Post COVID-19 clinical manifestations and its risk factors among patients in a Northern District in Kerala, India

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Abstract

Background: The novel virus SARS-CoV-2 has caused a pandemic of coronavirus disease 2019 (COVID-19). There is emerging evidence of post-COVID-19 manifestations among patients who sustain acute COVID-19. Most studies report fatigue, dyspnea, and myalgia as the common symptoms; however, currently, there is limited knowledge of these post-COVID manifestations and their risk factors, especially in India. **Methods:** A descriptive cross-sectional study was conducted among patients who had attended the district post-COVID clinic, Wayanad district, Kerala, from October 2020 to June 2021. Data were collected by direct/telephonic patient interviews and from their existing case records, using a pretested semi-structured proforma. **Results:** The sample size was 667. The mean age of the study population was 45 years (standard deviation [SD]: 14.55). The majority of the population presented with dyspnea (48%), fatigue (32%), and cough (25.6%). Mental health problems were also reported in 6% of participants. The respiratory system was commonly involved (61.2%). Around one-third of the patients (36.4%) had dyspnea on exertion and 11.8% had dyspnea at rest. One-fifth of the population reported aggravation of pre-existing co-morbidity and half of the respondents had persistence of at least one symptom after 6 months. There exist statistically significant associations between identified risk factors, especially gender, increasing age, the severity of COVID-19 infection, history of tobacco/alcohol use, and co-morbidities with outcomes. **Conclusion:** As post-COVID syndrome is a multisystem disease, integrated rehabilitation is required with targeted intervention for survivors based on their symptoms and needs.

Keywords: COVID-19, India, Kerala, long COVID, post-COVID clinic, post-COVID manifestations, post-COVID syndrome, risk factors

Introduction

COVID-19 is a novel disease caused by the severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2). Since its first description in December 2019, COVID-19 progressed into a major public health concern.[1] Patients suffered from symptoms such as fever, dry cough, and fatigue, which is mild in about 80% of cases; however, the severity may progress to develop respiratory distress.[2]

Recovery from COVID-19 occurs within 7–10 days in mild disease; it could take 3–6 weeks in severe illnesses. According to the Centers for Disease Control and Prevention, post-COVID-19 conditions are a wide range of new, returning, or ongoing health problems that people can experience for more than 4 weeks after

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initially being infected with the virus that causes COVID-19. Even asymptomatic can have post-COVID-19 conditions. These conditions are multisystem illnesses with different types and combinations of health problems for varying lengths of time and manifestations differ between patients and within patients over time. Follow-up of patients who recovered showed that one or more symptoms persist in a substantial percentage of people, even weeks or months after COVID-19.[3-6]A study done in Egypt revealed that only 10.8% of all subjects had no residual symptoms after recovery; however, a major proportion suffered from several symptoms and diseases.[2]

Many studies suggest that fatigue was the commonest symptom in the post-COVID period and the other reported long-term symptoms include dyspnea, chest pain, headache, loss of smell, loss of taste, arthralgia, myalgia, followed by depression, mood swings, anxiety, insomnia, itching, palpitations, anorexia, tingling fingertips, and brain fog. Critical manifestations such as stroke, renal failure, myocarditis, and pulmonary fibrosis were also reported. The most notable potential long-term effects involve the central nervous system, psychosocial, cardiovascular, pulmonary, hematologic, renal, and gastrointestinal manifestations, as well as the post-intensive care syndrome.[2,7-9] About 40% of patients with COVID19 admitted to the hospital developed acute respiratory distress syndrome (ARDS). Pulmonary fibrosis is a well-recognized sequela of ARDS.[10] In patients with less severe pulmonary involvement, gastrointestinal symptoms, smell, and taste disturbances may play a role.[1] A retrospective cohort study shows that individuals discharged after acute COVID-19 had an increased risk of mortality, readmission, and multi-organ dysfunction compared with the general population. This was not confined to the elderly and not uniform across ethnic groups.[10] Advanced age and pre-existing conditions are predictors of poor outcomes in acute COVID-19; however, the epidemiology of post-COVID syndrome has been poorly defined because of the unclear medium and long-term pathophysiology across organ systems.[11]

As the COVID-19 pandemic is only 18 months old, there are only very few studies discussing the post-COVID-19 phase. Because some of the signs and symptoms in the post-COVID phase are subtle, people fail to recognize and report the same, which may have serious health implications in the future. The knowledge regarding the epidemiology of post-COVID-19 among the recovered is very limited.

