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Research Article

'Long COVID'-Frequency and Pattern of Persistent Symptoms in COVID Patients-A Follow-up Study from a Single Centre

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ABSTRACT

Background: SARS-CoV-2 novel coronavirus infection resulted in major pandemic globally, with substantial medical, social, financial and psychological effects. Initially thought of as acute viral illness only was later realized causing midterm and possible long term deleterious effects on affected individuals. These effects have been given multiple terms i.e., long COVID, post COVID syndrome etc. To understand prevalence and pattern of long COVID symptoms and their relationship with various patient and primary disease related factors this study was done on 300 COVID-19 diagnosed patients at a single hospital of Noida. **Materials and Methods:** 200 admitted and 100 patients under home quarantine diagnosed at the facility 3-4 months back were interviewed telephonically or in follow up OPD using a pretested questionnaire. **Results:** 112 females and 188 males participated with mean age of 41.89 years. 29.3% (88/300) patients complained of at least one symptom with weakness, dyspnea and fatigue being the most common complaints. Older patients, those with comorbidity and belonging to upper SE strata were more likely to suffer from post COVID symptoms. **Conclusion:** Effects of COVID-19 go beyond acute illness. Significant number of patients continue to suffer even months after primary illness. To study long term effects further studies with much longer follow up are needed.

KEYWORDS

Long COVID, post COVID syndrome, PACS, post COVID symptoms

INTRODUCTION

SARS-CoV-2 is a very novel virus, reportedly appeared in the human population at the end of 2019 only. It is responsible for coronavirus disease (COVID-19). It caused a major worldwide pandemic affecting whole world in multiple waves caused by different variants. It led to global healthcare crises taking a heavy toll on global population physically, financially as well as psychologically. Still there is no end visible to this global pandemic. As per WHO coronavirus dashboard there have been 27,07,91,973 cases globally till evening of 16th December, 2021 with 53,18,216 cumulative deaths. In last 24 hrs 7,13,591 new cases have been reported worldwide. India has also been affected badly with 3,47,10,628 confirmed cases till date and death of 4,76,135 Indians attributed to this dreaded illness[1].

SARS-CoV-2 infection leads to acute illness in which infected people usually develop symptoms 4-5 days after initial exposure. Common symptoms of acute COVID illness are fever, cough, sore throat, myalgias, loss of taste and smell. Initially it was thought of as an acute viral illness, affecting mainly respiratory system. Slowly understanding is developing that it affects multiple organ systems. Reports

also started coming that its effects can be long term. Many patients have persistent symptoms for a long time even after supposed recovery from COVID-19 infection. Some of the patients develop new symptoms also. The term used to describe presence of these persistent or new symptoms, even weeks or months later irrespective of the viral status is long COVID[2]. But there is insufficient knowledge regarding these symptoms and long-term effects of COVID-19. Understanding medical, psychological and rehabilitation needs of these patients will help in making strategies to enable them to make as full a recovery as possible.

Objectives of the study
*   To estimate the frequency and type of long COVID symptoms after COVID-19
*   To assess the relationship of various patient and primary disease related factors with long COVID symptoms

MATERIALS AND METHODS
This cross sectional study was conducted at Government Institute of Medical Sciences, Noida, a dedicated COVID Centre, from January to March, 2021. Institutional ethics committee clearance was taken before starting the study. A total of 300 patients were included. Sample size was based on convenient sampling method.

Population
All individuals who were previously diagnosed and/or treated at GIMS Greater Noida for COVID-19 in October and November, 2020 comprised study population.

Sampling
Consecutive sampling starting from 1st October as date of COVID diagnosis was done. Patient selection was done from hospital records.

Inclusion criteria
*   Patients admitted at GIMS, Noida with diagnosis of COVID-19
*   Patients diagnosed as COVID positive at GIMS, Noida and advised/opted for home quarantine

Exclusion criteria
*   Patients below 12 years of age
*   Patients not willing to be part of study
*   Patients admitted for some other emergency procedure and found to be COVID positive
*   COVID positive females admitted for caesarean/ delivery were also excluded from the study
*   Patients unable to understand the questionnaire or communicate

Two hundred admitted and 100 patients who opted for home quarantine were included in the study. 63 patients were interviewed personally while remaining 237 patients were interviewed telephonically. In-depth in person or telephonic interview using a pretested questionnaire was used for data collection. These interviews were carried out in follow up OPD or telephonically at the convenience of participants.

