

Assessment of Post-Covid Symptoms in Covid-19 Recovered Patients: A Prospective Cohort Study in a Tertiary Care Centre of South India

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Abstract

Background: The post-Covid symptoms among patients hospitalised with covid has to be determined for elucidating the spectrum of illness which persists even after the apparent recovery. The understanding of the post-Covid symptoms will help us to better manage aftermath of the pandemic.

Aim: To determine the incidence of post-Covid symptoms in a cohort of inpatients who recovered from COVID-19 from a tertiary care centre in South India.

Method: 120 survivors from patients admitted with COVID 19 were prospectively followed up for 6 weeks after their discharge from the hospital. The cohort included 50 patients requiring Intensive care unit (ICU) care and 70 ward patients. The follow-up was conducted on the second and sixth week after discharge with a structured questionnaire. The questionnaire was filled by the patient/bystanders during their visit to the hospital for follow-up at 2 weeks and through telephone follow up at 6 weeks.

Results: Mean age of the cohort was 55 years and 55% were males. 58.3% had mild covid and 41.7% had moderate to severe covid infection. 60.8% (n=73) of patients had at least one persistent symptom at sixth week of discharge. 50 (41.7%) patients required intensive care during their inpatient stay. Presence of persistent symptoms at 6 weeks was not associated with severity of illness, age or requirement for intensive care. Fatigue was the most common reported persistent symptom with a prevalence of 55.8% followed by weight loss (22.5%) and dyspnoea (20%). Female sex (OR 2.4, 95% CI: 1.03–5.58, $p = 0.041$) and steroid administration during hospital stay (OR: 4.43; 95% CI: 1.9–10.28, $p = 0.001$), were found to be significant risk factors for the presence of post-Covid symptoms at 6 weeks as revealed by logistic regression analysis.

Conclusion: 60.8% of inpatients treated for covid had post-Covid symptoms at 6 weeks post- discharge from hospital. Female sex and steroid administration during hospital stay were identified as predictors of persistence of post-Covid symptoms at 6weeks.

Background

The COVID-19 posed unprecedented challenges for our generation. We were caught off guard and had to learn the various aspects of the virus such as transmissibility, variants, severity, management, etc. as the pandemic evolved [1]. Our understanding of the disease is still limited and those aspects which were not of primary concern at the height of the pandemic started getting attention as healthcare regained the balance of resources [2]. Presentations of multisystem inflammatory syndrome (MIS-C) in children and multisystem inflammatory syndrome (MIS-A) in adults gave us the clarity that the covid negativity is not a hardtop but just the beginning of a new chapter called post-Covid and the associated health issues [3]. If the economic and social impact of the covid was devastating the presence and persistence of the post-Covid symptom aggravates the situation [4]. To resolve or control the situation we need to understand the post-Covid symptoms and the morbidity and mortality it can result in so that the healthcare system could be better equipped to deal with this aftermath of the illness [5].

The COVID-19 illness ranged from mild disease presenting with fever, sore throat, runny nose, myalgia, headache, dry cough, loss of smell or taste, loose stool, loss of appetite, fatigue, and sleep disturbances to severe disease which can cause breathlessness and hypoxia due to acute respiratory distress syndrome (ARDS) to multiple organ dysfunction syndrome (MODS) due to Cytokine storm [6, 7]. Thrombotic complications like myocardial infarction (MI), stroke, and deep vein thrombosis (DVT) with pulmonary embolism (PE) were also noticed [8]. Those with mild illness while being managed in home-based care with comorbidities and risk factors often get hospitalized due to the severe disease or fearing the progression to severe disease [9]. Despite that a large population of COVID-19 patients is getting recovered and discharged from the hospital, the health status of patients after recovery is barely described in the literature, and this condition is termed as “long Covid” or “post-Covid syndrome” [10, 11].

The post-Covid symptoms observed in patients recovered from Covid, irrespective of the severity of the disease i.e., asymptomatic, mild, or severe. The post-Covid symptoms can range from fatigue, myalgia, dyspnoea, dry cough, loss of smell and taste to thrombotic complications [12, 13]. The frequency with which these complications happen has to be studied along with the risk factors which could predict the persistence of the post-Covid symptoms. The identification of the risk factors can act as potential facets of intervention that could result in a reduction of mortality and morbidity associated with the post-Covid sequelae [14]. The principal aim of this single-centre study was to determine the prevalence of post-Covid symptoms at 6 weeks post-hospitalization.