The existing very few studies have not included much of South Indian populations, including rural and indigenous people such as the tribes of Wayanad District, Kerala. Wayanad district harbors people predominantly belonging to the ancestral South Indian ethnicity. Hence, differences in the manifestations of post-COVID symptoms in this particular group of people, differing in cultural, socio-economic, and ethnic background, should be studied in detail. The establishment of post-COVID clinics will help in the understanding and characterization of the epidemiology of the disease, which will in return help in the

appropriate management of the patient. It may also redefine the public health intervention required and necessitate a change in policy-making and resource planning.[11] The objectives of the study were to describe the post-COVID clinical manifestations and determine their association with identified risk factors among patients, who attended the district post-COVID clinic, from October 2020 until June 2021, functioning at District TB Center Wayanad.

Materials and Methods

Study design, setting, population

A descriptive cross-sectional study was conducted among patients who had attended the district post-COVID clinic of District TB center, Mananthavady, Wayanad district, Kerala from October 2020 to June 2021.

Nearly a fifth of the population of Wayanad comprises SC/ST community and it is one of the hundred districts in India to be included in the Rashtriya Sam Vikas Yojana (Backward District Initiative by NitiAyog). They are socio-economically weak, necessitating help from Public Sector establishments, and other voluntary organizations. Wayanad was the first district in Kerala to start the "District post-COVID Clinic" as per the guidelines laid by the Ministry of Health and Family Welfare, Government of Kerala.[12] Post-COVID clinic discovered various symptoms in the COVID-19 survivors of both the first and second wave, a large chunk of which belonged to the rural population. Hence, the post-COVID clinic can provide first-hand information to the District Health administration to have a detailed data analysis to evaluate the health care Institutions under it.

Sample size and sampling technique

Non-probability sampling technique was applied to include data of 700 patients, which satisfied the inclusion and exclusion criteria. Only the data of patients who were residents of Wayanad District and who were previously diagnosed with COVID-19 either by RT-PCR or antigen testing were included in the study. Patients who declined to participate during the telephonic interviews and those who were currently COVID-19 positive were excluded from the study.

Data collection procedure

Data from the out-patient case sheets of patients who attended the District post-COVID clinic within the study period, were collected. Data were collected by direct/telephonic patient interviews and from their existing case records at the District post-COVID clinic, using a pretested semi-structured proforma as the study tool. Study variables, such as socio-demography, history of comorbidities, addictions, previous history of COVID-19 with its symptoms, clinical categorization, hospitalization and treatment history, presenting post-COVID symptoms and signs, relevant system-wise clinical examination findings, and relevant investigation results, were collected. The outcome variables were post-COVID clinical manifestations,

aggravation of comorbidities, and persistence of symptoms after 6 months.

Ethical considerations

Data were collected after getting approval from Institutional Ethics Committee with Ref. no. IEC/GMCM/87. Administrative approval was obtained from the District Medical Officer, Wayanad, for conducting the study. Informed consent was obtained before starting the telephonic interviews. The confidentiality of participants was maintained throughout the study.

Data analysis

All data were entered in MS Excel and analyzed using the SPSS 16 statistical software. Quantitative data such as age and time taken for COVID-19 negativity were described as mean with standard deviation, minimum and maximum values. Qualitative data are expressed as frequency and percentage. Possible associations of clinical manifestations and outcomes with the identified risk factors were calculated. Categorical variables were compared using the Chi-square test. Statistical significance was set at a two-sided $P < 0.05$. Binary logistic regression was used to identify the predictors of outcome.