*   Disease severity was classified as:
    *   **Asymptomatic:** Patients with no symptoms attributable to COVID infection
    *   **Mild:** Upper respiratory tract symptoms (and/or fever) without shortness of breath or hypoxia
    *   **Moderate:** Respiratory rate >24/min Spo2 90-93% on room air
    *   **Severe:** Respiratory rate >30/min Spo2 <90% on room air

Statistical analysis
*   Continuous variables were described as mean (standard deviation) and median (interquartile range), while categorical variables were presented as numbers and percentage
*   To study relationship between various patient and disease related variables and persistent symptoms Chi-square test and Fisher's exact test were used. $p < 0.05$ was taken as significant

RESULTS
Out of total 300 participants 118 were females while 182 were males. Age of participants ranged from 12-90 years with mean of 41.89 ± 17.85. Maximum participants belonged to 21-35 years age group. Sixty eight patients had some comorbidity with maximum being diabetes mellitus (40) and hypertension (24). Total 88 (29.3%) patients complained of 1 or more symptoms. One patient had developed petechial skin rashes while another young patient developed avascular necrosis of head of femur. While less than 1 out of four patients (23.18%) with asymptomatic or mild illness reported long COVID symptoms, more than half (50.9 and 50%, respectively) with moderate or severe disease were still suffering (Table 2). Detailed results are presented in Table 1 and 2.

Table 1: Socio-demographic and clinical profile of participants, frequencies of post COVID symptoms

Sociodemographic profile	N-300	Percentage	Post COVID symptoms	N-300	Percentage
			No	212	70.67
			Yes	88	29.33
Age			**Number of symptoms**		
<20 years	22	7.33	One	38	12.67
21-35 years	115	38.33	Two	34	11.33
36-50 years	62	20.67	Three	12	4.00
51-65 years	63	21.00	Four	3	1.00
>65 years	38	12.67	Five	1	0.33
Gender			**Symptom**		
Female	118	39.33	Fatigue	18	6.00
Male	182	60.67	Weakness	49	16.33
S-E status			Dyspnoea	19	6.33
Lower middle	144	48.00	Fever	6	2.00
Lower	5	1.67	Cough	10	3.33
Middle	117	39.00	Loss of taste	1	0.33
Upper middle	34	11.33	Headache	3	1.00
Disease severity			Sore throat	1	0.33
Asymptomatic	33	11.00	Body aches	16	5.33
Mild	200	66.67	Joint pains	6	2.00
Moderate	63	21.00	Insomnia	3	1.00
Severe	4	1.33	Palpitations	6	2.00
Comorbidity			Diarrohea	2	0.67
DM	41	13.67	Pain abdomen/chest	8	2.67
Hypertension	24	8.00	Anxiety	7	2.33
CAD	8	2.67	Confusion	2	0.67
Others	20	6.67			

Table 2: Correlation between socio-demographic and clinical profile of patients and long COVID symptoms

	Follow up symptoms (No)		Follow up symptoms (Yes)		Total			
	Number	Percentage	Number	Percentage	Number	Percentage	Chi-square	p-value
Gender								
Female	89	75.42	29	24.58	118	100	2.1234	0.145
Male	123	67.58	59	32.42	182	100		
Age								
<20 years	12	54.54	10	45.45	22	100	12.7156	0.013
21-35 years	91	79.13	24	20.87	115	100		
36-50 years	44	70.97	18	29.03	62	100		
51-65 years	45	71.43	18	28.57	63	100		
>65 years	20	52.63	18	47.37	38	100		
Mean age	40.55 years SD-16.75		45.14 SD-19.99		41.89 SD-17.85			0.043# ANOVA
Socioeconomic status								
Lower/L. Middle	121	81.21	28	18.79	149	100	15.913	<0.01
Middle	71	60.68	46	39.32	117	100		
Upper middle	20	58.82	14	41.18	34	100		
Disease severity								
Asympt/mild	179	76.82	54	23.18	233	100	19.0828	<0.01
Moderate	31	49.21	32	50.79	63	100		
Severe	2	50.00	2	50.00	4	100		
Comorbidity								
Any No	172	74.14	60	25.86	232	100	5.9498	0.015
Any Yes	40	58.82	28	41.18	68	100		
DM No	188	72.31	72	27.69	260	100	2.5333	0.111
DM Yes	24	60.00	16	40.00	40	100		
CAD No	212	72.60	80	27.40	292	100	19.8007	4.3399E-05*
CAD Yes	0	0	8	100	8	100		(Fishers exact)
Hypertension No	201	72.83	75	27.17	276	100	7.761	<0.01
Hypertension Yes	11	45.83	13	54.17	24	100		
Oxygen/assisted ventilation								
No	185	76.13	58	23.87	243	100	18.4272	<0.01
Yes	27	47.37	30	52.63	57	100		

DISCUSSION

COVID-19 pandemic caused by SARS-CoV-2 resulted in substantial morbidity as well as mortality globally. A large majority of infected people developed mild or moderate illness, while about 5% only got criticalyl ill[3].