Methods

Study setting

This was a single-centre hospital-based prospective observational study conducted at a 1300 bedded academic tertiary care referral centre in South India from February 2021 to July 2021. The hospital had dedicated isolation facility comprising Intensive care units and non-intensive care locations for treating patients admitted with COVID. The study was approved by Institutional Ethics Committee and informed signed consent was taken before patient enrolment.

Study Population

The study population comprised of adult (>18 years) patients who are diagnosed with COVID-19 and was admitted in the inpatient COVID location and subsequently got discharged from the hospital were screened for inclusion criteria. (Fig. 1). Patients who are being younger than 18 years old, death, pre/post-surgical patients, patients who were transferred to non-covid inpatient location for continuation of care for indications other than covid, and end of life care were excluded from the study.

In-hospital Data Collection

The data collection included demographic characteristics like age, sex, social history, and co-morbidities. The study also recorded COVID specific parameters included the severity of COVID-19 infection, level of clinical care received (ICU or non-ICU locations), length of hospital stay (LOS), vaccination status, disease symptoms and treatment details including antiviral, anticoagulation and steroid administration in COVID-19 patients.

Follow-up After Discharge

A questionnaire was prepared to assess the post-Covid symptoms in patients after their discharge from the hospital. The follow-up was conducted on 2 weeks (first follow-up) and 6 weeks (second follow-up) after discharge. The Post-Covid symptoms were grouped into 'Potentially infection-related symptoms' and 'Acute Post Covid symptoms' based on the 2 weeks and 6 weeks timelines post-discharge respectively [15]. Information regarding the current symptoms, and working status of each patient was obtained. Face-to-face interview and questionnaire filling was performed during their visit to the hospital for follow-up. Patients who were not able to come for a review were followed up telephonically. The collected data were entered in a pre-designed data collection form and populated in a Microsoft Excel sheet for further analysis.

Statistical analysis

Statistical analysis was performed using IBM SPSS version 20.0 software. Categorical variables are indicated using frequency and percentage. Numerical variables are presented using mean and standard deviation. To test the statistical significance of the comparison of categorical variables between two subject groups, a Chi-square test with continuity correction was applied. To test the statistical significance of the difference in the mean values of numerical variables between two subject groups, the student's t-test was used. Logistic regression was employed to identify the predictors of presence of symptoms lingering at 6 weeks. A p-value of <0.05 was advised statistically significant.

Results

Among the 454 patients who were screened and assessed for eligibility, 334 patients were excluded. (Fig. 1). Thus, a total of 120 patients were involved in the study that included 70 and 50 patients who received clinical care at non-ICU and ICU locations respectively.

Demographic details and infection specific characteristics of patients are depicted in Table 1. The mean age of study patients was found to be 54.95 ± 17.5 and 55% (66) were males. The mean LOS of study patients was 16.08 ± 10.1 days. Among the study cohort, 58.3% (n=70) had mild infection, 16.7% (n=20) had moderate infection and 25% (n=30) had severe infection.

Table 1
Demographic data and COVID-19 characteristics of patients

Variables	Overall	Non-ICU patients	ICU patients
Total no.	120	Mild-70 (58.3%)	Moderate-20 (16.7%) Severe-30 (25%)
Age, years (mean)	54.95±17.5	51.79±19.7	59.38±13.2
<40y	27 (22.5%)	22 (31.4%)	5 (10%)
40-60y	47 (39.2%)	24 (34.3%)	23 (46%)
>60y	46 (38.3%)	24 (34.3%)	22 (44%)
Sex			
Male	66 (55%)	30 (42.9%)	36 (72%)
Female	54 (45%)	40 (57.1%)	14 (28%)
Social history			
Alcohol consumption	13 (10.8%)	6 (8.6%)	7 (14%)
Smoking	14 (11.7%)	7 (10%)	7 (14%)
Length of hospital stay	16.08±10.1	9.26±2.7	25.64±8.9
Charlson Comorbidity Index (CCI)			
Mild (1-2)	31 (25.8%)	18 (25.7%)	13 (26%)
Moderate (3-4)	31 (25.8%)	14 (20%)	17 (34%)
Severe (≥5)	17 (14.2%)	10 (14.3%)	7 (14%)
New onset of diabetes	6 (5%)	4 (5.7%)	2 (4%)
Oxygen requirement	49 (40.8%)	1 (1.4%)	48 (96%)
Vaccination status			
First dose	6 (5%)	6 (8.6%)	0
Second dose	0	0	0
Symptoms at admission			
Respiratory symptoms	101 (84.2%)	51 (72.9%)	50 (100%)
Constitutional symptoms	75 (62.5%)	47 (67.1%)	28 (56%)
GI symptoms	17 (14.2%)	9 (12.9%)	8 (16%)
Loss of smell/ taste	9 (7.5%)	6 (8.6%)	3 (6%)
Location: At the end of second paragraph of results			