Results

Socio-demographic profile

The total sample size was 691. Only 4.6% of the population was less than 18 years of age and none of the participants in this age category had symptoms that persisted after 6 months, hence less than 18 years were excluded from further analysis making the final sample size 667.

Out of 667, the majority (99%) belonged to the general category and 1% was contributed by the tribal population. The mean age group of the study population with a standard deviation was 45 ± 14.55 with a range of 18–83. They were classified into three age categories. Half of the population belonged to 18–44 years, 30% in the 45–59-year group, and 20% were ≥60 years. More than half of the population was male.

Around half of the population had a history of some comorbidity. Common comorbidities were hypertension, pre-existing lung conditions such as reactive and restrictive airway diseases, and diabetes mellitus. Among the people with comorbidities, the majority had single comorbidities. One-fourth of the population had a history of either tobacco or alcohol use [Table 1].

Information on previous COVID-19 infection

The mean time taken for COVID-19 negativity with standard deviation among respondents (*n* = 574), who were tested as part of discharge policy was 10.6 ± 3.07 days with a median of 10 days. The history of clinical categorization at the time of COVID-19 infection revealed that the majority of the population was category A, followed by category B, and category C. This

corresponds to the hospitalization status. All in categories B and C were hospitalized (43.2%). Only around 1/10 needed intensive care unit (ICU) admissions. Nearly 15% received oxygen. Among them, only small proportions were in invasive and non-invasive ventilation [Table 2].

Table 1: Socio-demographic profile	
Variable	Number (%)
Age distribution of study participants (*n*=667)	
18-44 years	335 (50.2)
45-59 years	202 (30.3)
60 years and above	130 (19.5)
Gender distribution of study participants (*n*=667)	
Male	386 (57.9)
Female	281 (42.1)
History of comorbidity (*n*=667)	
No	359 (53.8)
Yes	308 (46.2)
Common types of comorbidity	
Hypertension (*n*=667)	125 (18.7)
Previous respiratory system conditions (*n*=667)	94 (14.1)
Diabetes mellitus (*n*=664)	91 (13.7)
Dyslipidemia (*n*=667)	26 (3.9)
Coronary artery disease (*n*=667)	24 (3.6)
Thyroid abnormalities (*n*=667)	22 (3.3)
Number of comorbidities (*n*=308)	
Single comorbidity	201 (65.3)
Multiple comorbidities	107 (34.7)
History of use of tobacco and alcohol (*n*=667)	
No	496 (74.4)
Yes	171 (25.6)
Type of addiction (*n*=171)	
Tobacco	95 (55.5)
Alcohol	76 (44.5)

Table 2: Details of previous COVID-19 infection	
Variable	*n* (%)
Clinical category (*n*=666)	
Category A (mild)	379 (56.9)
Category B (moderate)	150 (22.5)
Category C (severe)	137 (20.6)
Required ICU admission (*n*=665)	
Yes	57 (8.6)
Administered anti-viral (*n*=664)	
Yes	71 (10.7)
Administered steroid (*n*=664)	
Yes	61 (9.2)
Administered HCQ (*n*=664)	
Yes	14 (2.1)
Administered oxygen (*n*=665)	
Yes	99 (14.9)
Required non-invasive ventilation (*n*=661)	
Yes	1 (0.2)
Required invasive ventilation (*n*=659)	
Yes	4 (0.6)
Administered convalescent plasma (*n*=664)	
Yes	13 (2)

Acute COVID-19 clinical manifestations

The most common symptom was fever, followed by dyspnea, loss of smell, loss of taste, and cough [Figure 1].

Post COVID-19 symptomatology

The majority of the population presented with dyspnea, followed by fatigue and cough. A tenth of the population had sleep-related problems and 6.6% had self-reported psychiatric problems. Common psychiatric problems were mood disorders and anxiety. Partial or complete loss of taste and loss of smell was also reported [Figure 2].

