

Original Research Article

Comprehensive assessment of short- and long-term clinical outcomes of COVID-19 patients post discharge from a tertiary care designated COVID-19 hospital in South India

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ABSTRACT

Background: The aim of our study was to describe the symptomatology, health consequences and sequelae upto one year after symptom onset among hospital survivors with COVID-19.

Methods: A 3rd, 6th and 12-month follow-up of covid-19 survivors was done between 25-9-2020 and 24-9-2021. A 3rd month follow-up was done by telephonic conversation with the patients or care givers and their responses were recorded. At 6-month and 12-month follow-up visit, survivors were interviewed with questionnaires on symptoms and health related quality of life (HRQoL) and received a physical examination, a 6-minute walking test and other relevant investigations. The primary outcomes were symptoms, modified British Medical Council (mMRC) score, HRQoL and distance walked in 6 minutes (6MWD).

Results: 196 COVID-19 survivors completed both the visits. Median follow-up time was 187 days after symptom onset for 6-month visit and 353 days after symptom onset for 12-month visit. The proportion of patients with at least one sequelae symptom decreased from 143 (73%) at 6 months to 99 (51%) at 12 months ($p < 0.01$), the decrease was observed in all the symptoms studied in the patients. Breathlessness on exertion was the most commonly observed symptom which fell from 133 (68%) at 6 months to 82 (42%) at 12 months (0.001). The proportion of patients with fatigue or muscle weakness fell from 105 (54%) at 6 months to 70 (36%) at 12 months (< 0.01). No significant difference in median 6MWD between 6 months and 12 months was observed.

Conclusions: Most hospital survivors with COVID-19 had a good physical and functional recovery over time but some of the symptoms persisted at 12 months follow-up.

Keywords: COVID-19, HRQoL, 6MinWD, mMRC, Sequelae, Survivors

INTRODUCTION

The COVID-19 pandemic which originated from Wuhan, China in December 2019 and spread worldwide resulting in a pandemic has resulted in a wide spectrum of clinical manifestations ranging from asymptomatic to symptomatic (cold, cough, running nose, fever of varying degrees etc.) to severe acute respiratory illness (SARI), ILI, respiratory failure requiring ICU care and ventilator support to death across all ages. However, the short- and long-term clinical implications and outcomes of the

patients post discharge from the hospital needs to be assessed periodically for the development of any clinical/psychological problems/complications. Long-haul COVID or post-acute sequelae of SARS-CoV-2 infection (PASC) constitutes the continuation or emergence of persistent COVID-19 related symptoms past the time of acute infection with a wide range of symptoms in patients who experienced critically severe, moderate or mild symptoms.^{1,2} While some research links PASC to patients with severe disease, most studies show that PASC is more prevalent among patients with mild or

moderate COVID-19 infection.³⁻⁵ According to the National Institute for Health and Care Excellence (NICE), the definition of Long COVID is the presence of signs and symptoms that develop during or after an infection consistent with COVID-19, continuing for more than 12 weeks, and are not explained by an alternate diagnosis.⁶ These include myalgias, weakness, sleep disturbances, shortness of breath, loss of taste and smell, headaches, physical and psychological disturbances, cognitive impairment.^{7,8} The outcomes of COVID-19 survivors with comorbidities needs to be ascertained by regular assessment of their health condition for development of new health problems/worsening of existing comorbid conditions/re-infection etc. The importance of this study lies in the fact that COVID-19 infection is a new infection worldwide and there are only few studies which follow-up the survivors and assess their health status periodically and report any complications thereafter. It may help formulate rehabilitation measures, policy decisions, resource allocation if any complications do occur among the subjects during the study period (1 year). In such a case the study period may be extended further for 3 to 5 years.

Objectives

To collect data about sequelae symptoms and health status and study the short and long-term (upto 1 year) clinical outcomes of COVID-19 patients post discharge from the hospital.

METHODS

Source of data

Covid-19 survivors discharged from Victoria Hospital attached to BMC and RI.

Methods of collection of data

COVID-19 infected survivors post discharge from the hospital between 25-9-2020 and 24-9-2021 were recruited for this longitudinal, prospective cohort study (1 year follow-up). The demographics, admission/clinical /discharge data and investigation reports of patients were collected from the medical records section. A 3rd month follow-up was done by telephonic conversation with the patients or care givers and their responses were recorded by the counselor. Then the patients were called (telephone, E-mail, SMSs) at selected intervals (6- and 12-months interval) and requested them to attend the outpatient clinic at Victoria Hospital, Department of General medicine. During the 6-month and 12-month follow-up visits, the COVID-19 survivors were interviewed with questionnaires on symptoms and health related quality of life (HRQoL) and received a thorough physical examination, subjected to a 6-minute walk test and the results noted in ACC/AHA standard format along with other necessary investigations. They were required to report their health status post discharge including any

adverse health consequences, reinfection, or development of any new health related issues of both body and mind at the follow-up visits.

Inclusion criteria

Adult (>18 years) COVID-19 survivors (clinically and microbiologically-PCR or radiologically-HRCT confirmed cases) post discharge from the hospital, willing to give consent and attend the hospital OPD for follow-up.

