International Journal of General Medicine

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ORIGINAL RESEARCH

A Comprehensive Assessment of Self-Reported Post COVID-19 Symptoms Among Beneficiaries of Hospital Employee Scheme at a Tertiary Healthcare Institution in Northern India

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Purpose: With millions of people being affected by COVID-19, people living with post COVID-19 clinical symptoms (PCS) are expected to rise further. The primary aim of the study was to comprehensively assess self-reported PCS and its associated risk factors among beneficiaries of Hospital Employee Scheme of a tertiary healthcare institution in Delhi.

Patients and Methods: An online cross-sectional study was conducted using a semi-structured questionnaire developed by employing nominal group technique among individuals aged 18 years and above who were novel SARS-CoV-2 positive from January to April 2021. Participants were telephoned first, before sending the online survey link. Socio-demographic data, information on PCS along with potential risk factors, pre-existing morbidities, vaccination status, severity of acute illness and management were collected between June and July 2021. PCS was presented as relative frequency; Chi-Square test and odds ratio; adjusted values were used to rule out any association between PCS and predictors.

Results: In total, 773 of 1801 eligible participants responded to the survey (completion rate 42.9%), with a median age of 34 years (IQR 27–44). Males accounted for 56.4% and PCS was present in 33.2%. The most prevalent symptoms were fatigue (79.3%), arthralgia (33.4%), myalgia (29.9%), hair loss (28.0%), headache (27.2%), breathlessness (25.3%), and sleep disturbance (25.3%). The prevalence of PCS was reduced to 12.8% at 12 weeks. Female gender, older age, oxygen supplementation, severity of acute illness, and pre-existing co-morbidities were positively associated with PCS. Vaccination (second dose) reduced the odds of developing PCS by 39% compared to unvaccinated participants (aOR 0.61; 95% CI 0.40–0.96).

Conclusion: PCS affects almost all organ systems of the body, regardless of the severity of acute COVID-19 illness. Two doses of vaccine hel reduce the development of PCS.

Keywords: COVID-19, post COVID-19 symptoms, long COVID-19, cross-sectional study, Northern India

Introduction

The World Health Organization declared COVID-19 a pandemic on March 22, 2020, approximately 3 months after the first case of the disease was identified.[1,2] Since then, the disease continues to spread in an unprecedented manner across the world causing the loss of millions of lives. As of July 4, 2022, more than 546 million people were affected and nearly 6.3 million people lost their lives due to the disease.[3] In India, approximately 43.5 million people have been infected with the virus and more than 525,000 of them have died.[4]

While the countries continue to grapple with the rising number of COVID-19 cases, there is growing evidence on lingering COVID-19 symptoms extending up to a few months from the date of initial diagnosis among the survivors. Multiple studies,

Received: 20 July 2022
Accepted: 7 September 2022
Published: 20 September 2022

including self-reported and systemic reviews, have illustrated that around 50–87% of the hospitalized patients experience at least one or more post COVID-19 symptoms (PCS) for several weeks.[5–9] For example, a self-reported online survey in Korea reported that 52.7% of the respondents have shown at least one persistent COVID-19 symptom.[6] Another study showed that 20% of the patients experienced PCS lasting more than 3 months.[10] A self-reported Swedish web questionnaires study reported 1 out of 10 with long-term symptoms for at least 4 weeks.[8] Such persisting and debilitating symptoms following COVID-19 mean that the adverse consequences of the pandemic do not end with recovery, and continue much beyond the acute phase of illness.[5]

As the pandemic continues to spread globally, the number of people living with PCS will increase over time. Although the natural history of COVID-19 is not completely known, it is now well recognized that COVID-19 is a multiorgan systemic disease with broad spectrum of manifestations.[5] With millions of individuals recovering, the long-term consequence of COVID-19 is likely to become an additional burden on the healthcare delivery system, especially in low- and-middle-income countries. Understanding PCS and associated risk factors is crucial to reorient the model of care to make it more responsive to the emerging needs. Hence, information on PCS is essential to guide development of appropriate infrastructure and manpower, thereby designing management strategies and patient care plans in hospitals and rehabilitation facilities. The present study aimed to comprehensively assess self-reported PCS and associated risk factors among beneficiaries of Employee Hospital Scheme of a tertiary healthcare institution in Northern India.

Materials and Methods

Study Population

This cross-sectional study was conducted among adult population (those aged 18 years and above) who were beneficiaries of Hospital Employee Scheme (EHS) of a tertiary healthcare institute in Northern India. The institute is one of the biggest tertiary canters in the country with more than 15,000 employees and more than 3100 beds expanding across various medical subspecialties. The EHS was established in the institute to provide free healthcare services to hospital employees and their dependents. During the COVID-19 pandemic, the hospital staff and their dependents have received free COVID-19 care services for both outpatients and in-patients, including COVID-19 vaccination. The inclusion criteria for the study were positive report of SARS CoV-2 test from January 1, 2021 to April 30, 2021, and having recovered from the illness. This list of COVID-19 recovered individuals (2037) was obtained from the Department of Hospital Administration of the institution during the month of June 2022. From this list, we excluded participants aged below 18 years, individuals who could not contact telephonically before sending the link and participants not using or not having knowledge of WhatsApp. The variables recorded were age, sex, date of diagnostic testing for COVID-19, and relevant contact details (like telephone numbers). The required minimum sample size was estimated based on the seroprevalence among adults of 47.2% in megacities in December 2020,[11] with a relative precision of 10%, power of 80%, 95% confidence interval and a nonparticipation rate of 20%. The final estimated sample size calculated was 773 individuals.