The commonly observed co-morbidities in the study cohort were hypertension (39.1%), diabetes mellitus (39.2%), and 5% were diagnosed with new onset of diabetes. Six patients (5%) had taken the first dose of the covishield vaccine. Most of the patients exhibited respiratory symptoms (84.2%) and constitutional symptoms (62.5%) during the hospital stay (Fig. 2).

During the second week, 78.3% (n=94) of patients remained symptomatic with at least one listed symptom among fatigue (67.5%), dyspnoea (30%), cough (20.8%), sleep disturbance (17.5%), loss of appetite (16.7%), and weight loss (13.3%) (Table 2) (Fig. 2). During the sixth week, 60.8% (n=73) of patients remained symptomatic. At 6 weeks of follow-up, fatigue was the most commonly reported symptom with a prevalence of 55.8% followed by weight loss (22.5%), dyspnoea (20%), loss of appetite (10.8%), and cough (10%) (Table 3 (Fig. 2). Anxiety/depression was reported in 8.3% and 5% of patients during the 2nd and 6th week respectively. None of the patients had a fever at 6 weeks follow-up.

Table 2
 Characterization of post-discharge persistent symptoms during the second week

Symptoms	Overall	Ward patients	ICU patients	P value
Fatigue	85 (67.5%)	44 (62.9%)	37 (74%)	0.121
Dyspnoea	36 (30%)	17 (24.3%)	19 (38%)	0.106
Anxiety/ depression	10 (8.3%)	5 (7.1%)	5 (10%)	0.577
Fever	2 (1.7%)	1 (1.4%)	1 (2%)	0.999
Headache	10 (8.3%)	5 (7.1%)	5 (10%)	0.577
Cough	25(20.8%)	10 (14.3%)	15 (30%)	0.037*
Myalgia	12 (10%)	6 (8.6%)	6 (12%)	0.537
Arthralgia	11 (9.2%)	5 (7.1%)	6 (12%)	0.363
Chest pain	2 (1.7%)	1 (1.4%)	1 (2%)	0.999
Loose stools	11 (9.2%)	6 (8.6%)	5 (10%)	0.789
Loss of appetite	20 (16.7%)	9 (12.9%)	11 (22%)	0.185
Weight loss	23 (13.3%)	7 (10%)	16 (18%)	0.003*
Sleep disturbances	21 (17.5%)	9 (12.9%)	12 (24%)	0.113
Runny nose	2 (1.7%)	1 (1.4%)	1 (2%)	0.999
Loss of smell	7 (5.8%)	4 (5.7%)	3 (6%)	1.000
Loss of taste	9 (7.5%)	5 (7.1%)	4 (8%)	0.999
Blurred vision	1 (0.8%)	1 (1.4%)	0	1.000
Skin rashes	1 (0.8%)	0	1 (2%)	0.865
Infections	5 (4.2%)	1 (1.4%)	4 (8%)	0.335
Oxygen requirement	3 (2.5%)	0	3 (6%)	0.138
Hospitalization	7 (5.8%)	3 (4.3%)	4 (8%)	0.645
Able to work	10/37 (27%)	8/24 (33.3%)	2/13 (15.4%)	0.328
Location: At the end of 3rd paragraph of results				

Table 3
 Characterization of post-discharge persistent symptoms during the sixth week

