Incidence and predictors of long Covid-19 in hospitalized patients: A cohort study

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ABSTRACT

Background. Long-term Covid-19 symptoms have the potential to negatively impact health and quality of life. We evaluated the incidence and predictors of long Covid-19 among hospitalized patients.

Methods. We prospectively collected clinical data of 393 patients diagnosed as Covid-19 positive and admitted to our hospital. At 1-year follow-up, all vital parameters and laboratory investigations were recorded. A multiple logistic regression model was used to determine predictors of long Covid-19.

Results. Long Covid-19 was found in 34.4% of patients at 1-year follow-up. Most commonly reported symptoms were joint pain (40%), fatigue (33%), and dyspnoea (22.9%). Severity of disease at the time of admission (1.5; 95% Confidence Interval [CI] 1.09–2.2; p=0.01), high body-mass index (BMI) (1.1; 95% CI 1.03–1.13; p=0.003) and increased age (1.02; 95% CI 1.00–1.04; p=0.02) were independent predictors of long Covid-19 on follow-up.

Conclusion. Almost one-third of patients were diagnosed with long Covid-19 at 1-year follow-up. Severity of disease at the time of admission, increased BMI, and increased age were independent predictors of long Covid-19.

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INTRODUCTION

The long-term effects of severe acute respiratory syndrome corona virus 2 (SARS-CoV-2) are frequently denoted interchangeably as long Covid and post-Covid syndrome. Clinical guidelines were proposed for the diagnosis and management of long Covid-19 in April 2021.[1] Most observational studies using patient health records and clinical data show that the prevalence of long Covid following acute SARS-CoV-2 infection is 10%–30%, with signs and symptoms occurring after hospital discharge. Chest pain, fatigue, dyspnoea, hair loss, depression, headache, muscle pain, cough, and joint pain are the most common reported long Covid symptoms.[1–3] Furthermore, long Covid results in a wide range of manifestations, affecting different organs and systems in the body. The presence of co-morbid conditions increases the risk of developing long Covid symptoms.[4] Our aim was to determine the incidence and predictors of long Covid at 1-year follow-up among patients admitted with a diagnosis of Covid-19.

METHODS

In this prospective observational study, we collected clinical data of 393 patients admitted and diagnosed with Covid-19 disease at a tertiary cardiac care hospital from 27th March to 27th May 2021.

Patients diagnosed to have Covid-19 based on a positive reverse transcriptase polymerase chain reaction (RT-PCR) test, radiology, and laboratory findings, and admitted to our institution based on the guidelines of the Government of India, Ministry of Health and Family Welfare, were included in this study.[5] Patients with missing data were excluded.

Their baseline characteristics, laboratory findings, treatment, and outcome data were recorded. We scheduled a follow-up, 1 year after diagnosis of Covid-19 disease at our hospital. Long Covid was defined as the persistence of symptoms beyond 4 weeks of SARS-CoV-2 infection, which are not explained by other causes.[6] Classification of Covid as mild, moderate, and severe was done as per the Ministry of Health and Family Welfare, Government of India.[5]

At the time of follow-up, pulse, blood pressure, temperature, respiratory rate, and peripheral capillary oxygen saturation (SpO_2) were recorded. Electrocardiograms (ECGs) and 2D ECGs were performed on all patients. Additionally, blood was drawn for complete blood count, C-reactive protein, D-dimer, and HbA1c. Lipid profiles were measured using International Federation of Clinical Chemistry (IFCC)—approved enzymatic methods with a commercially available kit on an auto-analyser (ARCHITECH PLUS ci4100, Germany)—Lipid levels were classified according to the classification suggested by the National Cholesterol Education Program (NCEP) and the Adult Treatment Panel III (ATP III) guidelines.[7] The institutional ethics committee approved this study (UNMICRC/Allied/2021/18).

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Statistical analysis

Using SPSS 26.0 software (IBM, Inc., Chicago, IL, USA), the categorical variables were expressed as frequencies (percentages), and the continuous variables were expressed as mean (SD). The Chi-square test was used for categorical variables. Pearson correlation was used to find out the correlation between the variables. A logistic regression model was used in a multivariate analysis. A p-value <0.05 was considered statistically significant.