Grading of dyspnea

Around one-third of patients had dyspnea on exertion and more than one-tenth had dyspnea at rest [Table 3].

Post COVID-19 involvement of different systems

Major systems involved in the post-COVID-19 phase were the respiratory system, followed by the musculoskeletal and gastrointestinal systems. Fibrotic changes were seen on imaging in 2% of patients with respiratory system involvement. Other systems involved are shown in Figure 3. Common symptoms of respiratory system involvement were cough, dyspnea on exertion and at rest, and exacerbation of previous lung problems. Myalgia, arthralgia, and exacerbation of arthritis were the common musculoskeletal problems. Acute gastritis, vomiting, loss of appetite, and diarrhea were the common symptoms of gastrointestinal involvement. Anosmia, parosmia, insomnia, headache, paresthesia/numbness, and confusion were the common manifestations of central nervous system involvement. Common dermatology manifestations were itching, skin rashes, and hair loss. Partial vision damage was the major ocular problem and erectile dysfunction in males was the major genital problem encountered [Figure 3].

Major post-COVID outcomes

The major post-COVID outcomes described were the aggravation of comorbidity and persistence of symptoms after 6 months of COVID-19 infection. Among the respondents, one-fifth of the population reported aggravation in comorbidity as a result of COVID-19 infection. Among these, the majority had exacerbation of pre-existing lung diseases. New onset/exacerbation of diabetes mellitus and hypertension were the other changes in comorbidities detected. Symptoms (mostly mild) persisted after 6 months for around half of the respondents. The main symptoms that persisted were dyspnea, cough, fatigue, insomnia, partial loss, or altered taste/smell sensation after 6 months of recovery [Table 4].

Table 3: Grading of dyspnea (*n*=667)	
Dyspnea coding	*n* (%)
No dyspnea	345 (51.7)
Dyspnea at rest	79 (11.8)
Dyspnea on exertion	243 (36.4)

Associations between risk factors and symptomatology

The association between gender and psychiatric problems shows that females are at 2.85 times more risk than males. Headache was reported more by people aged <60 years compared to the age group ≥60 years. Similarly, as the severity of the clinical category progresses, the post-COVID headache proportions were decreasing. It was more reported in persons belonging to the previous category-A COVID group. In contrast to this, as the category progressed from A to C, the chance of post-COVID fatigue increased significantly. Post-COVID-19 patients who had previously taken steroids as part of the COVID treatment were at 2.38 times more risk for developing dyspnea and 1.92 times risk for fatigue, compared to their counterparts [Table 5].
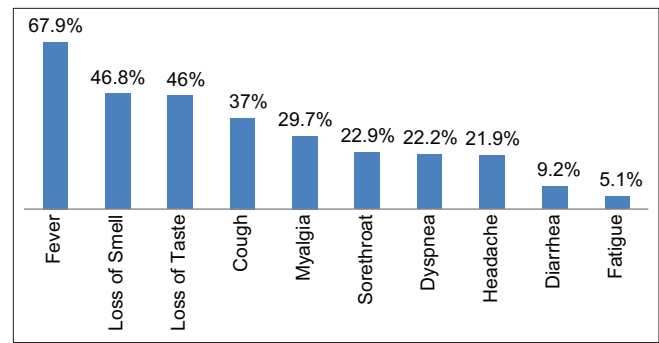

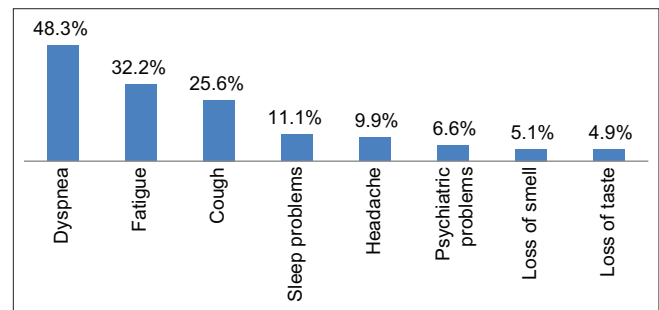
Figure 1: Symptomatology of acute COVID-19 (*n*=663)