Symptoms	Overall	Ward patients	ICU patients	P value
Fatigue	67 (55.8%)	38 (54.3%)	29 (58%)	0.512
Dyspnoea	24 (20%)	11 (15.7%)	13 (26%)	0.165
Anxiety/ depression	6 (5%)	3 (4.3%)	3 (6%)	1.000
Headache	3 (2.5%)	1 (1.4%)	2 (4%)	0.767
Cough	12 (10%)	5 (7.1%)	7 (14%)	0.217
Myalgia	6 (5%)	3 (4.3%)	3 (6%)	1.000
Arthralgia	4 (3.3%)	2 (2.9%)	2 (4%)	1.000
Chest pain	1 (0.8%)	0	1 (2%)	0.865
Loose stools	4 (3.3%)	2 (2.9%)	2 (4%)	1.000
Loss of appetite	13 (10.8%)	7 (10%)	6 (12%)	0.728
Weight loss	27 (22.5%)	13 (18.6%)	7 (14%)	0.223
Sleep disturbances	11 (9.2%)	5 (7.1%)	6 (12%)	0.363
Loss of smell	4 (3.3%)	2 (2.9%)	2 (4%)	1.000
Loss of taste	4 (3.3%)	2 (2.9%)	2 (4%)	1.000
Blurred vision	1 (0.8%)	1 (1.4%)	0	1.000
Infections	2 (1.6%)	2 (2.9%)	0	1.000
Oxygen requirement	0	0	0	-
Hospitalization	4 (3.3%)	3 (4.3%)	1 (2%)	0.864
Able to work	19/37 (51.4%)	13/24 (54.2%)	6/13 (46.2%)	0.573
Location: At the end of 3rd paragraph of results				

Acute Post-Covid Symptoms were reported among 70% (35) and 54.3%(38) among the patients requiring ICU care and non-ICU care respectively during IP stay. (Table 4).

Table 4
Prevalence of post-Covid symptoms during the follow-up period

Frequency	Overall	Ward patients	ICU patients
Second week-Potentially infection-related symptoms			
Presence of symptoms	94 (78.3%)	49 (70%)	45 (90%)
No symptoms	26 (21.7%)	21 (30%)	5 (10%)
One symptom	9 (7.5%)	7 (10%)	2 (4%)
Two symptoms	28 (23.3%)	17 (24.3%)	11 (22%)
More than two symptoms	57 (47.5%)	25 (35.7%)	32 (64%)
Sixth week-Acute post-Covid symptoms			
Presence of symptoms	73 (60.8%)	38 (54.3%)	35 (70%)
No symptoms	47 (39.2%)	32 (45.7%)	15 (30%)
One symptom	18 (15%)	9 (12.9%)	9 (18%)
Two symptoms	28 (23.3%)	15 (21.4%)	13 (26%)
More than two symptoms	27 (22.5%)	14 (20%)	13 (26%)
Location: At the end of 4th paragraph of results.			

Comparison between post-Covid symptoms of the non-ICU and ICU patients during the 2nd-week exhibited statistically significant difference in cough ($p=0.037$) and weight loss ($p=0.003$). At the time of the first follow-up, 2.5% (3) patients had persistent hypoxia necessitating supplemental oxygen. Hospitalization due to post-discharge symptoms was reported in 11 patients (9.2%) during the follow-up period of 6 weeks. Among 37 patients in the whole cohort who are employed, 27% (10) and 51.4% (19) were able to re-join work at 2 weeks and 6 weeks respectively post-discharge from hospital.

Among the symptoms, the maximal reduction at 6 weeks was observed for fatigue at 11.7% compared to 2 weeks follow up. Weight loss exhibited an increase of prevalence by 3.3% during the sixth week from the second week follow-up.

Association of baseline characteristics and COVID-19 treatment with the presence of symptoms at 6 weeks post-discharge is depicted in Table 5. Among patients discharged from ICU, a higher proportion of females (92.9%) remained symptomatic at 6 weeks of follow-up as compared to males (61.1%, $n=22$) (OR 8.27, 95% CI 0.97-70.2, $p=0.04$). Among patients admitted in non-ICU location, anti-viral treatment during hospital stays ($p=0.007$) and steroid administration during hospital stay ($p<0.001$) and patients receiving steroids at discharge ($p=0.04$), were significantly associated with the presence of post-Covid symptoms at 6 weeks.

