15.2%)	0.971
	Dyspnoea	33 (6.1%)	4 (5.1%)	0.727	17 (6.1%)	16 (6%)	4 (5.1%)	0.94
	Chest pain	54 (9.9%)	7 (8.9%)	0.77	25 (9%)	29 (10.9%)	7 (8.9%)	0.716
	Palpitation	15 (2.8%)	2 (2.5%)	0.91	7 (2.5%)	8 (3%)	2 (2.6%)	0.932
	Insomnia	87 (16%)	10 (12.7%)	0.449	36 (12.9%)	51 (19.2%)	10 (12.7%)	0.098
	Head Ache	115 (21.1%)	16 (20.3%)	0.863	61 (21.9%)	54 (20.2%)	16 (20.5%)	0.89
	Lack of concentration	107 (19.6%)	8 (10.1%)	0.042	53 (19%)	54 (20.2%)	8 (10.3%)	0.129
	Paraesthesia	14 (2.6%)	2 (2.5%)	0.984	7 (2.5%)	7 (2.6%)	2 (2.5%)	0.996
	Anxiety	53 (9.7%)	7 (8.9%)	0.808	27 (9.7%)	26 (9.8%)	7 (8.9%)	0.97
	Depression	71 (13%)	7 (8.9%)	0.295	29 (10.4%)	42 (15.8%)	7 (8.9%)	0.094
	Anorexia	56 (10.3%)	8 (10.1%)	0.968	26 (9.3%)	30 (11.3%)	8 (10.1%)	0.752
	Indigestion	54 (9.9%)	7 (8.9%)	0.77	27 (9.7%)	27 (10.2%)	7 (8.9%)	0.942
	At least one	406 (74.5%)	55 (69.6%)	0.357	195 (69.9%)	212 (79.4%)	54 (69.6%)	0.025
Quality of life (mean ± S.D)		0.94 ± 0.1	0.96 ± 0.07	0.006	0.95 ± 0.09	0.92 ± 0.11	0.96 ± 0.07	0.000

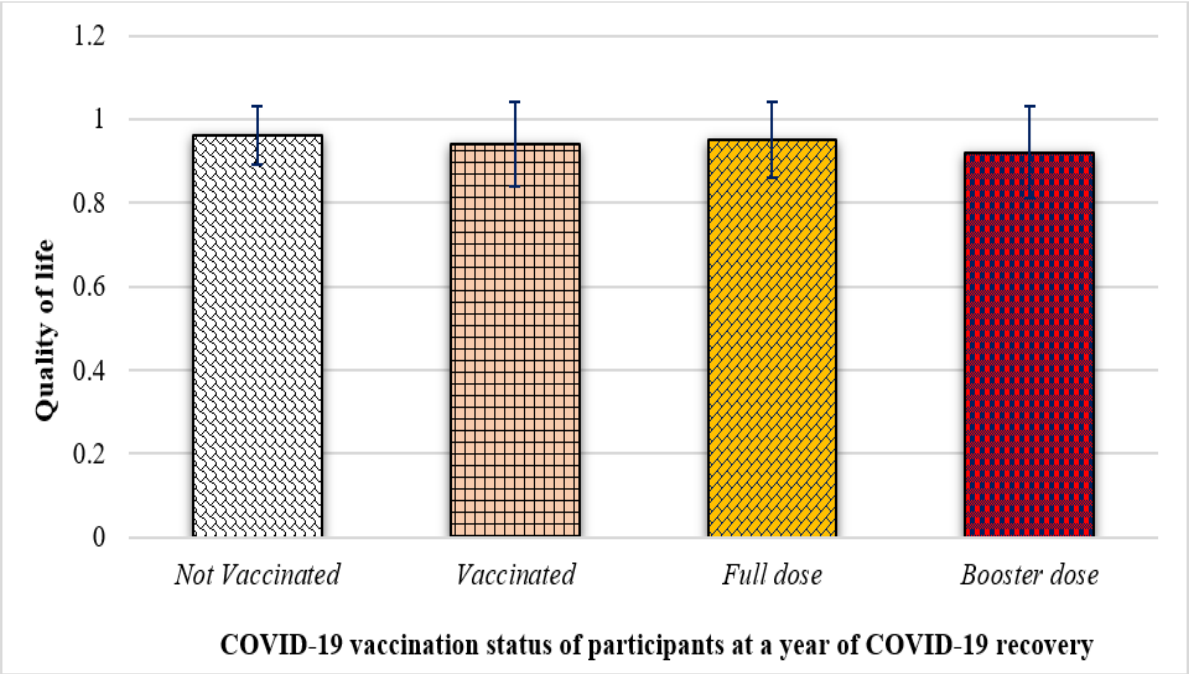

Figure 3: Impact of COVID-19 vaccination on quality of life.