Figure 2: Post-COVID-19 symptomatology (*n*=667)
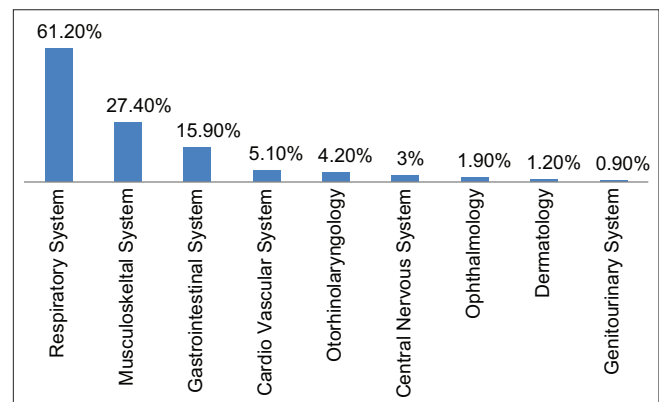

Figure 3: Post-COVID-19 involvement of different systems (*n*=667)

Association between risk factors and persistence of at least one symptom

There were statistically significant associations between the persistence of at least one symptom after 6 months among survivors and various risk factors such as age group, clinical categories, steroid use, ICU admission, tobacco/alcohol use, and presence of comorbidities such as pre-existing lung diseases, diabetes mellitus, and hypertension. Patients in the age group ≥60 years were at 43.4 times high risk than those in <60 years age category. As the category of acute COVID-19 progressed, the proportion of people with persistence also increased. Patients, who were previously admitted to the ICU were 16 times more at risk for persistence of at least one symptom. Another significant finding was that persistence was 8.9 times higher in persons who had taken steroids during their COVID-19 period. Persons with a history of comorbidities were at six times more risk than those without comorbidities. Patients with a history of tobacco/alcohol use were 2.7 times at risk of developing persistence. [Table 6]

Association between risk factors and aggravation in comorbidities

The other outcome was aggravation/new onset of comorbidity status. The patients with pre-existing lung diseases and convalescent plasma recipients were around four times riskier for aggravation of comorbidity status compared to their counterparts [Table 7].

Predictors of persistence of symptoms after 6 months

Binary logistic regression revealed that the model was fitted well and the predictors were patients who had received oxygen during their COVID-19 period, presence of any comorbidity, presence of diabetes mellitus, history of tobacco/alcohol use, age group ≥60 years, previous history of loss of smell, and previous history of loss of taste [Table 8].

Discussion

In this descriptive cross-sectional study, post-COVID-19 patients who had attended the District post-COVID clinic, for 9 months and satisfied the selection criteria were surveyed for post-COVID-19 manifestations and their association with

Table 4: Major post-COVID outcomes

Post-COVID aggravation of comorbidity (*n*=337)	
Aggravation in comorbidity	**n (%)**
Yes	70 (20.8)
No	267 (79.2)
Type of comorbidity aggravated (*n*=70)*	
Preexisting lung diseases	36 (51.4)
Diabetes mellitus	21 (30)
Hypertension	12 (17.1)
Persistence of at least one symptom after 6 months (*n*=490)	
Symptoms persisting after 6 months of COVID-19	**n (%)**
Yes	226 (46.1)
No	264 (53.9)