Table 5
Association of baseline characteristics and COVID-19 treatment with presence of symptoms at 6 weeks post-discharge

Variables	Whole cohort			ICU			Ward		
	Presence	Absence	P value	Presence	Absence	P value	Presence	Absence	P value
Age	73 56.71±16.16	47 52.21±19.52	0.173	35 61.34±12.79	15 54.8±13.49	0.109	38 52.45±17.86	32 51±21.87	0.761
Gender									
Male	37 (56.1%)	29 (43.9%)	0.16	22 (61.1%)	14 (38.9%)	0.04*	15 (50%)	15 (50%)	0.5
Female	36 (66.7%)	18 (33.3%)		13 (92.9%)	1 (7.1%)		23 (57.5%)	17(42.5%)	
CCI score (Mean±SD)	73 2.30±1.91	47 1.79±2.04	0.164	35 2.74±1.85	15 1.87±2.26	0.158	38 1.89±1.90	32 1.75±1.96	0.756
Anti-viral treatment									
During hospital stay	55 (70.5%)	23 (29.5%)	0.006*	31 (70.5%)	13 (29.5%)	0.51	24 (70.6%)	10 (29.4%)	0.007*
During discharge	4 (57.1%)	3 (42.9%)	0.565	2 (50%)	2 (50%)	0.34	2 (66.7%)	1 (33.3%)	0.5
Anti-coagulants									
During hospital stay	51 (64.6%)	28 (35.4%)	0.168	29 (69%)	13 (31%)	0.54	22 (59.5%)	15 (40.5%)	0.24
During discharge	31 (70.5%)	13 (29.5%)	0.073	20 (69%)	9 (31%)	0.55	11 (73.3%)	4 (26.7%)	0.08
Steroids									
During hospital stay	45 (75%)	15 (25%)	0.001*	33 (68.8%)	15 (31.3%)	0.48	12 (100.0%)	0	<0.001*
During discharge	16 (66.7%)	8 (33.3%)	0.60	11 (57.9%)	8 (42.1%)	0.12	5 (100.0%)	0	0.04*
Location: At the end of results									

Female sex (OR 2.4, 95% CI: 1.03–5.58, $p = 0.041$) and steroid administration during hospital stay (OR: 4.43; 95% CI: 1.9–10.28, $p = 0.001$), were found to be significant risk factors for the presence of post-Covid symptoms at 6 weeks as revealed by logistic regression analysis.

Discussion

Our prospective study on 120 COVID-19 survivors from a tertiary care centre revealed persistence of acute post-Covid symptoms in 60.8% of patients in the cohort during the sixth week after discharge from the hospital. The predominant post-Covid symptoms included fatigue (55.8%) weight loss (22.5%) and dyspnoea (20%) and 10% of the cohort reported constitutional symptoms like loss of appetite, sleep disturbance, and cough. The prevalence of post-Covid symptoms was not significantly different between the patients requiring and not requiring intensive care during their inpatient stay.

A university hospital based study in UK followed up 100 subjects at 4-8 weeks after discharge reported fatigue (72% in ICU patients and 60.3% in ward patients) and dyspnoea (65% in ICU patients and 42.6% in ward patients) as most common post-discharge symptoms in their study [11]. In a single centre prospective cohort study by Jacobs et al in USA, 55% of COVID-19 survivors had persistent fatigue, 51% had muscle pain and 45.3% had dyspnoea 35 days post-discharge [16]. A similar study conducted in the UK by Mandal S et al revealed 69% of survivors had persistent fatigue, 53% had dyspnoea and 34% had dry cough 54 days post-discharge [17]. Our study observations at 42 days (6 weeks) post-discharge were overall in lieu with these publications regarding prevalence of post-Covid symptoms. However, our cohort had a lower prevalence of respiratory symptoms such as dyspnoea and cough at 20% and 10% respectively. We did not observe

fever among post-Covid symptoms in our cohort similar to previously published studies from Bangladesh and Netherlands [10, 18]. Appearance of new post-Covid symptoms at 2 weeks among the patients in our cohort included anxiety/depression, weight loss, sleep disturbance, blurred visions, skin rashes and infections in comparison to symptomatic presentation during the time of admission.

Increased prevalence of post-Covid symptoms (60.8%) could denote increased time to symptom recovery in COVID-19 patients as compared to community-acquired pneumonia patients whose symptomatic recovery was 97% by 10 days [19]. An additional longitudinal study comprised of 201 community-acquired pneumonia patients found that dyspnoea settled after 14 days of symptom onset and fatigue after 20 days [20]. The protracted symptomatic status of the patients represents the underrepresented clinical milieu of the disease out of the initial acute phase. Recent studies have even reported post-Covid symptoms even 120-180 days post-discharge [21].

