

Six-month Morbidity and Mortality in Patients after Recovery from COVID-19

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ABSTRACT

Background: This telephonic survey was aimed to identify the proportion of coronavirus disease-2019 (COVID-19) patients who died from any cause, within 6 months of discharge from a tertiary COVID-19 care hospital. We also analyzed whether any clinical and/or laboratory variables were associated with post-discharge mortality.

Materials and methods: All adult patients (age ≥ 18 years) who had been discharged during the period between July 2020 and August 2020 from a tertiary COVID-19-care hospital after initial hospitalization for COVID-19 were included. A telephonic interview was conducted 6 months after discharge to assess morbidity and mortality in these patients.

Results: Out of the 457 patients who responded, 79 patients (17.21%) were symptomatic, and breathlessness was found as most common symptom (6.12%). Fatigue was noted in (5.93%) of study patients, followed by cough (4.59%), sleep disturbances (4.37%), and headache (2.62%). Of the 457 patients who responded, 42 patients (9.19%) required expert medical consultation for their persistent symptoms. Thirty-six patients (7.88%) required re-hospitalization for post-COVID-19 complications within 6 months of discharge. A total of 10 patients (2.18%) succumbed within 6 months of their discharge from the hospital. 6 patients were males and 4 females. Most of these patients (7/10) succumbed in the second month after discharge. Seven patients had moderate-to-severe COVID-19 disease and most of these (7/10) had not been treated in the intensive care unit (ICU).

Conclusion: Post-COVID-19 mortality figures were not very high in our survey despite the high perceived risk of thromboembolic events after recovery from COVID-19. A significant proportion of patients reported persistent post-COVID-19 symptoms. Breathing difficulty was the most common symptom noted by us, closely followed by fatigue.

Keywords: Hospitalization, Mortality, Post-COVID-19, Symptoms.

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HIGHLIGHTS

- This is probably the first study from India which looked at post-COVID-19 mortality.
- Proportion of patients who succumbed to any reason after recovery from COVID-19 (post-COVID-19 mortality) was not very high.
- Almost 17% of post-COVID-19 patients were symptomatic even after 6 months of recovery.
- Breathlessness is the most common post-COVID-19 symptom followed by fatigue.

INTRODUCTION

With the world still battling coronavirus attacks, the number of patients who have survived severe COVID-19 is also increasing. These patients, however, continue to battle with many symptoms of the illness, long after they have clinically tested negative for the disease. They are called as long-haulers. In the days to come, it will be an important challenge to manage these cases simply because of the huge numbers. coronavirus disease-2019 sequelae may vary from mild symptoms such as nonspecific fatigue and body aches to severe forms requiring long-term oxygen therapy and even lung transplantation due to lung fibrosis. A significant number of patients are reporting cardiac abnormalities and strokes leading to marked impairment in the quality of life (QoL). Studies have reported that around 70–80% of patients declared COVID-19 free and recovered from the acute crisis, still present with the persistence of at least one symptom.^{1,2}

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The aims and objectives of this study were to identify the proportion of COVID-19 patients who died due to any cause within 6 months of discharge from our tertiary COVID-19-care hospital. We also wanted to assess the clinical and laboratory variables associated with mortality, if any.

The concept of long COVID-19 is quickly gaining cognizance because not only do patients tend to have prolonged or persistent symptoms even after testing negative for COVID-19 but also because rehospitalizations and deaths due to post-COVID complications continue to occur. Even though the COVID-19 pandemic continues to rage on, the death rates due to this disease have decreased significantly in most parts of the world. Not many studies, however, have investigated the fate of patients who have been discharged,

including the pattern of hospital readmissions after initial COVID-19 hospitalization.^{3,4} There is not enough literature on mortality after discharge following COVID-19 hospitalization. We could only find one study that assessed mortality in COVID-19 patients discharged after initial hospitalization.

MATERIALS AND METHODS

After obtaining ethical committee approval, we embarked upon this observational telephonic survey-based study. All the adult patients (age ≥18 years) who had been discharged in the period between July 2020 and August 2020 from All India Institute of Medical Sciences (AIIMS), Patna, Bihar, India after initial hospitalization for COVID-19 were included. Clinical and laboratory data of hospitalization for COVID-19 were retrieved from the medical records department of our hospital. Patients less than 18 years, pregnant women, and individuals with missing phone numbers or clinical details were excluded. An interview was scheduled at a time convenient to the patient and or relative and all questions were then asked as per the protocol of this study. Patients or their attendants were telephonically called in the period between February 2021 and March 2021 for those discharged in the period between July 2020 and August 2020, respectively. Oral consent was obtained for a telephonic survey after explaining the aims and objectives of the call. The data collected during telephonic interviews and clinical details of COVID-19 hospitalization retrieved from medical record department (MRD) were used for analysis. A questionnaire was designed to have only closed-ended answers that include post-COVID-19 symptoms, history of post-COVID-19 hospitalizations, and any mortality. Pretesting of the questionnaire was done, and supervised calls were made before the beginning of actual data collection.