Study Definitions

Post COVID-19 clinical symptoms: Symptom(s) that persisted beyond 4 weeks from the date of SARS-CoV-2-positive test conducted using either Reverse Transcriptase Polymerase Chain Reaction (RTPCR) or Cartridge Based Nucleic Acid Amplification Test (CBNAAT). Further, according to the timeframe, post COVID-19 symptoms were classified as short-term post COVID-19 symptoms (ST-PCS): symptoms present beyond 4 weeks after the SARS-CoV-2-positive test and lasting less than or up to 12 weeks; and long-term post COVID-19 symptoms (LT-PCS): symptoms present beyond 12 weeks after the SARS-CoV-2-positive test.

Data Collection

A semi-structured questionnaire was developed for the study. The questionnaire was digitized using Google Forms.[12] Google Forms is an online data collection tool that is commonly used for surveys.[13,14] A nominal group technique was used to develop the questionnaire. One researcher developed the first draft of the study tool after extensive review of the relevant published papers to ensure all possible PCS. One expert each was requested to review the tool from the specialties of endocrinology, internal medicine, psychiatry, ophthalmology, and pulmonary medicine, respectively. The questionnaire was revised based on the feedback received from the experts during the group discussions (in person and

online). The questionnaire included demographic information, and various possible risk factors for post COVID-19 manifestations. The final section of the questionnaire consisted of a list of possible post COVID-19 symptoms that were categorized based on organ systems. Before standardization, pre-testing of the questionnaire was done among non-study participants who had recovered from COVID-19. The English language was translated into Hindi by a translator, and back translated into English to ensure the accuracy of the translation.

The data were collected between June 16, 2021 and July 30, 2021. A minimum gap of 4 weeks was ensured between data collection and COVID-19 testing date of participants. All participants meeting the inclusion criteria were contacted telephonically and were requested to participate in the survey. The respondents who were using WhatsApp™ platform (Facebook Inc, Cambridge, MA, USA) were sent the survey link using the same number. If any participant did not use WhatsApp™ on their phone, they were requested to provide an alternative mobile number with WhatsApp™ installed. This was done to enhance the participation rate. If any respondent could not provide a WhatsApp number, or could not read both the English and Hindi languages, we requested the participants for a suitable time to call for telephone-based data collection if they are willing to participate.

WhatsAppTM is a popular medium for communication and has been used in many studies as an electronic platform for communication.[15–17] Once the survey link was shared, the participants were requested to save the sender number first and then to activate the survey link. Prior to inclusion in the survey, participants were required to offer informed e-consent. A total of three reminders at a gap of 1–2 days were sent to participants who did not respond to the survey link sent to them earlier.

Ethics Statement

The present study was reviewed and has been approved by the Institute Ethics Committee of All India Institute of Medical Sciences, New Delhi (Ref. No.: IEC-365/04.06.2021).

Data Management and Analysis

The responses were automatically collected in a Google spreadsheet linked to the data collection form. The data were analysed using STATA version 15 (StataCorp 2015, Stata Statistical Software: Release 15, College Station, TX: StataCorp LP). The participants were divided into two groups, namely participants with post COVID-19 symptoms and participants without symptoms for further analysis.

Descriptive analysis was performed to summarize the findings. Continuous variables were presented as the mean and standard deviation for normal distribution, whereas median and interquartile range (IQR) were used for variables that were not distributed normally. Post COVID-19 manifestations were presented as relative frequency. Furthermore, post COVID-19 symptoms were categorized into 15 different groups according to different organ systems. The duration of symptoms was estimated from the date of confirmed test and date of response of the participants. Categorical data were presented as absolute counts, percentages and were further compared using the Chi Square and Fisher's exact test. Continuous variables were compared using *t*-test. Univariable and multivariable logistic regression models were used to explore explanatory variables associated with post COVID-19 symptoms. The results were presented as odds ratios and adjusted odds ratios (ORs and aORs), along with 95% confidence intervals. Variables that were significant at $p<0.10$ in the univariable regression analysis were included in the multivariate model. Since it was a web-based survey, the checklist for Reporting Results of Internet E-Surveys (CHERRIES) was followed while reporting the data.[18]

Results

Characteristics of the Study Population

We were able to send the survey link to 1801 eligible participants after exclusion. Of this, a total of 773 individuals offered consent and completed the survey questionnaire (completion rate 42.9%). The median age of the respondents was 34.0 (IQR 27.0–44.0) years. The male respondents were 56.4%. The body mass index was equal to or more than 25 kg/m^2 for 319 (41.3%) respondents. The most commonly reported blood group was B Rhesus positive (31.8%), followed by O Rhesus positive (25.7%). Slightly more than half of the respondents (51.1%) were currently employed in the hospital, and nearly 80% of them were

graduate or above in education. A total of 134 (17.3%) respondents smoked or chewed tobacco products and 229 (29.6%) consumed alcohol (Table 1).

One-quarter (24.7%) had received the second dose of the vaccine at the time of the survey. Approximately three-fourths of participants (75.2%) reported that they had either asymptomatic or mild acute COVID-19, and 2.71% reported that they experienced severe acute COVID-19 (Table 1). Approximately 169 (21.9%) participants reported that they were managed in the hospital. Of these, 23 (2.9%) required oxygen supplementation during management. Furthermore, 8.3% of the participants considered themselves to have poor or very poor overall health status following COVID-19 illness.