The majority of patients in the study were in the age group 51-60 years with a mean age of 55 years. Although patients with age >50 years are proven to run the consequential risk of developing severe illness if they contract the infection due to physiological changes that come with aging and potential underlying health conditions, this was not found to be a significant factor in determining the incidence of post-Covid symptoms in our cohort [22]. Despite the existing publications portraying the major role of comorbidities and LOS in the development of post-discharge Covid symptoms, our data failed to show any significant association with these covariates [23]. In our study female sex and steroid administration during hospital stay were found to be significant risk factors for the presence of post-Covid symptoms at 6 weeks. A similar observation regarding the female sex as a risk factor for developing post-Covid symptoms can be seen in a prospective cohort study conducted by Mahmud R et al [10].

All the patients in the ward who had steroid administration during stay (17%, 12/70) and at discharge (7%, 5/70) were observed to have developed post-Covid symptoms at 6 weeks post-discharge from hospital. This indicates potential role for steroid stewardship programmes that focuses on optimizing the use of steroids in COVID patients with special reference to non-intensive care requiring mild cases given the increased risk of lingering post COVID symptoms after discharge.

Despite the possibility of post-intensive care syndrome interfering with the post-Covid syndrome assessment, the lack of a significant difference in the prevalence of post-Covid symptoms at 6 weeks among ICU and non-ICU requiring patients in our study suggests that patients discharged from non-ICU locations with relatively less COVID-19 severity could also develop post-Covid symptoms similar to patients discharged from ICU [24].

Limitations

This study has many limitations. Our conclusion is based on the data from a single tertiary care centre catering to morbidly ill patients. This study was limited to COVID-19 survivors who were hospitalized. Since the period of the follow-up was limited to 6 weeks, the duration of the persistence of the symptoms of the long Covid could not be determined. The study observations could not be extended to vaccinated patients as the majority of the study cohort were non vaccinated.

Conclusion

Our study revealed a high prevalence of post COVID symptoms at a minimum of six weeks post discharge among inpatients who recovered from COVID. Female sex and steroid administration during hospital stay were identified as predictors of persistence of post-Covid symptoms at 6weeks. HealthCare systems across the globe has to account for the tail wagging phenomenon of post- Covid syndrome and needs to strategize the management and rehabilitation of those suffering from this extended illness.

Abbreviations

MIS-C
Multisystem Inflammatory Syndrome in Children
MIS-A
Multisystem Inflammatory Syndrome in Adults
ARDS
Acute Respiratory Distress Syndrome
MODS
Multiple Organ Dysfunction Syndrome
MI
Myocardial Infarction

DVT
Deep Vein Thrombosis
PE
Pulmonary Embolism
LOS
Length of hospital Stay
ICU
Intensive Care Unit
CCI
Charlson Comorbidity Index

Declarations

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Authors contributions

DTS and MM involved in conceptualization, manuscript writing, review and editing. CVN and AA involved in data collection and follow-up. CVR involved in writing manuscript, literature search and references. CVR, PP, RPR, AA were responsible for project implementation. FE done the data analysis and involved in review and editing of manuscript. PP and RPR involved in literature search, manuscript writing and references.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethical approval and consent to participate

The study was approved by Institutional Ethics Committee (Approval No: IEC AIMS 2021-PHARM-095) and informed signed consent was obtained from the patients or bystanders during their follow-up period. The study was conducted in accordance to the regulations and guidelines of Amrita Institute of Medical Science and Research Centre, Kochi.

Consent for publication

Not applicable

Competing interests

The authors declare no conflict of interest for this work.