Operational Definitions

- Symptomatic: Patients who continued to have at least one post-COVID-19 symptom persisting from the time of discharge till the time of interview.
- Asymptomatic: Patients who did not have any post-COVID-19 symptoms for at least the last 4 weeks.
- Post-COVID-19 symptoms: Dyspnea, cough, and fatigue.

Questionnaire

- Q1. Do you have any of the following symptoms: Cough, dyspnea, and fatigue?
 - Yes/No (Which of the following?)
- Q2. Do you have a symptom not mentioned above?
 - Yes/No (Which symptom? Headache, Insomnia, etc.?)
- Q3. Did you require expert medical consultation for post-COVID-19 symptoms?
 - Yes/No
- Q4. Did you require re-hospitalization at any hospital, after recovery from COVID-19?
 - Yes/No
- Q5. Is the patient discharged from hospital still surviving?
 - Yes/No
- Q6. If he has succumbed, then what time (in months) after discharge did he succumb?
 - A number

Statistical Analysis

Statistical analysis was done using OpenEpi or statistical procedures for social service (SPSS) software, version 20. Most of the data were dichotomous categorical variables which were

Table 1: Baseline characteristics of study patients

	Total (n = 457)	Proportion (%)
Male:Female	359:98	78.5:21.44
Asymptomatic	378	82.71
Symptomatic	79	17.21
Dyspnea	28	6.12
Cough	21	4.59
Fatigue	23	5.93
Sleep disturbances	20	4.37
Headache	12	2.62
Required medical consultation	35	7.65
Required hospitalization	36	7.88
Post-COVID-19 deaths	10	2.18

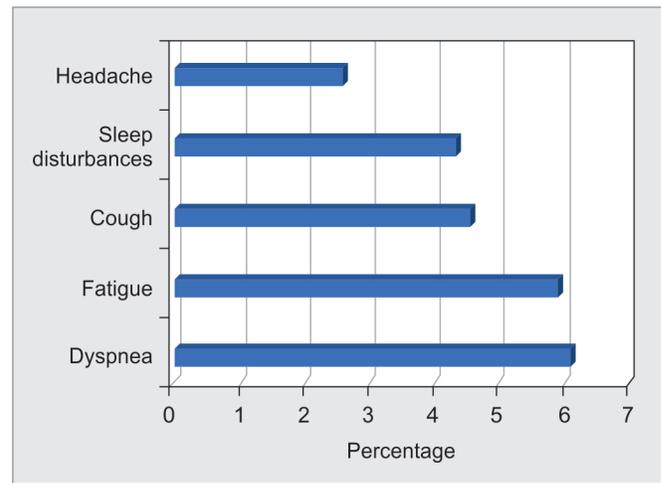


Fig. 1: Post-COVID-19 symptoms

expressed as percentages. Non-parametric tests were applied to them. The continuous data were expressed in mean and standard deviation. Chi-squared test analysis was also used for categorical variables and *t*-tests were used for the comparison of continuous variables. The variables after suitable statistical analysis with *p* <0.05 have been considered as statistically significant for the study.

RESULTS

A total of 984 patients were admitted to our hospital during the study period. Out of these, 729 patients were discharged and included in our study. The remaining 255 patients succumbed during hospitalization itself. Out of 729 patients, we were able to connect with only 457 patients. In the remaining 272 patients, either an incorrect phone number had been provided or their phones were unreachable despite more than three attempts. Some patients also refused consent to participate in the survey.

In the telephonic survey, we noted that out of the 457 patients who responded, 79 patients (17.21%) were still symptomatic with complaints of either cough, dyspnea, or fatigue. Dyspnea or breathing difficulties were noted to be the most common symptoms seen in 6.12% of total responders, followed by fatigue in 5.93%, and cough was noted in 4.59%. Some patients reported sleep disturbances (4.37%), and headaches (2.63%). (Table 1; Fig. 1). Of all