RESULTS

We found the incidence of long Covid-19 to be 34.4% after hospital discharge at 1-year follow-up. The baseline characteristics and risk factors of the patients are given in Table 1.

At presentation, 37 (9.4%) patients had ground glass opacity, 16 (4.1%) had local patchy, and 77 (19.6%) patients had bilateral patchy consolidation on the chest X-ray. 77 (19.6%) patients had a 'severe' score on computed tomography (CT-SS) of the chest. During the illness, patients were managed in the hospital according to disease severity and many patients received Remdesivir (71.5%) and steroids (65.1%). Tocilizumab (5.1%) and immunosuppressant (3.1%) drugs were also used. At the time of admission, 174 (44.3%) patients required oxygen; 67 (17%) patients were on non-rebreather mask (NRBM) and 7 (1.8%) patients required high flow nasal cannula (HFNC). 35 (8.9%) patients needed bi-level positive airway pressure (BiPap) support.

At 1-year follow-up, 135 (34.4%) patients had post-Covid symptoms. Most patients reported joint pain (40%) and fatigue (33.3%; Table 2).

Other common symptoms were dyspnoea (22.9%), postural orthostatic tachycardia (POTS) (11.1%), hair loss (5.9%), chest pain (4.4%), weakness (3.7%), pedal oedema (2.2%), and mucormycosis (2.2%). New onset hypertension was detected in 32.3% of patients at 1-year follow-up.

Based on the presence of post-Covid-19 symptoms at 1-year follow-up, we classified patients into two groups: those with absence of long Covid (65.6%) and those with long Covid (34.4%) and compared their clinical features (Table 3).

At follow-up, most patients (86%) had a normal ECG (Table 4). 1.8% patients had T-wave inversion, 2.5% had left bundle branch block (LBBB), and 1.8% had right bundle branch block (RBBB). An echocardiogram (Echo) was also obtained. Baseline left ventricular ejection fraction (LVEF) was 55%–60% in the majority of patients (86%). We compared the baseline Echo of patients who had low LVEF: 26 patients (6.6%) had LVEF of 30%–50% at the 1-year examination and 24 (6.1%) had low LVEF even at first hospitalization. Only 2% patients had below 30% LVEF. 14.8% patients had diastolic dysfunction. 82.4% had pulmonary hypertension.

On regression analysis, older age (56.64 years), female gender (39.3%), in-hospital complications (13.3%), presence

TABLE 1. Demographic characteristics and risk factors

Variable	*n*=393 (%)
Mean (SD) age (years)	54.23 (12.7)
Gender	
Male	272 (69.2)
Female	121 (30.8)
Diabetes type 2	112 (28.5)
Hypertension	141 (35.9)
Hypothyroidism	31 (7.9)
Chronic kidney disease	8 (2)
Severe CT severity score	77 (19.6)
Mean (SD) body mass index (kg/m²)	26.70 (4.62)
In-hospital complications	35 (8.9)

CT computed tomography

TABLE 2. Comparison of baseline characteristics and risk factors in long Covid-19 and without long Covid-19

Variable	No long Covid-19	Long Covid-19	p value
	n=258 (%)	*n*=135 (%)	
Mean (SD) age (years)	52.97 (12.71)	56.64 (12.37)	0.006*
Male	190 (73.6)	82 (60.7)	0.009*
Female	68 (26.4)	53 (39.3)	
Diabetes mellitus	64 (24.8)	48 (35.6)	0.03*
Hypertension	86 (33.3)	55 (40.7)	0.18
Chronic kidney disease	5 (1.9)	3 (2.2)	0.85
Smoking	3 (1.2)	4 (3)	0.38
Mean (SD) BMI (kg/m²)	26.16 (4.72)	27.73 (4.26)	0.001*
In Hospital complication	17 (6.6)	18 (13.3)	0.04*
Mean (SD) days of hospitalization	8.06 (4.6)	9.95 (6.09)	0.05
Severity of Covid-19			
Mild	124 (48.1)	50 (37)	0.05
Moderate	118 (45.7)	66 (48.9)	0.63
Severe	16 (6.2)	19 (14.1)	0.02*
Severe CTSS	48 (18.6)	29 (21 .5)	0.58
ICCU admission	8 (3.199)	5 (3.7)	0.98
Requirement of steroid	162 (62.8)	94 (69.6)	0.17
CRP-Q (>5 mg/L)	227 (88)	125 (92.6)	0.21
D-dimer (>500 ng/L)	157 (60.9)	101 (74.8)	0.008*
Truponin-1 (3 UNL)	21 (81)	26 (19.3)	0.002*
HbA1c (>6.5)	78 (30.2)	61 (45.2)	0.005*