Post-COVID-19 Symptoms

One-third of the participants, ie, 257 (33.2%), reported that they had at least one or more ST-PCS (4 weeks or more), but this number was reduced to 99 (12.8%) at 12 weeks or more and to 15 (0.90%) at 16 weeks or more since SARS-CoV-2

Table 1 Characteristics of the Study Population (N=773)

Characteristics	Observation	Post COVID-Symptoms		
	n (%)	Yes (%)	No (%)	
	N=773	n=257 (33.2)	n=516 (66.8)	P value
Age (years)				
18–25	149 (19.3)	26 (17.4)	123 (82.6)	0.0001
26–45	462 (59.8)	177 (38.3)	285 (61.7)	
46–60	146 (18.9)	45 (30.8)	101 (69.2)	
61–70	12 (1.06)	7 (58.3)	5 (41.7)	
>71	4 (0.5)	2 (50.0)	2 (50.0)	
Gender				
Male	436 (56.4)	123 (28.2)	313(71.8)	0.0007
Female	337 (43.6)	134 (39.8)	203 (60.2)	
Blood groups				
A+	142 (20)	49 (34.5)	93 (65.5)	0.36
A-	3 (0.4)	0 (0)	3 (100)	
AB+	86 (12.1)	26 (30.2)	60 (69.8)	
AB-	4 (0.6)	1 (25)	3 (75)	
B+	246(34.7)	99 (40.2)	147 (59.8)	
B-	16 (2.3)	5 (31.3)	11 (68.8)	
O+	199 (28.1)	61 (30.7)	138 (69.3)	
O-	13 (1.8)	3(23.1)	10(76.9)	
Do not know	64 (8.3)	13	51	
Body mass index (kg/m^2)				
Normal or underweight (≤24.9)	413 (53.4)	154 (33.9)	300 (66.1)	0.21
Overweight (25–29.9)	248 (32.1)	86 (34.7)	162 (65.3)	
Obese (≥30)	71 (9.2)	17 (23.9)	54 (76.1)	

(*Continued*)

Table 1 (Continued).

Characteristics	Observation	Post COVID-Symptoms		
	n (%)	Yes (%)	No (%)	
	N=773	n=257 (33.2)	n=516 (66.8)	P value
Educational level				
Secondary and below	60 (7.8)	17 (28.3)	43 (71.7)	0.13
Higher secondary level	121 (15.7)	35 (28.9)	86 (71.1)	
Graduate	354 (45.8)	112 (31.6)	242 (68.4)	
Postgraduate	233 (30.1)	91 (39.1)	142 (60.9)	
Prefer not to specify	5 (0.06)	-	-	
Workplace/occupation				
Hospital employee	395 (51.1)	156 (39.5)	239 (60.5)	0.0002
Non-Hospital employee	378 (48.9)	101 (26.7)	277 (73.3)	
Smoking/tobacco products consumption				
Yes	134 (17.3)	31 (23.1)	103 (76.9)	0.006
No	639 (82.7)	226 (35.4)	413 (64.6)	
Alcohol consumption				
Yes	229 (29.6)	70(30.6)	159 (69.4)	0.30
No	544 (70.4)	187(34.4)	357 (65.6)	
Place of COVID-19 test conducted				
Government	743 (96.1)	249(33.5)	494 (66.5)	0.43
Private	30 (3.9)	8(26.7)	22 (73.3)	
Places of COVID-19 management				
Non-Hospital	604 (78.2)	206 (80.2)	398 (77.1)	0.44
Hospital	169 (21.8)	51 (30.2)	118 (69.8)	
Severity of COVID-19 disease (self-rated)				
Asymptomatic	138 (17.8)	21 (15.2)	117 (84.8)	0.0001
Mild	443 (57.3)	154 (34.8)	289 (65.2)	
Moderate	171 (22.1)	71 (41.3)	101 (58.7)	
Severe	21 (2.71)	11(55)	9(45)	
Management for COVID-19				
Managed with oxygen	23 (2.98)	15 (65.2)	8 (34.8)	0.0001
Managed without oxygen	750 (97.0)	242 (32.3)	508 (67.7)	
COVID-19 vaccination at the time survey				
Not vaccinated before COVID-19 infection	407 (52.7)	142 (34.9)	265 (65.1)	0.05
1st dose before COVID-19 virus infection	175 (22.6)	65 (37.1)	110 (62.9)	
2nd dose before COVID-19 virus infection	191 (24.7)	50 (26.5)	141 (73.5)	

(*Continued*)

Table 1 (Continued).

Characteristics	Observation	Post COVID-Symptoms		
	n (%)	Yes (%)	No (%)	
	N=773	n=257 (33.2)	n=516 (66.8)	P value
Comorbidities among participants				
Yes	261 (33.8)	110 (42.1)	151(57.9)	0.0002
No	512 (66.2)	147 (28.7)	365 (71.3)	
Self-rating following COVID-19 illness				
Good health	709 (91.7)	215 (30.3)	494 (69.7)	0.0001
Poor or very poor health	64 (8.3)	42 (65.6)	22 (34.4)	

test positivity. Few respondents rated their severity of PCS as mild (58.0%), moderate (34.6%), or severe (4.93%; Table 2). During acute phase of COVID-19 illness, 68.1%, 27.6% and 4.2% had asymptomatic or mild, moderate and severe acute illness, respectively among participants who experienced PCS (Table 2). Another 80.2% of the PCS respondents were not hospitalized during the acute COVID-19 illness (Table 1).

Table 2 Characterization of Post COVID-19 Symptoms (n=257)

Symptom Groups	n	Relative Frequency (%)
Unspecific post COVID-19 syndrome		
Weakness/Tiredness	204	79.4
Weight loss	46	17.9
Fever	34	13.2
Unable to do routine activities	25	9.7
Weight gain	2	0.78
Retching	1	0.39
Respiratory		
Difficulty in breathing	65	25.3
Cough	64	24.9
Chest heaviness/tightness	1	0.39
Cardiovascular syndrome		
Palpitations	41	15.9
Cold and chills legs/ body	13	5.06
Swelling or oedema in lower limbs	12	4.67
Sweating and night sweating	11	4.28
High blood pressure (new)	8	3.11
Tachycardia	3	1.17

(*Continued*)

Table 2 (Continued).