*Multiple responses

Table 5: Association between risk factors and clinical manifestations

Association between gender and psychiatric problem			
Gender	**Psychiatric problem (*n*=667)**		
	Yes *n* (%)	**No *n* (%)**	
Female	29 (10.3)	252 (89.7)	χ^2=10.93 at df 1 with a *P* value of 0.001, OR=2.85 (1.5-5.4)
Male	15 (3.9)	371 (96.1)	
Association between age group and headache			
Age group	**Headache (*n*=667)**		
	Yes *n* (%)	**No *n* (%)**	
≥ 60 years	6 (4.6)	124 (95.4)	χ^2=5.05 at df 1 with a *P*- value of 0.025, OR=0.39 (0.16–0.91)
< 60 years	60 (11.2)	477 (88.8)	
Association between previous COVID-19 clinical category and clinical manifestations			
Category	**Headache (*n*=666)**		**Fatigue (*n*=666)**	
	Yes *n* (%)	**No *n* (%)**	**Yes *n* (%)**	**No *n* (%)**
Category A	48 (12.7)	331 (87.3)	105 (27.7)	274 (72.3)
Category B	13 (8.7)	137 (91.3)	48 (32)	102 (68)
Category C	4 (2.9)	133 (97.1)	61 (44.5)	76 (55.5)
	χ^2=11.11 at df 2 with a *P* value of 0.004		χ^2=13.06 at df 2 with a *P* value of 0.001	
Association between previous steroid use and clinical manifestations			
Previous steroid use	**Dyspnea (*n*=664)**		**Fatigue (*n*=664)**	
	Yes *n* (%)	**No *n* (%)**	**Yes *n* (%)**	**No *n* (%)**
Yes	41 (67.2)	20 (32.8)	28 (45.9)	33 (54.1)
No	279 (46.3)	324 (53.7)	185 (30.7)	418 (69.3)
	χ^2=9.73 at df 1 with a *P* value of 0.002, OR=2.38 (1.36-4.16)		χ^2=5.89 at df 1 with a *P* value of 0.015, OR=1.92 (1.13-3.27)	

Table 6: Association between risk factors and persistence of at least one symptom after 6 months

Risk factors	Persistence of at least one symptom after 6 months		Statistical inference
	Yes *n* (%)	No *n* (%)	
Association between age group and persistence of symptoms after 6 months (*n*=490)			
≥ 60 years	103 (95.4)	5 (4.6)	χ^2=1.35 at df 1 with a *P* value of
< 60 years	123 (32.2)	259 (67.8)	<0.001, OR=43.38 (17.24-109.16)
Association between clinical categories and persistence of symptoms after 6 months (*n*=489)			
Category A	90 (34.6)	170 (65.4)	χ^2=47.85 at df 2 with a *P* value
Category B	59 (46.8)	67 (53.2)	of <0.001
Category C	77 (74.8)	26 (25.2)	
Association between steroid use and persistence of symptoms after 6 months (*n*=488)			
Steroid use - Yes	39 (86.7)	6 (13.3)	χ^2=32.47 at df 1 with a *P* value of
Steroid use - No	187 (42.2)	256 (57.8)	<0.001, OR=8.89 (3.69- 21.45)
Association between ICU admission and persistence of symptoms after 6 months (*n*=488)			
ICU admission -Yes	44 (91.7)	4 (8.3)	χ^2=44.05 at df 1 with a *P* value of
ICU admission -No	182 (41.4)	258 (58.6)	<0.001, OR=15.59 (5.51-44.16)
Association between comorbidity and persistence after 6 months (*n*=490)			
Comorbidity - Yes	163 (67.6)	78 (32.4)	χ^2=88.32 at df 1 with a *P* value of
Comorbidity - No	63 (25.3)	186 (74.7)	<0.001, OR=6.17 (4.17-9.14)
Association between preexisting respiratory condition and persistence after 6 months (*n*=490)			
Respiratory condition - Yes	45 (62.5)	27 (37.5)	χ^2=9.11 at df 1 with a *P* value of
Respiratory condition - No	181 (43.3)	237 (56.7)	0.003, OR=2.18 (1.30-3.65)
Association between hypertension and persistence after 6 months (*n*=490)			
Hypertension - Yes	81 (82.7)	17 (17.3)	χ^2=65.79 at df 1 with a *P* value of
Hypertension - No	145 (37)	247 (63)	<0.001, OR=8.12 (4.63-14.23)
Association between diabetes mellitus and persistence after 6 months (*n*=487)			
Diabetes mellitus - Yes	62 (88.6)	8 (11.4)	χ^2=59.66 at df 1 with a *P* value of
Diabetes mellitus - No	162 (38.8)	255 (61.2)	<0.001, OR=12.2 (5.69-26.14)
Association between dyslipidemia and persistence after 6 months (*n*=490)			
Dyslipidemia- Yes	16 (88.9)	2 (11.1)	χ^2=12.03 at df 1 with a *P* value of
Dyslipidemia- No	210 (44.5)	262 (55.5)	0.001, OR=9.98 (2.27-43.9)
Association between coronary artery disease and persistence after 6 months (*n*=490)			
Coronary artery Disease -Yes	19 (90.5)	2 (9.5)	χ^2=15.56 at df 1 with a *P* value of
Coronary artery Disease -No	207 (44.1)	262 (55.9)	<0.001, OR=12.02 (2.77-52.21)
Association between tobacco/alcohol use and persistence after 6 months (*n*=490)			
Tobacco/alcohol use Present	79 (64.2)	44 (35.8)	χ^2=21.66 at df 1 with a *P* value of
Tobacco/alcohol use-Absent	147 (40.1)	220 (59.9)	<0.001, OR=2.69 (1.76-4.11)