long-term COVID. Previous studies by Peghin *et al.* and Tsuchida *et al.* have reported elevated immunogenicity, antibody titers, and reactogenicity in individuals with a history of COVID-19 infection.[22,23]

The main ongoing symptomatic COVID-19 manifestations of individuals were cough, fatigue, myalgia, and headache. Fatigue, headaches, insomnia, and hair loss were the main post-COVID syndromes six months after recovery, and headache, fatigue, lack of concentration, and hair loss were the main post-COVID syndromes a year of COVID-19 recovery. Similar to the findings of this study, Indian researchers reported myalgia, fatigue, shortness of breath, and headache as the primary persistent symptoms.[2,24]

The study found that the COVID-19 recovered individuals experienced a gradual improvement in their QoL between the baseline and the follow-up periods of six and twelve months (0.90 ± 0.13 vs. 0.93 ± 0.11 vs. 0.94 ± 0.1) (Table 2 and Figure 3). The QoL among mild to moderately COVID-19-recovered individuals was significantly higher than severe to critical at a month post-COVID-19 recovery (0.91 ± 0.13 vs. 0.88 ± 0.15, p <0.05) (Figure 3). There were no significant differences in QoL between illness severity at 6 and 12 months post-COVID-19 recovery (p >0.05). Arab-Zozani *et al.*, reported a lower QoL compared to this study; however, it is important to note that they did not specify the timeframe of their study concerning COVID-19 recovery.[25,26] The analysis of the percentage of individuals reporting problems affecting their QoL in each EQ-5D-5L dimension revealed that pain or discomfort was the most frequent issue reported at one month, mobility at six months, and pain or discomfort again at twelve months after recovery. The findings reported in the study by Huang *et al.*[18] were consistent with the findings of the present study. In each of the EQ-5D-5L dimensions, anxiety or depression emerged as the most often reported problem by Arab-Zozani *et al.* and Nguyen HC *et al.*,[25,26] The study found that individuals who had received the COVID-19 vaccination demonstrated a lower QoL in comparison to not vaccinated (0.94 ± 0.1 vs. 0.96 ± 0.07). Individuals who had received a booster dosage show this pattern even more (0.92 ± 0.11). This indicates that receiving the COVID-19 vaccination affects QoL.

The strength of our study is that individuals with comorbidities were excluded, reducing the chance of symptom overlap for long-term COVID manifestations. Additionally, we specifically evaluated the influence of COVID-19 vaccinations on long-term COVID symptoms and health-related quality of life among individuals who had previously recovered from COVID-19.

Our research has several limitations since it is single-centric which only covers a small portion of Southern India. The generalizability of our findings to larger groups may be limited as a result. Additionally, we did not specifically focus on acute COVID-19 symptoms or the persistence of these symptoms as ongoing manifestations in our study. We may have identified the persistent COVID-19 symptom from the newly emerging long-term COVID manifestation by looking at the acute COVID-19 symptoms.

CONCLUSION

The prevalence of long-term COVID-19 symptoms was notable, affecting 87.3% of patients after one month. However, it decreased to 72.1% after six months and remained relatively unchanged at

73.9% after one year. The main ongoing symptomatic COVID-19 manifestations of individuals were cough, fatigue, myalgia, and headache. Fatigue, headaches, insomnia, and hair loss were the main post-COVID syndromes six months after recovery, and headaches, fatigue, lack of concentration, and hair loss were the main post-COVID syndromes a year after COVID-19 recovery. Individuals who had recovered from COVID-19 experienced a gradual improvement in their health-related quality of life between the baseline and the follow-up periods of six and twelve months. The study also found that individuals who had received the COVID-19 vaccination demonstrated an increase in long-term COVID manifestation and a lower health-related quality of life in comparison to those who had not.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

AH & RC: Adichunchanagiri Hospital and Research Centre; **BP:** Blood pressure; **BMI:** Body mass index; **CTRI:** Clinical Trials Registry of India; **COPD:** Chronic obstructive pulmonary disease; **QoL:** Quality of life; **RT-PCR:** Reverse transcriptase polymerase chain reaction; **SPSS:** Statistical Package for the Social Sciences.

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