Table 2: Comparison of post-COVID-19 symptomatic and asymptomatic patients

	Symptomatic (n = 79)	Asymptomatic (n = 378)	p-value
Age	49.35 ± 15.6	46.91 ± 15.6	NS
Male %	63 (79.74)	295 (78.04)	NS
COVID severity			
Mild	32 (40.50)	260 (68.78)	<0.00001
Moderate	41 (51.89)	91 (24.07)	<0.00001
Severe	06 (7.59)	27 (7.14)	NS
Comorbidity			
DM	22 (27.84)	104 (27.51)	NS
HT	21 (26.58)	91 (24.07)	NS
CAD	1 (1.26)	19 (5.02)	NS
CKD	–	9 (2.38)	
COAD	2 (2.53)	9 (2.38)	NS
Treatment related			
Oxygen supplementation	45 (56.96)	127 (33.59)	<0.0001
Ward	73 (92.40)	340 (89.94)	NS
ICU requirement	6 (7.59)	38 (10.02)	NS
Duration of hospitalization (days)	11.36 ± 5.77	11.62 ± 5.70	NS

DM, diabetes mellitus; HT, hypertension; CAD, coronary artery disease; CKD, chronic kidney disease; COAD, chronic obstructive airway disease; ICU, intensive care unit

the patients who responded, 42 patients (9.19%) required expert medical consultation for these symptoms. 36 patients out of the 457 (7.88%) required re-hospitalization for post-COVID-19 complications within 6 months of discharge. A total of 10 patients (2.18%) succumbed within 6 months of their discharge from our hospital (Table 1).

We compared the clinical characteristics of patients who were symptomatic and asymptomatic patients after discharge (Table 2). Most of the patients who had recovered after a mild infection, remained symptom-free (asymptomatic) (68.78% vs 40.50%, $p < 0.00001$). Patients with moderate COVID-19 illness were more symptomatic (51.89% vs 24.07%, $p < 0.00001$) in the 6 months after discharge. Analyzing the comorbidities present in patients who had been discharged, we found that no particular comorbidity specifically influences whether a patient would remain symptomatic or asymptomatic. However, patients who had received oxygen therapy during their stay were more symptomatic post-discharge than those that did not need any oxygen ($p < 0.005$). A total of 10 patients had succumbed to the infection and medical records of the 10 patients who succumbed were analyzed in greater detail. Although we did not ask for the specific antecedent and immediate cause of their deaths in the telephonic survey, Table 3 summarizes some clinical and laboratory characteristics of these patients who had succumbed to the disease postdischarge.

DISCUSSION

The spectrum of COVID-19 ranges from being an asymptomatic infection to severe life-threatening viral pneumonia requiring hospital admission, and death.⁵⁻⁷ The symptoms are similar to those observed during previous severe acute respiratory syndrome [(SARS)-associated coronavirus 2 (SARS-CoV-2)] and Middle East respiratory syndrome (MERS) outbreaks.⁸ However, COVID-19 is a

new disease and uncertainty remains regarding its possible long-term effects on morbidity and mortality.

Our observations indicate that approximately one-fifth (17.21%) of interviewed patients remained symptomatic even after 6 months of discharge. There were 25 patients who had more than one symptom after discharge. Varying degrees of dyspnea or breathing difficulty was the most common post-COVID symptom reported in this study. This was followed by fatigue and lethargy. Huang et al.⁹ have described the clinical follow-up for 6 months of 1,733 adult patients discharged from their hospital after COVID-19. They have reported a much higher proportion of patients 76% (1,265 of 1,655) who complained of at least one persistent symptom, as compared to our study figures of 17.21%. They noted that fatigue or muscle weakness was the most frequently reported symptom (63%). In our subset, fatigue was reported in smaller numbers as compared to dyspnea. Another North Indian study including more than 1000 patients with a follow-up period of at least 3 months showed myalgia (10.9%), fatigue (5.5%), shortness of breath (6.1%), and cough (2.1%) as the common symptoms.¹⁰ The higher prevalence of dyspnea in our study could be due to a higher prevalence of underlying comorbidities such as chronic respiratory disorder, physical deconditioning, and more sedentary life. Post-COVID-19 symptoms are not only limited to severe COVID-19 but also limited to mild disease. We have found a persistence of symptoms such as fatigue and cough in almost one-third of patients who recovered from mild COVID-19 a month back.¹¹

Donnelly et al.¹² in their study have reported that 27% of survivors after COVID-19 hospitalization either required readmission or died within 60 days after discharge. This is again a much higher rate than that noted in our study. We observed that only 36 (7.88%) of discharged patients either needed rehospitalization or succumbed due to any cause. We believe one reason could be a scarcity of post-COVID-19-care beds in this part of the country.