identified risk factors. The study reveals that the majority of the patients experienced dyspnea followed by fatigue and cough. These findings are consistent with studies done in Italy where fatigue and dyspnea were the predominant post-COVID symptoms and in China where the most common symptom was fatigue and severe patients had pulmonary diffusion abnormality.[13,14] Similar findings were seen in a study done in Haryana and a prospective study done in New Delhi.[15,16] In our study, one-tenth of the population had dyspnea at rest. Long-term lung damage such as irreversible dyspnea is one of the feared features of COVID-19.[17]

According to Higgins *et al.*,[9] other long-term effects of COVID-19 were the mental health impact on survivors, including anxiety, depression, Post Traumatic Stress Disorder (PTSD), sleep disturbances/insomnia, and chronic fatigue syndrome. Our study also reveals that a significant proportion of patients also experienced sleep disorders and self-reported psychiatric problems. Similar findings were seen in a study done in China.[14] In a study done in Spain, insomnia persisted in most patients 1 year after acute COVID-19 and was more common among hospitalized patients.[18]

Table 7: Association between risk factors and aggravation of comorbidities			
Risk factors	Aggravation of comorbidities Yes n (%)	Aggravation of comorbidities No n (%)	Statistical inference
Association between preexisting respiratory condition with aggravation of comorbidities (n=337)			
Respiratory condition - Yes	36 (38.3)	58 (61.7)	χ^2=24.33 at df 1 with a P value of <0.001, OR=3.82 (2.2-6.62)
Respiratory condition - No	34 (14)	209 (86)	
Association between convalescent plasma recipient status with aggravation of comorbidities (n=337)			
Plasma received -Yes	5 (50)	5 (50)	χ^2=5.28 at df 1 with P value of 0.02, OR=4 (1.12-14.23)
Plasma received - No	65 (20)	260 (80)	

Table 8: Predictors of persistence of symptoms after 6 months among survivors using Binary logistic regression			
Predictors of persistence of symptoms after 6 months Model fit: Nagelkerke R square=60.6%			
Variables	Persistence of at least one symptom after 6 months		
	Odd's ratio	95% CI for OR	P
Oxygen required (ref: not required)	14.89	5.9-37.61	<0.001
Any comorbidity - Yes (Ref: No)	3.71	2.15-6.39	<0.001
Diabetes mellitus - Yes (Ref: No)	5.56	2.16-14.32	<0.001
History of tobacco/alcohol use - Yes (Ref: No)	1.90	1.03-3.53	0.040
Age group - ≥60 years (Ref: <60 years)	60.84	18.13-204.22	<0.001
Previous history of loss of smell- Yes (Ref: No)	0.23	0.05-0.95	0.043
Previous history of loss of taste- Yes (Ref: No)	5.29	1.25-22.31	0.023