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Figures

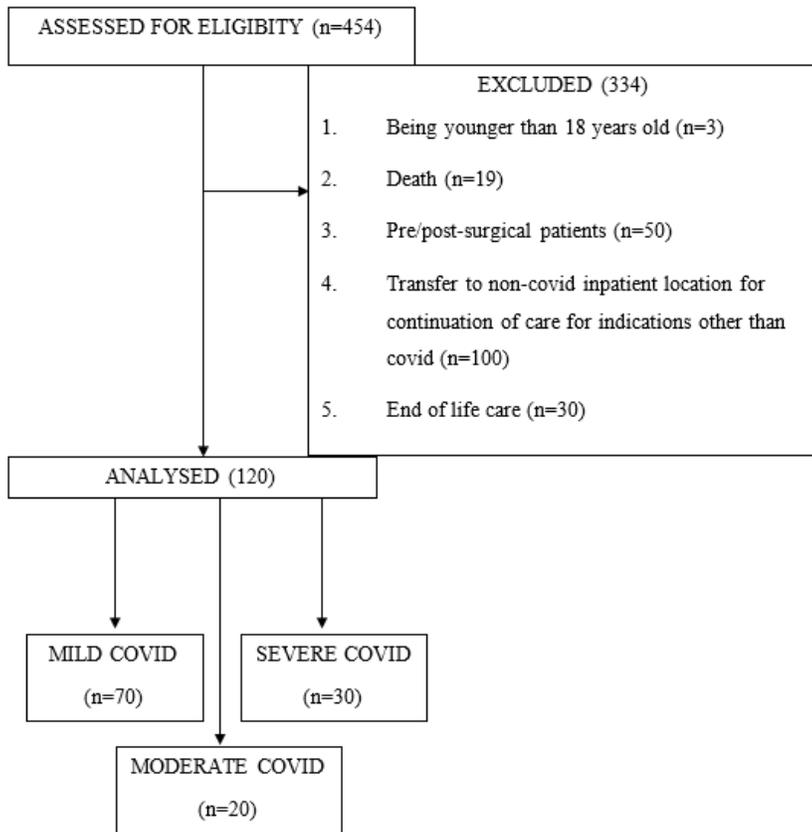


Figure 1

Patient selection for this prospective cohort study

Location: At the end of study population heading which comes under methods

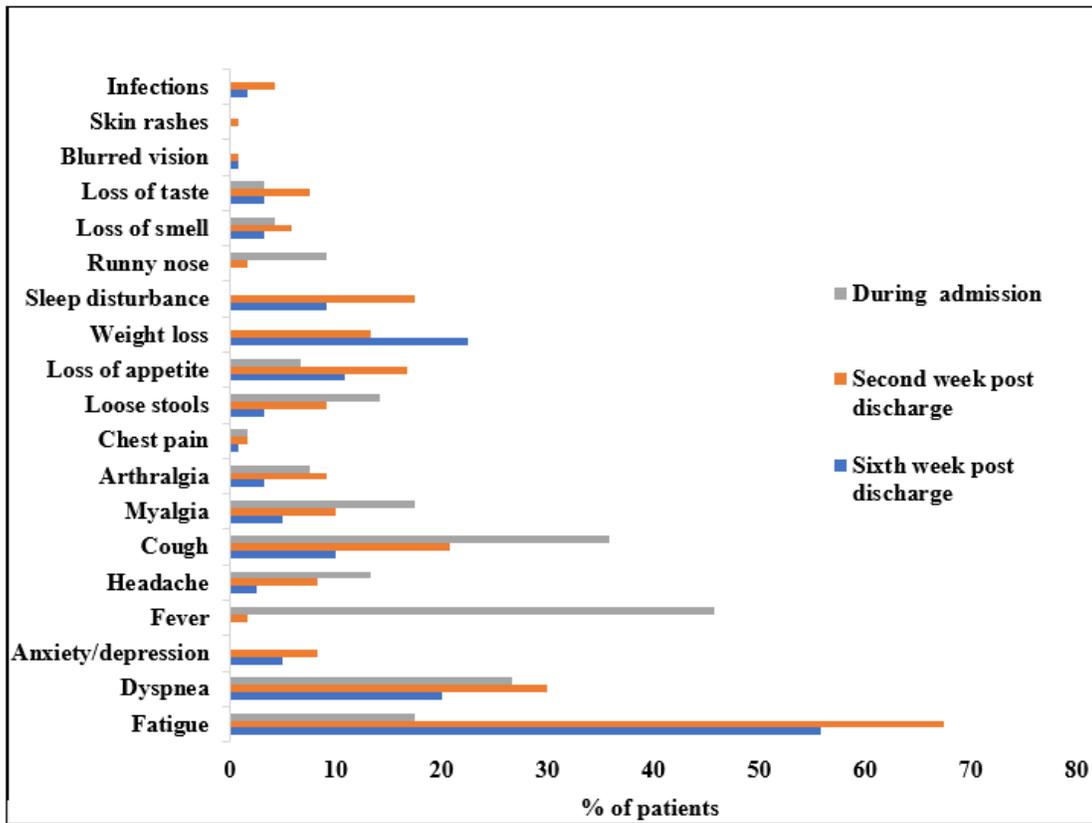


Figure 2

Percentage of patients with COVID-19 related symptoms during hospital admission and at the time of follow-up.

Location of figure: After the 3rd paragraph of results