* p<0.05 ECG electrocardiogram CTSS computed tomography severity score BMI body mass index
ICCU intensive cardiac care unit CRP-Q C-reactive protein–quantitative UNL upper normal limit

TABLE 3. Electrocardiogram and echocardiographic findings at follow-up (*n*=393)

Item	*n* (%)
Electrocardiogram	
Normal	338 (86)
Sinus tachycardia (>100/minute)	4 (1)
Sinus bradycardia (<60/minute)	13 (3.3)
Left bundle branch block	10 (2.5)
Right bundle branch block	7 (1.8)
T-wave inversion	7 (1.8)
Non-specific ST-T changes	14 (3.6)
Atrial fibrillation	4 (1)
Echocardiography	
Normal LVEF (55% to 60%)	339 (86.3)
LVEF (30% to 50%)	26 (6.6)
Previous echocardiography: Normal	2
Previous echocardiography: Low LVEF (35%)	24
LVEF (≤30%)	8 (2)
Previous echocardiography: Normal	0
Previous echocardiography: Low LVEF (35%)	8
Pulmonary hypertension	324 (82.4)
Diastolic dysfunction	58 (14.8)

LVEF left ventricular ejection fraction

TABLE 4. Symptoms at the time of follow-up (*n*=135)

Symptom	*n* (%)
Joint pain	54 (40)
Fatigue	45 (33.3)
Dyspnoea	31 (22.9)
Chest pain	6 (4.4)
Hair fall	8 (5.9)
Weakness	5 (3.7)
Pedal oedema	3 (2.2)

of diabetes (35.6%), high BMI (27.73 kg/m^2) and severity of Covid-19 disease (14.1%) at the time of admission were significantly associated with the risk of developing long Covid-19. The use of steroids and duration of hospitalization were also higher in the long Covid group but were not significant (Table 5).

We determined the cut-off values for BMI and age from the receiver operating characteristic curve (ROC). Our cut-off value of BMI >25.9 kg/m^2 showed an area under the curve (AUC) of 0.61 (95% CI 0.56–0.66, p=0.0003) with 67.9% sensitivity and 54.4% specificity. At the age of >60 years, the AUC was 0.57 (95% CI 0.52–0.62, p=0.03), with 43% sensitivity and 67.8% specificity, among those who had Covid.

At 1-year follow-up, low haemoglobin was found in 7 (1.8%), raised CRP-Q (>5 mg/L) in 3 (0.8%), and raised D-dimer (>500 ng/L) in 67 (17%) patients. Among the lipid profile were increased level of triglyceride (TG) in 147 (37.4%), high density lipoprotein cholesterol/low density lipoprotein cholesterol ratio (LDL/HDL ratio) in 146 (37.2%), very low-density lipoprotein (VLDL) in 109 (27.7%), cholesterol in 101 (25.7%), total lipids (TL) in 108 (27.5%), low density lipoprotein cholesterol (LDL-C) in 96 (24.4%) and low high-density lipoprotein cholesterol (HDL-C) levels in 200 (50.9%) patients. According to the NCEP guidelines, 73% patients had dyslipidaemia. HbA1c was also increased in 87 (22.1%) patients. New onset of type 2 diabetes was seen in 3.85% of the patients. D-dimer levels were also increased in 67 (17%) patients.