Existing evidence suggests that COVID-19 is a multisystem disease with long-term effects, Post-COVID effects encompass a broad spectrum including pulmonary, cardiovascular, neuromuscular, and neuropsychiatric/psychiatric systems.[17,19,20] Similarly, in this study also, almost all the systems were involved. The respiratory system was the major system involved, followed by the musculoskeletal and gastrointestinal systems. These findings are consistent with a study done in Haryana after the first wave, which shows that the post-COVID complications were related mainly to the respiratory system.[19] A review article also suggests that post-COVID syndrome is mainly characterized by musculoskeletal, pulmonary, digestive, and neurological involvement including depression.[21]

According to studies by Raveendran *et al.*[20] and Sykes *et al.*,[22] female gender, increasing age, and presence of comorbidities increase the risk of developing the post-COVID syndrome and females were significantly more likely than males to report anxiety, low mood, fatigue, and sleep disturbance. Similarly in our study, females were at more risk of psychiatric problems. Also, increasing age, progression of clinical category, and steroid intake during acute COVID-19 were significant risk factors for post-COVID symptoms. The severity of post-COVID manifestations was correlated to the severity of the infection and the presence of comorbidities.[23]

In our study, the persistence/partial loss of smell or taste was another significant symptom. Persistent anosmia is one of the most common post-COVID symptoms, which is caused by the post-viral injury to the olfactory bulb.[19]

In this study, at least one symptom persisted after 6 months for half of the patients after recovery. Similar findings are seen in an Italian study where 87.4% reported persistence of at least one symptom, particularly fatigue and dyspnea and a meta-analysis also suggested that up to 48% of patients persisted with respiratory symptoms.[13,21] Oxygen requirement during COVID-19, age ≥60 years, presence of addictions, presence of comorbidities, diabetes mellitus, loss of smell, and loss of taste were the predictors for the persistence of symptoms in our study. Similar findings were observed in a study by Kayaaslan *et al.*,[17] where hospital admission for acute COVID-19, severe COVID-19, and presence of comorbidity were independent predictors for symptom persistence.

In this study, hypertension was the most common comorbidity identified among the participants, followed by co-existing respiratory conditions and diabetes mellitus. A significant proportion of patients had aggravation of comorbidities and among them, those with pre-existing lung diseases were at around four times more chance of the aggravation of comorbidity status compared to their counterparts. According to Raveendran and Misra, the COVID-19 pandemic has resulted in poor control of diabetes, progression of pre-diabetes to diabetes, an increase in the number of new-onset diabetes, and a rise of corticosteroid-induced diabetes.[24]

Conclusion

The most common symptoms reported by the post-COVID patients were dyspnea, followed by fatigue and cough. A significant proportion also reported mental health problems and insomnia. The respiratory system was the most common system affected in the post-COVID period. There is a significant aggravation of comorbidities and at least one symptom persisted for half of the study participants after 6 months of recovery. There exist statistically significant associations between identified risk factors especially gender, increasing age, the severity of COVID-19 infection, history of tobacco/alcohol use, and comorbidities with outcomes.

This knowledge regarding post-COVID symptoms and their associations will help in the early diagnosis and treatment at

the community level. All subjects recovering from COVID-19 should undergo long-term monitoring for their symptoms and condition improvement. Follow-up in the post-recovery period is important due to its resulting disruption of the quality of life and the health care should be planned as multidisciplinary care with representation from specialists (respiratory medicine, cardiology, and rehabilitation medicine) and cognate disciplines (including physiotherapy, occupational therapy, psychology, and dietetics) to address the patient as a whole.

Key messages

- Most post-COVID patients encountered numerous symptoms ranging from mild to severe.
- Significant involvements of different organ systems were seen.
- Alleviating the symptoms and improving the quality of life for those affected should be highly regarded.
- Interdisciplinary cooperation is needed for comprehensive care in the outpatient setting.

Conflicts of interest

There are no conflicts of interest.

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