Symptom Groups	n	Relative Frequency (%)
Chest pain	1	0.39
Stroke (new)	1	0.39
Musculoskeletal		
Joint pain	86	33.5
Muscle pain	78	30.3
Leg pain	2	0.78
Back pain	2	0.78
ENT symptoms		
Loss or decreased of smell	58	22.6
Sore throat	56	21.8
Loss of taste	48	18.7
Altered smell	18	7.00
Hearing loss	10	3.89
Nasal congestion or blockage	21	8.17
Ringing in the ears	12	4.67
Sinusitis or pain in the sinus	9	3.50
Itching in the ear	1	0.39
Runny nose	1	0.39
Otitis externa	1	0.39
Ocular symptoms		
Itching in the eyes	25	9.73
Near vision impairment	20	7.78
Burning eyes	18	7.00
Redness in eyes	17	6.61
Feeling of dryness in eyes	15	5.84
Distance vision impairment	10	3.89
Feeling of painful in eyeball	16	6.23
Foreign body sensation in the eyes	6	2.33
Double vision	1	0.39
Asthenopia	1	0.39
Periorbital pigmentation	1	0.39

(*Continued*)

Table 2 (Continued).

Symptom Groups	n	Relative Frequency (%)
Gastrointestinal		
Loss of appetite	41	15.9
Loose motion	34	13.2
Abdominal cramps/pain	26	10.1
Nausea/vomiting	23	8.94
Acidity or gastritis	7	2.72
Increased appetite	2	0.78
Constipation	2	0.78
Hepatobiliary		
Liver problems/Abnormal liver function test	9	3.50
Abnormal in lipid profile	1	0.39
Neurological symptoms		
Headache	70	27.2
Sleep disorders	65	25.3
Loss of memory	36	14.0
Unable to concentrate	48	18.7
Dizziness	21	8.17
Tingling or peripheral neuropathy	1	0.39
Mental health symptoms		
Anxiety or apprehension	35	13.6
Mood swing or disorders	27	10.5
Fear or panic attack	18	7.00
Depression	15	5.84
Dermatological symptoms		
Hair loss or falls	74	28.8
Skin rashes	19	7.39
Discoloration of fingers/toes	9	3.50
Itching whole body	1	0.39
Acne	1	0.39
Black fungus	1	0.39
Dry skin	1	0.39
Nail discoloration	1	0.39
Herpes	1	0.39

(*Continued*)

Table 2 (Continued).

Symptom Groups	n	Relative Frequency (%)
Oral symptoms		
Dry mouth	23	8.95
Gum or Teeth pain	14	5.45
Oral ulcer	3	1.17
Sensitive to cold water	2	0.78
Bleeding gum	2	0.78
Endocrine problems		
Diabetes (New)	6	2.33
Thyroid problem (new)	2	0.78
Behavioral problems		
Increase of mobile phone/computers/tablets	64	24.9
Loos of motivation	17	6.61
Not willing to interact with friends	11	4.28
Started alcohol consumption	2	0.78
Decrease of mobile phone	1	0.39
Started using tobacco/ smoking	1	0.39
Renal problems		
Kidney function deranged (New)	1	0.39
Self-reported severity of COVID-19 illness		
Asymptomatic	21	8.17
Mild	154	59.9
Moderate	71	27.6
Severe	11	4.28
Severity of post COVID-19 symptoms (n=81)		
Mild	47	58.0
Moderate	28	34.6
Severe/very severe	4	4.93
Cannot say	2	2.47

Abbreviation: ENT, Ear, Nose,Throat.

Among individuals with post-COVID-19 symptoms, 85.6% reported non-specific post COVID-19 symptoms (NPCS, Table 2). This was followed by musculoskeletal manifestations (49.8%), otorhinolaryngological symptoms (47.5%), neurological symptoms (47.0%), cardiorespiratory symptoms (42.4%), gastrointestinal symptoms (36.2%), ocular symptoms (31.9%), dermatological symptoms (31.5%), and cardiovascular symptoms (24.5%) and mental health symptoms (23.7%). The remaining organ system-specific symptoms, including behavioural changes, oral health problems, and hepatobiliary, and endocrine, kidney function abnormalities, were reported by less than 20% of the respondents (Figure 1). Overall, the

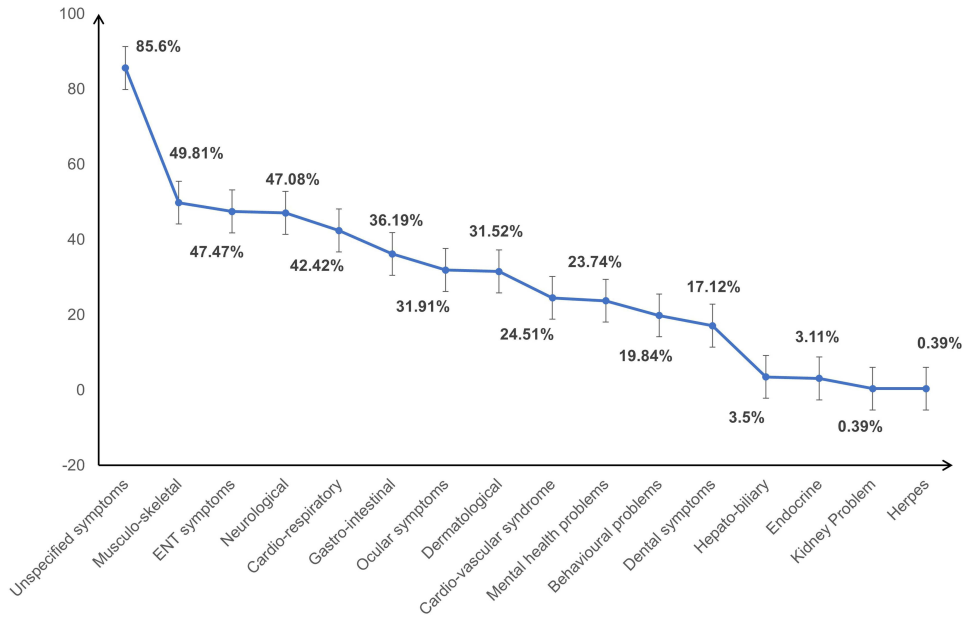

Figure 1 Organ specific categorization of post-COVID-19 symptoms (N=257).

commonly reported symptoms were fatigue, arthralgia and myalgia, hair loss and headache, cough, breathlessness, sleep disorders, sore throat and decreased sense of smell and taste (Figure 2).