Table 3: Characteristics of post-COVID-19 deaths

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7	Case 8	Case 9	Case 10
Age	39	1	55	64	59	55	40	47	66	60
M/F	F	F	M	M	F	M	F	M	M	M
Timing after discharge (months)	2	2	2	2	2	2	1	2	3	1
COVID-19 severity	Mild	Severe	Moderate	Mild	Moderate	Severe	Severe	Severe	Moderate	Mild
Comorbidity				D	H, C	D, H, CKD	H, CKD	D	C	D
Treatment										
Oxygen therapy	No	YES	YES	NO	YES	YES	YES	YES	YES	NO
Ward (W)/ICU	W	ICU	W	W	W	ICU	ICU	W	W	W
Investigations										
TLC (/mm ³)	7.99	15.7	13.29	9.27	12.3	10.9	9.05	8.71	12.23	14.12
Neutrophil (%)	63	91	88.3	87.3	75	89.5	61	94.7	93	71.3
Lymphocyte (%)	23.8	6	8	7.6	25	8.7	34	4.5	5.8	23.4
Inflammatory marker										
CRP (<5 mg/L)	NA	NA	NA	NA	2.4	324.2	31	NA	26.4	49.2
Ferritin (<322 ng/mL)	454.8	NA	431	1670	598	1650	1793	NA	817	729.39
LDH (<460 U/L)	NA	NA	NA	NA	117	1339.54	NA	NA	1133	NA
D-dimer (<0.02 ng/mL)	NA	NA	0.86	NA	2.15	3.42	4.9	NA	5.9	2.83

C, cancer; D, diabetes; CKD, chronic kidney disease; H, hypertension; TLC, total leukocyte count; NA, not applicable (data could not be retrieved)

The fact that the proportion of people who died ($n = 10$) is very close to the proportion of people who were re-hospitalized ($n = 26$), as noted in our study, bears testimony to this unfortunate fact. The number of hospitalized patients should have been much higher than those that succumbed. In Bihar, the eastern state of India, it was exceedingly difficult to get beds for post-COVID-19 care once declared COVID-19 negative. This is because most private nursing homes and small hospitals had been closed due to the nationwide shutdown as well as the fear and paranoia of the owners. Even the hospitals catering to COVID-19 patients had shut doors to non-COVID-19 patients for fear of the spread of the disease to a vulnerable population due to mixing. We believe that patients who needed hospitalization might be finding it very difficult because the very few hospitals which were taking care of non-COVID-19 patients were either full or exorbitantly costly. Indeed, the plight of even palliative care patients due to the lockdown has been staggering¹³. We could not communicate with almost a fifth of the patients who had been discharged from the hospital. These could be the least accessible and least resourceful patients. This group could be more symptomatic. More may have succumbed to disease and thus the true mortality and mortality figures could be higher.

Analyzing the 10 mortalities, 6 patients were males and 4 were females. Most of these patients (7/10) succumbed in the second month after discharge. Two patients died within the first month of the discharge and one patient expired in the third month. Out of the 10 deaths, 3 patients had only mild disease, 3 had moderate disease and four patients had severe COVID-19 infections. A total of 5 out of the 10 (50%) were diagnosed as diabetics but 3 out of the 10 (30%) patients had no comorbidities documented. Most of these patients, that is, 7 out of 10 (70%) had not required intensive care treatment and they had been discharged from the ward itself. One of these patients had severe COVID-19 which was managed in the ward itself. Three patients who succumbed had required ICU care before discharge. Although we did not specifically ask for the antecedent or immediate cause of death in these patients, we retrieved their hospital records for assessment. Although a record of inflammatory markers could not be obtained from all patients, we did note an elevation in levels of C-reactive protein (CRP), lactate dehydrogenase (LDH), ferritin, and D-dimer (Table 3).

Persistent symptoms after COVID-19 can have a bearing on medical management and drug usage among these mentally traumatized patients. Although understanding of the disease is continually being updated, till the time we know with clarity about the disease pathophysiology, it would be prudent to err on the side of caution and aggressively manage any persistent symptoms.

The strength of this study is that hardly any Indian study has looked into mortality figures after recovery from COVID-19 infection considering the perceived increased risk of thromboembolic events.

There are several limitations of this study. First, it was a telephonic survey, where data could not be validated and is thus prone to reporting bias. More than one-fifth of patients could not be engaged in the survey and this group of patients might be more symptomatic and more patients may have died in this group given the difficulty in reaching out to them. The true mortality and morbidity figures are thus more likely to be higher. This survey is from a single center and at a time when healthcare delivery was overwhelmed by the number of COVID-19 patients presenting to this tertiary care center. Discharge criteria were more relaxed to treat as many sick COVID-19 patients as possible. Some post-discharge symptoms thus may not be the same in the population when surveyed at a different time.



CONCLUSION

A significant proportion of patients had persistent post-COVID-19 symptoms after discharge from the hospital in our study. Breathing difficulty was the most common symptom noted, closely followed by fatigue. We did not find any significant correlation between any specific comorbidity or laboratory value that could predict the persistence of the COVID-19 symptoms after discharge. The proportion of patients who died after recovery from COVID-19 was lower in our study compared to that reported in the literature.

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