Exclusion criteria

Patients who were lost to follow-up or died or bed bound unable to mobilize or mental disorders.

Methodology

After obtaining institutional ethical committee clearance, the patients were recruited randomly as per inclusion criteria mentioned above and a written informed consent was taken and called at regular intervals by the counsellor for follow-up.

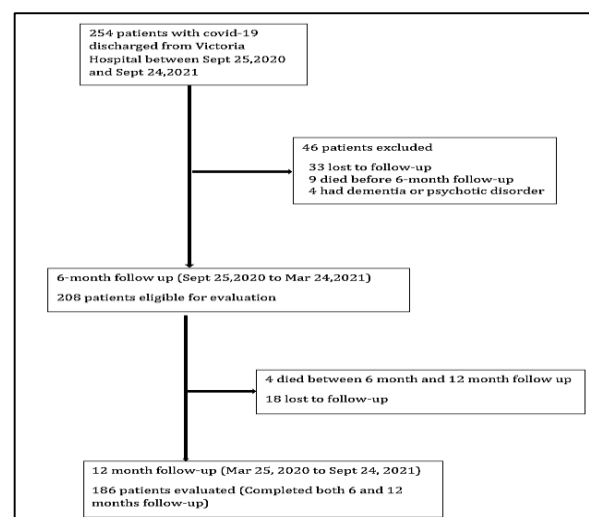


Figure 1: Flow chart of COVID-19 patients.

Flow chart shows above 254 patients with COVID-19 discharged from Victoria Hospital between September 25,2020 and September 24,2021 were recruited for the study. A 3rd month follow-up was done by telephonic conversation with the patients or care givers and their responses were recorded. Patients having symptoms and requiring medical check-up were called to the hospital for further tests or treatment. 196 participants who attended the 6-month and 12-month follow-up visits were included in the final analysis.

Statistical analysis

Demographic characteristics and long-term health consequences of COVID-19 in patients are presented as

median for continuous variables and expressed as absolute values along with percentages as categorical variables. For the comparison of demographic and clinical characteristics among participants chi-square test, Fisher's exact or Mann-Whitney U test were used when appropriate. For the comparison of symptoms, exercise capacity and health-related quality of life between 6-month and 12-month follow-up Wilcoxon signed-rank test or McNemar test were used when appropriate. All significance tests were two sided and a p-value of less than 0.05 was considered statistically significant unless stated otherwise. All statistical analyses were done with SAS (version 9.4).

RESULTS

Table 1 shows the demographic and clinical characteristics of 196 patients who attended both visits. Median follow-up time was 187 days (175-199) after symptom onset for 6-month visit and 353 days (332-374) after symptom onset for 12-month visit.

Table 1: Characteristics of COVID-19 patients who completed both 6-month and 12-month follow-up (n=196).

Variables	N (%)
Age (years)	56 (38-74)
Sex	
Men	112 (57)
Women	84 (43)
Cigarette smoking	
Never smoker	145 (74)
Current smoker	17 (9)
Former smoker	34 (17)
Alcohol abuse	82 (42)
Comorbidity	
Diabetes mellitus	74 (38)
Hypertension	62 (32)
CAD	15 (8)
CVA	12 (6)
Malignancy	8 (4)
COAD	16 (9)
CKD	9 (5)
Treatment received in hospital	
Corticosteroids	120 (61)
Antivirals	122 (62)
Hydroxychloroquine	157 (80)
Antibiotics	161 (82)
Length of hospital stay (days)	12 (9-18)
ICU admission	10 (5%)
Length of ICU stay (days)	15 (8-19)

The median age of patients was 56 years (38-74) and 112 (57%) were men and 84 (43%) women. 10 (5%) patients were admitted to the ICU with a median length of ICU stay of 15 (8-19) days. A significant number of patients were smokers 51 (28%) (current or former) and had

history of alcohol abuse 82 (42%). Diabetes mellitus 74 (38%), hypertension 62 (32%), chronic obstructive airway disease 16 (9%) and coronary artery disease 15 (8%) were the major comorbid conditions reported in the study participants. Majority of the patients received hydroxychloroquine 157 (80%), antibiotics (82%) and supportive measures as they were in the standard treatment protocol and a few also received corticosteroids 120 (61%) and antiviral drugs 122 (62%).

Table 2: Sequelae symptom during 6-month and 12-month follow-up comparison.

Sequelae symptoms	6-month N (%)	12-month N (%)	P value
Breathlessness on exertion	133 (68)	82 (42)	<0.001
Dyspepsia	70 (36)	41 (21)	0.43
Myalgia	82 (42)	47 (24)	0.2
Polyarthralgia	60 (31)	39 (20)	0.14
Headache	23 (12)	17 (9)	0.31
Dizziness	21 (11)	12 (6)	0.04
Taste Disorder	17 (9)	13 (7)	0.1
Chest Pain	13 (7)	9 (5)	0.3
Sleep Difficulties	12 (7)	9 (5)	0.5
Skin rash	13 (7)	8 (4)	0.04
Smell disorder	12 (7)	8 (4)	0.05
Swallowing difficulty	11 (6)	6 (2)	0.06
Decreased appetite	11 (6)	5 (2)	0.01
Low mood or depression	10 (6)	9 (5)	0.02