Characterization of Post COVID-19 Symptoms

Nonspecific Post COVID-19 Symptoms (NPCS)

Fatigue (79.4%) was the most common manifestation among all post-COVID symptoms (Figure 2). The next most frequent amongst nonspecific post-COVID-19 symptom was weight loss (17.9%), followed by fever off and on (13.2%), and inability to perform routine activities (9.7%, Figure 1). Two respondents (0.78%) reported loss of weight after the COVID-19 disease.

Respiratory Symptoms

Considering the respiratory manifestations, approximately 25.3% of the participants reported breathlessness, followed by cough (24.9%). One person reported with chest tightness and heaviness.

Cardiovascular Symptoms

Among the cardiovascular symptoms, 16.0% of the respondents reported that they had palpitations followed by feeling cold and chills in the body and lower limbs (5.06%), 4.3% reported sweating at night and 4.7% for swelling of the lower limbs and another 3.1% reported hypertension. Three participants (1.2%) reported tachycardia, and one each reported chest pain and stroke as post-COVID-19 symptoms.

Musculo Skeletal Systems

There were few musculoskeletal manifestations experienced by the participants. The most common were arthralgia (33.46%) and myalgia (30.35%), followed by low back pain (0.78%) and leg pain (0.78%).

ENT Symptoms

Several oto-rhino-laryngological post-COVID-19 symptoms have been reported. The most frequent manifestations included loss or decreased sense of smell (22.57%) and sore throat (21.79%), followed by loss of taste (18.68%). Other reported oto-rhino-laryngological manifestations were altered smell (7.0%), nasal blockage (8.17%), tinnitus (4.67%, 12/257), pain in sinus areas (3.5%), etc. Itching ears and otitis externa were noted in one participant each.

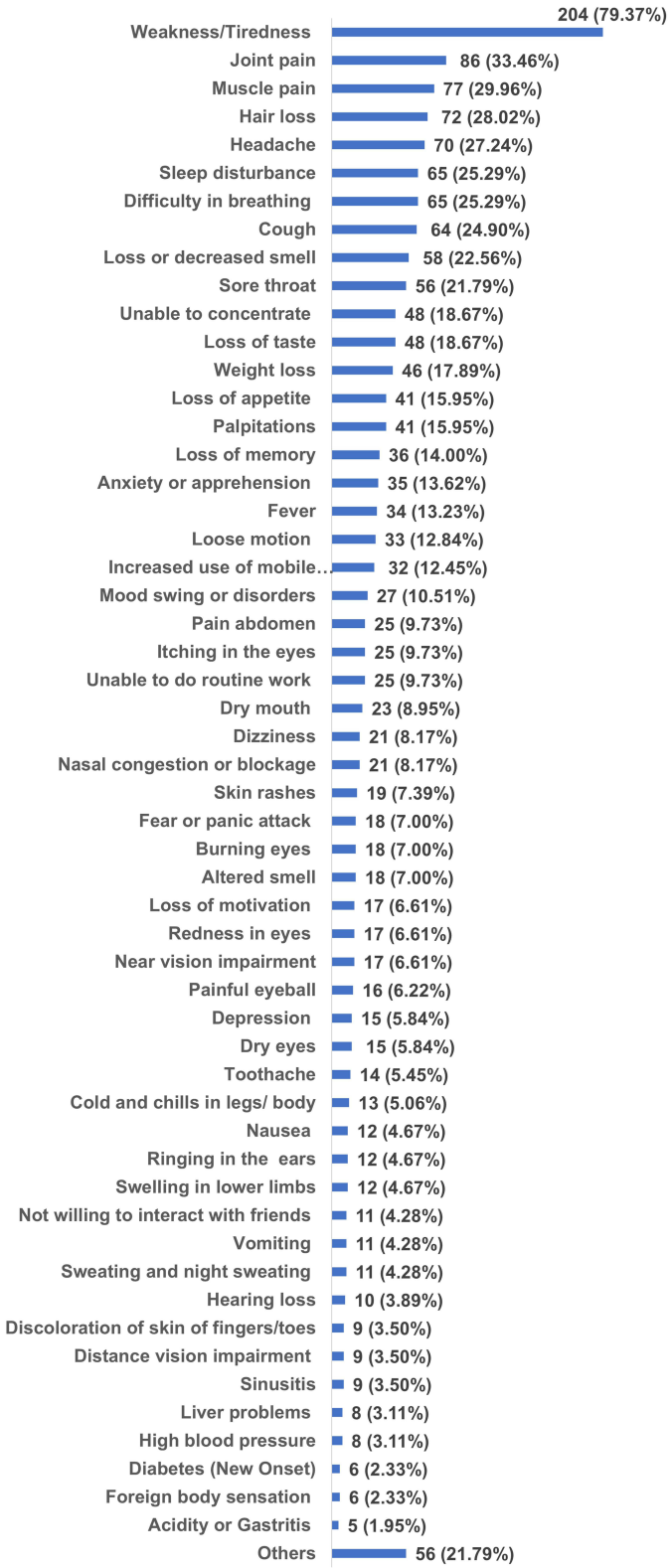

Figure 2 Frequency of self-reported post COVID-19 symptoms among study participants (N=257).

Eye Symptoms

Itching in the eyes (9.73%) was the most frequently reported post-COVID-19 ophthalmological manifestation, followed by near vision impairment (7.78%), burning eye sensation (7.0%), red eyes (6.61%), and pain in eyes

(6.23%). Other reported post COVID-19 eye symptoms were dryness in eyes (5.84%), distance vision impairment (3.89%) and foreign body sensation (2.33%), whereas diplopia, asthenopia and dark periorbital circle was reported by one respondent each.