DISCUSSION

This prospective observational study was designed to address post-recovery symptoms in patients who experienced acute symptoms of Covid-19. Many hypotheses have been proposed for the pathophysiology of long Covid, but the mechanism is still unclear.[8]

Long Covid generally manifests as a combination of disorders and complications. People recovering from Covid-19 sometimes show symptoms of a condition called postural orthostatic tachycardia syndrome (POTS). Typical arrhythmias can occur in individuals with Covid, and long-term Covid-19 has been associated with tachycardia. Common symptoms of Covid-19 POTS are tachycardia, headaches, and dyspnoea. A recently published review suggests that POTS is commonly associated with fatigue and connective tissue disorder. Our study found an 11.1% incidence of post-Covid-19 POTS; several studies have reported a higher prevalence of POTS.[9,10]

A recent study reported joint pain as a generalized long-term symptom of Covid-19.[11] One north Indian study reported that 15.6% patients had joint pain post-Covid from three to six months, 20.8% at six weeks to three months, and 28.6% after 3 months. We also found that 13.7% patients had joint pain as a long Covid symptom post-Covid disease.[12]

Symptoms such as fatigue are common (33.3%) long-term complaints post-Covid-19 recovery. In studies conducted in Italy, the UK, and France, fatigue was found to be the most common post-Covid-19 manifestation.[13–15] César Fernández-

TABLE 5. Regression analysis for factor associated with the risk of developing long Covid

Variables	Exp (B)	95% C.I. for Exp (B)		p value
		Lower	Upper	
Disease severity	1.50	1.09	2.2	0.01*
BMI (kg/m²)	1.10	1.03	1.13	0.003*
Age (years)	1.02	1.00	1.04	0.02*
Gender	0.55	0.34	0.89	0.02*
Diabetes mellitus type 2	0.65	0.39	1.08	0.09
In-hospital complications	0.49	0.23	1.03	0.06
D-dimer (>500 ng/L)	0.56	0.35	0.90	0.02*
Troponin-1 (>42)	0.44	0.23	0.83	0.01*
HbAlc (%) (>6.5)	0.57	0.37	0.89	0.01*

*p<0.05 BMI body mass index HbA1c glycosylated haemoglobin CI confidence interval

de-las-Peñas *et al.* describe the incidence of persistent fatigue and dyspnoea in the largest multicentre study published with a long-term follow-up period in hospitalized Covid-19 survivors.[16]

There are many different types of hair loss and a multitude of factors that can contribute to it. One proposed theory for post-Covid-19 hair loss is that interleukin-6 (IL-6), a pro-inflammatory cytokine, may play a role.[17] A Saudi Arabian study found 26% patients reporting hair loss at 3-months follow-up.[18] We found that 5.9% patients had hair fall as a long-term Covid symptom.

A case series reported that 9 patients who recovered from Covid-19 completely developed pedal oedema.[19] We found that only 2.2% patients had pedal oedema after Covid-19 recovery. Another Indian study reported that diabetes and widespread use of corticosteroids in the background of Covid-19 appears to increase mucormycosis.[20] We found 3 patients with mucormycosis, and all had diabetes and were treated with steroids.

We found new onset of hypertension in 32.3% and type 2 diabetes in 3.8% patients at 1-year follow-up. A recently published systematic review evaluated changes in blood pressure, sugar, and lipid profiles of Covid recovered patients at follow-up to identify new-onset of hypertension, diabetes, and dyslipidaemia.[21] Disease prevalence and risk factors for long Covid tend to be higher in females, increasing age, obesity, and poor sociodemographic factors.[22–24]

We found that BMI above 25.9 kg/m^2, and age >60 years were independent predictors of post-Covid symptoms. Thompson *et al.* reported that a high BMI increased the risk of long Covid.[23] Similarly, a study by Sudre *et al.* reported that patients with prolonged symptoms were more likely to be obese.[22] Davis *et al.* reported that hospitalized Covid-19 patients presented with more symptoms post-Covid recovery, which is supported by our findings.[10] Our study results show that lipid profile values remained high during follow-up. Wrona *et al.* and Li *et al.* reported that LDL-C, triglycerides, and TC were significantly higher at follow-up.[21,25]

Limitations of our study include it being a single-centre experience, a small number of patients, and a lack of lipid profile data of the cohort at the time of admission.

Conclusion

The incidence of long Covid was 34.4% after hospital discharge at 1-year follow-up. Patients mainly developed symptoms like joint pain, fatigue, dyspnoea, or shortness of breath. Severity of disease at the time of admission, increased BMI, and age were independent predictors of long Covid.

Conflicts of interest. None declared

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