Table 2 shows the temporal trend in sequelae symptom, health-related quality of life and exercise capacity. The proportion of patients with at least one sequelae symptom decreased from 143 (73%) at 6 months to 99 (51%) at 12 months ($p < 0.01$), the decrease was observed in all the symptoms studied in the patients. Breathlessness on exertion (to usual daily activity) was the most commonly observed symptom which fell from 133 (68%) at 6 months to 82 (42%) at 12 months (0.001). Fatigue or muscle weakness was the next most commonly reported symptom at both visits, but the proportion fell from 105 (54%) at 6 months to 70 (36%) at 12 months (< 0.01). Many symptoms significantly resolved over time in the total cohort (Table 2). Additionally, more patients had anxiety or depression 10 (6%) at 6 months versus 9 (5%) at 12 months ($p = 0.02$), among whom mild anxiety or depression was predominant.

Predicted values were calculated according to the method of Enright and Sherrill (8). The lower limit of the normal range was calculated by subtracting 153 m from the predicted value for men or by subtracting 139 m for women, p value indicates the comparison of consequences between 6 months and 12 months in total or each category of scale.

Table 3 shows that all the patients completed the 6-minute walk test at follow-up, however the proportion of patients with 6MWD less than lower limit of the normal range was 17 (9%) at 12 months which was statistically lower than 19 (10%) at 6 months (p=0.14). No significant difference in median 6MWD between 6 months and 12 months was observed.

Table 3: 6-minute walk test results.

	6-month	12-month	P value
Distance walked in 6-minutes (meters)	479 (438-490)	479 (438-490)	0.01
Percentage of predicted value§	78 (70-89)	84 (74-92)	0.21
Less than lower limit of normal range	19 (10%)	17 (9%)	0.14

Table 4: Modified British Medical Research Council scale.

mMRC score	6-month	12-month
0	3	0
>1	1	1

Table 4 shows the proportion of patients with dyspnoea characterized by mMRC score of 1 or more slightly increased from 39 (20%) at 6 months to 45 (23%) at 12-month visit.

Table 5: Quality of life was assessed using the EuroQol visual analogue scale ranging from 0 (worst imaginable health) to 100 (best imaginable health).

EQ-5D-5L questionnaire¶	6-month	12-month	P value
Mobility	10 (5%)	11 (6%)	0.05
Personal care	4 (2%)	3 (1%)	0.04
Usual activity	4 (2%)	2 (1%)	0.01
Pain or discomfort	37 (19%)	45 (23%)	<0.01
Anxiety or depression	41 (21%)	50 (26%)	0.12
Quality of life	74 (70-79)	76 (70-81)	0.03

Table 5 shows the data of COVID-19 patients who had problems with mobility, pain or discomfort, anxiety or depression and had lower self-assessment scores of quality of life at 12 months compared to the 6 months follow-up visit. Within 12 months after symptom onset two of the 196 patients developed ischemic stroke and one developed acute myocardial infarction.

DISCUSSION

This was a longitudinal cohort study of hospital survivors with covid-19 and describes the recovery and health consequences within 12 months after symptom onset.it

was found that most patients had a good physical and functional recovery during follow-up, however some of the symptoms persisted at 12 months post discharge from the hospital.

A similar study reported the recovery of about 87% of the COVID-19 patients post discharge, persistence of at least one or two symptoms was observed in 32% of the patients while the rest demonstrated three to four symptoms after two months of recovery.⁹ Commonly observed symptoms were fatigue (53%) low health related quality of life (44%), dyspnoea (43%) and arthralgia (27%). Other long term serious consequences were dysregulated sleep-wake cycle, cognitive impairment, profound unremitting anergia and chronic relapses of exhaustion together termed "post-exertional malaise".^{10,11} Any such persisting symptom after recovery from covid-19 should be seriously considered and treated as they may reflect severe post-covid syndrome.¹² Another study reported fatigue (26%), dyspnoea (20%) and muscle pain (8%) to be the most common symptoms present on discharge as well as on one year follow-up. Headache was also found to be a frequent complaint among sufferers that goes along for a more extended period of time that is, 7.5% on discharge and 1.3% after a year.¹³ A study reported dyspnoea and fatigue to be the most common symptoms that were often associated with joint or chest pain.⁶ In addition to these general symptoms, the involvement of major organs like the heart, lung and brain causing myocardial inflammation, myocarditis, cardiac arrhythmias, interstitial thickening and fibrosis, headache, vertigo, encephalitis, seizures, major mood swings and brain fog, have been reported with cases of end-organ damage.¹⁴⁻¹⁶

The sample size was small, attrition among the participants, follow-up of the study participants restricted to one year, subjective responses to questionnaire were some of the limitations.

CONCLUSION

Most hospital survivors with COVID-19 had a good physical and functional recovery over time but some of the symptoms persisted at 12 months follow-up. Ongoing longitudinal follow-up (beyond one year) is needed to better characterise the natural history and pathogenesis of long-term health consequences of COVID-19.

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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee BMC and RI

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