Gastrointestinal, Endocrine and Hepatobiliary and Kidney Symptoms,

A wide range of gastrointestinal symptoms was reported after recovery from COVID-19. Among them, loss of appetite (15.9%), diarrhea (13.2%), abdominal pain (10.1%), nausea and vomiting (8.94%) were the most prevalent manifestations. Other symptoms were acidity (2.72%) and an increase in appetite (0.78%) and constipation (0.78%). While 3.5% of the individuals reported liver function disorders, one participant reported abnormalities in kidney function tests.

Neurological Symptoms

Several post-COVID-19 neurological manifestations have been reported as shown in Table 2. Among them, the most frequently reported symptoms included headache (27.2%), sleep disturbance (25.3%), and inability to concentrate (18.7%), followed by loss of memory (14.0%). While 8.17% of the participants experienced dizziness, one had a tingling sensation in the body.

Mental Health

Among the post-COVID-19 mental symptoms, anxiety disorder (13.6%) was the most frequently reported symptom as shown in Table 2, followed by mood swings (10.5%), panicky attacks (7.0%) and depression (5.84%) among recovered participants.

Dermatological Symptoms

A variety of post-COVID-19 dermatological manifestations were being noted among participants. Of them, hair loss (28.79%) and skin rashes (7.39%) were the most common symptoms, followed by discoloration of fingers or toes (3.5%). The least frequent dermatological manifestations were acne, itching of the whole body, dryness of skin, and nail discoloration (Table 2). One person reported with Herpes zoster.

Dental Symptoms

Several oral manifestations have been reported among patients who have recovered from COVID-19. Dry mouth (8.95%) and pain in the gum or teeth (5.45%) were the most frequent post-COVID-19 oral health problems. Other less frequent oral manifestations were oral ulcer (1.17%), sensitivity to cold water (0.78%) and bleeding in the gum (0.78%).

Behavioral Problems

There were reports on changes in behaviors after recovery from COVID-19 (Table 2). Among them, the most prevalent were the increased use of electronic gadgets (24.9%) and loss of motivation (6.61%). Other less common post COVID-19-related behavioural changes were loss of interest in interacting with friends or peer groups (4.28%), new onset alcohol consumption and smoking or use of tobacco products (0.39%).

Pre-Existing Comorbidities Among Participants

Among the participants, 33.8% reported that they had at least one or more associated comorbidities before the COVID-19 disease (Figure 3). Hypertension (10.1%) was the most common comorbidity, followed by diabetes mellitus (6.33%). Other reported common comorbid conditions were thyroid problems (3.8%), migraine (3.6%), heart disease (2.46%) and asthma (2.46%). The remaining comorbidities were present in less than 2% of participants (Figure 3).

Factors Associated with Post-COVID-19 Manifestations

The univariable logistic regression model showed that several factors were associated with post-COVID-19 manifestations (Table 3). Younger age groups (absence of null value in 95% CI of OR; 2.94, 2.11 and 6.62 for age the group 26–45; 46–60; 61–70 years), male gender (OR: 0.59) individuals working other than the hospital (OR: 0.55), absence of co-morbidities (OR: 1.81) and those who received a second dose of the COVID-19 vaccine (OR: 0.61) had a lower risk for post-COVID-19 symptoms. Oxygen supplementation during treatment, and the severity of COVID-19 illness were positively associated with the development of PCS.

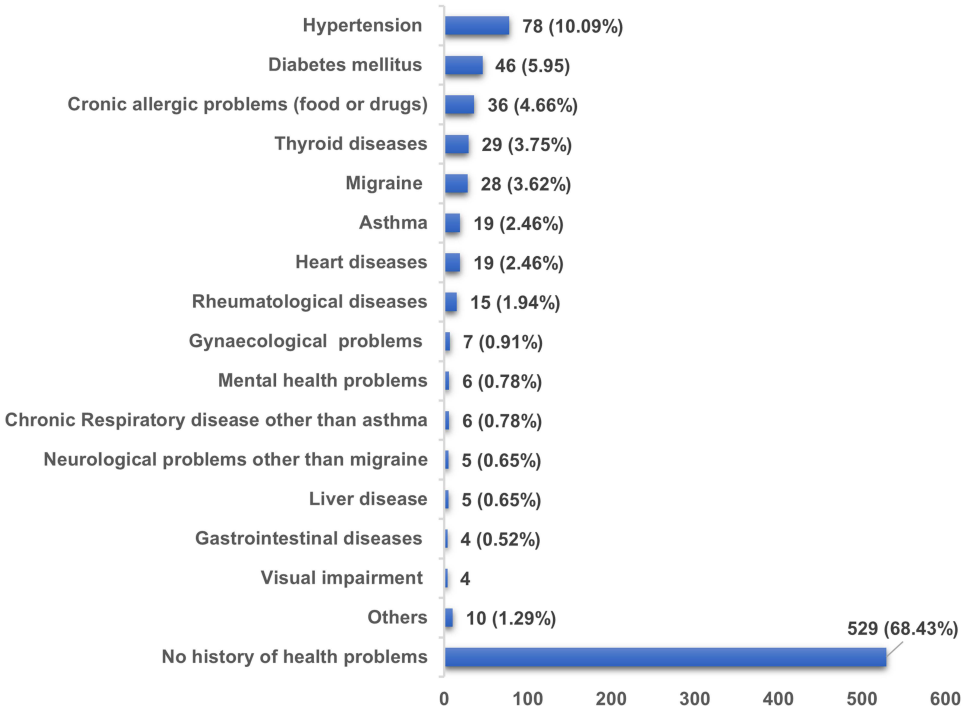

Figure 3 Pre-existing comorbidities (self-reported) among study participants (N=773).

The multivariate analysis (Table 3) showed that PCS was 1.57 times more likely to develop in pre-existing comorbid participants than in healthy participants, 4.07 times more likely in patients with oxygen supplementation during treatment from non-oxygenation patients. Further, about 2.23 times for mild and 2.66 times for moderate COVID-19 illness are more likely to develop PCS than in asymptomatic patients. Smokers compared to nonsmokers were found to have a protective effect in univariable analysis, but in the multivariable analysis, after adjusting for other explanatory variables, smoking was not associated with PCS.

Table 3 Factors Associated with Post COVID-19 Symptoms

Parameters	Regression Model		p-value
	Univariable OR (95% CI)	Multivariable OR (95% CI)	
Age (in Years)			
18–25	1		
26–45	2.94 (1.85–4.67)	2.38(1.42–4.00)	0.001
46–60	2.11(1.22–3.65)	1.46(0.76–2.84)	0.258
61–70	6.62(1.95–22.5)	4.88(1.32–18.10)	0.018
≥71	4.73(0.64–35.1)	6.39(0.65–62.78)	0.111
Gender			
Female	1		
Male	0.59 (0.44–0.80)	0.69(0.47–1.00)	0.051

(*Continued*)

Table 3 (Continued).

Parameters	Regression Model		p-value
	Univariable OR (95% CI)	Multivariable OR (95% CI)	
Educational level			
Postgraduate	1		
Graduate	0.72(0.51–1.02)	0.74(0.50–1.10)	0.133
Higher secondary level	0.64 (0.40–1.02)	0.87(0.49–1.54)	0.639
Secondary and below	0.62(0.33–1.15)	1.27(0.56–2.88)	0.567
Body mass index			
Normal or less	1		
Overweight or obese	0.92 (0.68–1.26)	0.82(0.58–1.16)	0.264
Workplace			
Hospital employee	1		
Non-hospital (other) employees	0.55 (0.41–0.76)	0.65(0.74–3.87)	0.026
Blood group (n=709)			
Negative Rh factor in blood group	1		
Positive Rh factor in blood group	1.61 (0.74–3.48)	1.69(0.74–3.87)	0.217
Smoking			
No	1		
Yes	0.55 (0.36–0.85)	0.60(0.33–1.06)	0.078
Alcohol consumption			
No	1		
Yes	0.84 (0.60–1.17)	1.22(0.77–1.92)	0.394
Presence of co-morbidities			
No	1		
Yes	1.81 (1.32–2.47)	1.57(1.08–2.29)	0.018
Oxygen requirement during treatment			
No	1		
Yes	3.93(1.65–9.41)	4.07(1.52–10.91)	0.005
Severity of COVID-19 disease			
Asymptomatic	1		
Mild	2.97(1.79–4.91)	2.23(1.28–3.89)	0.005
Moderate	3.92(2.25–6.82)	2.66(1.43–4.93)	0.002
Severe	6.81(2.52–18.43)	2.37(0.76–7.44)	0.139

(*Continued*)

Table 3 (Continued).

Parameters	Regression Model		p-value
	Univariable OR (95% CI)	Multivariable OR (95% CI)	
Status of COVID-19 vaccination			
Not vaccinated	1		
1st dose received before the infection	1.10(0.76–1.59)	0.91(0.59–1.40)	0.664
2nd dose received before the infection	0.66(0.4–0.97)	0.61(0.40–0.96)	0.031
Rating overall health status following COVID-19 illness			
Good health	1		
Poor or very poor health	4.37(2.56–7.53)	3.42(1.83–6.37)	<0.001

Abbreviations: OR, odds ratio; aOR, adjusted odds ratio; CI, confidence interval.

One of the important findings in the multivariable regression model was that the odds of developing PCS were lower among individuals who received a second dose of COVID-19 vaccine in comparison to unvaccinated individuals (aOR 0.61; 95% CI 0.40–0.96, Table 3). The multivariable logistic regression model revealed that older age group, female gender, healthcare staff, oxygen supplementation during COVID-19 management, cognitive or memory impairment, severity of acute COVID-19 illness, and unvaccinated status were independent risk factors for PCS (Table 3).

Discussion

The current study was conducted among SARS-CoV-2 positive individuals who tested positive and recovered 4 weeks or more before the date of inception of data collection. They were asked about the status of COVID-19 illness during the telephonic interview to ensure that the information collected was for PCS. As of now, it is practically challenging to compare the findings and the prevalence of PCS across various studies due to differences in assessment time since recovery, and variability in the duration while defining post COVID-19 symptoms. Therefore, the prevalence of PCS, to date, has ranged from 27.8% to 95.0% depending on the time of data collection after recovery.[6,7,19,20]

The present study showed that the prevalence of PCS was 33.2%, irrespective of the severity of COVID-19. This indicates that one in three individuals have persistent PCS after 4 weeks or more following the positive test. Furthermore, it is evident that many patients continue to experience persistent symptoms after COVID-19, irrespective of disease severity during acute illness and the requirement of hospitalization. Studies have reported multiple PCS in non-hospitalized patients after several months of recovery from COVID-19.[21,22] Although individuals reporting the severity of PCS were fewer in number, PCS ranged from mild to severe.

In the current study, the prevalence of PCS was slightly higher in males (56.4%) as compared to females (43.6%); however, females were more likely to develop PCS than males. The difference in physiological and socio-cultural factors may be possible explanation for this, but further study is warranted to explore the underlying reasons. A female preponderance of PCS has also been reported in other studies.[21,23] The present study also indicated that older individuals were more likely to develop PCS than younger age groups (Tables 1 and 3). Several studies also noted that increasing age is a risk factor for PCS.[19,20,24] Education, alcohol consumption, body mass index, and blood groups did not have any significant effect on the development of PCS.

The study noted that individuals working in the healthcare sector had a higher risk of developing PCS than individuals who were working in other sectors. In the multivariable regression analysis, non-healthcare staff are at lesser risk of having PCS than employees working in the hospital (OR: 0.65, Table 3).

Participants with moderate-to-severe COVID-19 illness are at a higher risk for PCS after recovery as shown in univariate analysis. A longitudinal follow-up study will be helpful to assess the duration of persistence for PCS among participants with severe acute illness.

In the present study, fatigue was the most common symptom among all the PCSs, reaching up to 80.3%. In the studies conducted elsewhere, including systemic reviews and meta-analyses, fatigue was the most frequently reported symptom with a prevalence ranging from 30% to 82.9%.[6,21,25,26] The remaining symptoms, such as arthralgia and myalgia, hair loss, headache, shortness of breath, sleep disturbance, cough, loss of smell and taste, were noted in between 20% and 34% of the participants. The pathophysiology behind such a wide range of manifestations is not yet clear, however, it indicates multiorgan involvement as in the acute phase of the illness. The possible immunological mechanism involving the multi-organ system following SARS-CoV-2 infection has been illustrated to explain the appearance of these long-lasting symptoms in other literature.[6,27]

The present study also showed that the odds of having PCS were reduced by 39% in individuals who had received two doses of COVID-19 vaccine compared to persons who did not receive any dose (Table 3). This is an additional beneficial finding for the COVID-19 vaccine that has already been found to reduce the risk of SARS CoV-2 infection and the severity of acute illness. Therefore, vaccination against COVID-19 should be encouraged among the eligible population as early as possible.

A small percentage of recovered patients also experienced both near and distance visual impairment, and dry eyes. It is not clear whether symptoms could be side effects of medication that were commonly used during the acute management or related to weakness of the ocular muscles. The study also indicated a strong association between pre-existing co-morbidities and the presence of PCS. Similar pre-existing co-morbidities such as hypertension, chronic respiratory diseases, and diabetes mellitus have shown to be determinants of the prolonged COVID-19 symptoms as illustrated in other studies.[24,28,29] Furthermore, our study showed that participants who were managed during the acute phase of COVID-19 illness with oxygen supplementation were more likely to develop PCS than participants who were managed without oxygen. A similar finding was shown in another study.[24]

Among psychosocial behavioral changes, a sizeable number of recovered subjects also reported anxiety, and mood disorders, including panic and depression in the current study. Various changes in behavioral aspects in the present study were noted, such as a substantial increase in the use of electronic gadgets being the most common, among the survivors. A link with mental and behavioural problems among recovered patients has also been reported in other studies.[6,25,28]

Overall, we observed that the PCS involved almost all organ systems of the body. Such multiorgan involvement in PCS has been described in other literature.[6,14,26] Similar results were reported in a mobile phone app-based study in the United Kingdom.[27] This implies that managing such widely variable symptoms requires a holistic multidisciplinary approach involving multiple specialties, including hospital and community-based rehabilitation programs to support healthcare and psychological needs for an extended time rather than organ-specific management.

To date, it is not yet fully understood how long the PCS will persist among COVID-19 survivors. In addition to our findings, various previous studies reported that SARS-CoV-2 can still infect individuals despite vaccination, although the severity of the disease is reduced. PCS can also affect individuals regardless of the severity of the acute phase of COVID-19 illness. Therefore, there is a need to develop a PCS care model that is suitable for resource limited countries. One such model is being run to manage PCS in the United Kingdom.[28,29] Individuals with PCS who have pre-existing comorbidities need a proper follow-up strategy because such persons are potential candidates for developing significant disabilities. In addition, a few patients who had recovered from COVID-19 also had newly detected diabetes, abnormal renal, liver, and thyroid function tests and stroke as in other studies.[24] These patients need to be investigated thoroughly per se, including those who report poor or very poor health following COVID-19 and need to be managed accordingly. Follow-up is necessary to know whether such conditions could be reversible in due course of time.

The limitations of our study include first, we relied on self-reported data so there may be potential for socially desirable responses or recall bias in participants. Since it was a cross-sectional study, we cannot rule out the casual relation of some of manifestations whether it was due to COVID-19 or persisting health problems. Second, we did not access the investigation records of the respondents. Therefore, the rating of severity of acute illness and management information were based on participants' responses. Furthermore, further study is warranted to assess any co-relation with metabolic disorders and cardio-respiratory symptoms. Third, our study may not be truly a representative of all communities since we procured the list from one institute, and we also could not collect data from the participants who were not using either smartphones or WhatsApp™.

Conclusion

The PCS affects a wide range of body organ systems, regardless of the severity of the acute phase of illness. Female gender, older age, oxygen supplementation during the acute illness, associated comorbidities, and severe acute illness are risk factors for PCS. Such persistent COVID-19 manifestations not only burden the affected individuals and their families but also pose challenges to healthcare and public health services. We suggest an integrated care model involving all relevant healthcare disciplines while managing PCS in the outpatient setting at every healthcare facility, rather than organ-specific approaches. Intuitively, our findings highlight the importance of vaccination in the reduction of PCS in individuals who have received two doses of the COVID-19 vaccine compared to unvaccinated individuals. Continuous follow-up will be important to assess further prolonged post COVID-19 health problems. A community-based rehabilitation programme, including psychological support, should be a part of post COVID-19 care.

Acknowledgment

We would like to thank all respondents who are employees of All India Institute of Medical Sciences, New Delhi, and their respective dependents for their participation in the post-COVID-19 survey. We thank data entry operator Mr Vikas for his efforts in converting the questionnaires into electronic versions using Google Forms and assistance in data cleaning. We also extend our gratitude to Mr Rajesh Sharma for his unconditional help in data analysis. Finally, we appreciate the staff working in database management of All India Institute of Medical Sciences, New Delhi, for their support in providing the list of participants for the study.

Funding

Indian Council of Medical Research, New Delhi funded (Project Grant no. 2021-6506/F1) this study. The funder does not have any role in the design and conduct of the present study. The investigators performed the present study among the individuals who were beneficiaries of a tertiary hospital health scheme.

Disclosure

The authors report no conflicts of interests in this work.

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