Initially it was thought of as an acute illness with recovery expected in 2 weeks for those with mild disease while those with more severe illness expected to take 4-6 weeks to recover. In 2nd quarter of 2020 reports started emerging that significant number of affected people continue to suffer from new or similar symptoms for weeks or months even after supposedly recovering from this acute viral illness. Multiple terms i.e., long COVID, post COVID syndrome, long haulers or post-acute sequelae of COVID have been used to describe it. It was initially recognised through reporting by patients themselves on social media[4]. In Mid 2020 newspapers also published first person accounts of difficulties in recovery from COVID illness[5]. The term long COVID was used first time by Elisa Perego from Lombardy, Italy to describe her experience[6]. The term long haulers was given by Yong and Watson[7,8].

In this study, patients were interviewed at least 3 months after initial diagnosis of COVID-19. The 88 (29.33%) out of 300 patients stated that they were still suffering from at least one symptom. Prevalence of post COVID symptoms has varied largely in reported literature. In an Italian study conducted in April and May, 2020, 87.4% of patients complained of suffering from at least one symptom especially fatigue and dyspnoea[9]. In this study, patients were assessed on an average of 60.3 days after appearance of 1st symptom. But in another survey done on 488 patients in Michigan, USA 159 (32.6%) only complained of persistent or new symptoms 2 months post discharge 10. This wide difference could be partly due to heterogeneity of participants regarding age, primary disease severity as well as associated comorbidity.

In this study, majority of patients (72 out of 88) complained of only 1 or 2 symptoms. Only 16 patients had 3 or more symptoms. One of the reason for lower prevalence of post COVID symptoms in this study could be that patients were interviewed 3-4 months later, while most other studies surveyed patients on average after 2 months[9-14].

Weakness was the most prevalent symptom in this study, followed by dyspnoea, fatigue and bodyaches, respectively (Table 1). Post COVID syndrome can give rise to symptoms related to multiple organ systems. It can be pulmonary (dyspnoea and decreased exercise capacity), cardiovascular (palpitations, chest pain and arrhythmia), neuropsychiatric (fatigue, myalgia, headache, sleep disturbances, loss of taste and smell, confusion and anxiety), dermatologic (hair loss and skin allergy), renal, gastrointestinal and haematological. We also noticed majority of these symptoms.

We did not find any difference between male and female participants regarding prevalence of post COVID symptoms. Although other surveys have reported higher prevalence of long COVID in females. They also found that, patients with post COVID symptoms are on average 4 years older than those without[15]. Our findings are in agreement with this observation. In this study, mean age of patients with long COVID symptoms was 45.14 years as compared to 40.55 years in those without such symptoms. Age difference between 2 groups was statistically significant as evidenced by p-value of 0.013 on chi-square analysis (Table 2). We also found significantly higher prevalence of long COVID in patients belonging to higher socioeconomic group as compared to those from lower socioeconomic strata. Although differences based on race and ethnicity have been evaluated in some studies, effect of socioeconomic status has not been investigated. This difference could be partly due to higher expectations of patients belonging to upper socioeconomic strata.

We also found patients who had moderate to severe illness and those who needed oxygen and/or assisted ventilation were significantly more likely to report post COVID symptoms. Huang *et al.*[16] at 6 month follow up of COVID-19 patients discharged from Wuhan hospital reported that patients with more severe disease (severity scale of 5-6) were more likely to have lung diffusion impairment, fatigue, muscle weakness, anxiety or depression[16]. Arnold *et al.*[12], in UK study at 12 week follow up also noticed patients with severe disease more likely to have higher possibility of persistent symptoms, abnormal chest x-ray and lung function studies[12].

We also noticed higher risk of post COVID symptoms in patients who had any previous comorbidity especially those suffering from hypertension. Risk of higher possibility of post COVID syndrome in patients with comorbidities has been reported by others also[17].

Majority of people with long COVID have achieved virologic clearance evident by negative RTPCR, indicating microbiological recovery[18]. Majority of these individuals also show biochemical and radiological recovery. On the basis of duration of symptoms, long COVID has been divided into 2 stages. Post-acute COVID where symptoms extend beyond 3 weeks, but less than 12 weeks and chronic COVID where symptoms extend beyond 12 weeks[19].

Determination of pathophysiology of long COVID symptoms, not being our study objective, was not investigated. It could be multifactorial. Various reasons ascribed to it are persistent chronic inflammation (convalescent phase), sequelae of organ damage (pulmonary fibrosis and chronic kidney disease), complications of associated co morbidities or adverse effects of medications. Non-specific effects of critical illness and hospitalization may be additive factors. Enforced isolation during COVID illness and Post traumatic stress may contribute to psychological issues. Persistent viremia due to uncleared infection, reinfection or relapse is an uncommon cause[20-24]. Thus pathophysiology of long COVID in each patient needs to be understood so as to provide individualized care as per requirement of that particular patient.

CONCLUSION

Effects of SARS-CoV-2 infection go beyond acute illness. Significant number of people continue to suffer from effects of post COVID syndrome for varying duration ranging from weeks to months. Older patients, those with more severe disease and patients with comorbidities are more likely to suffer from long COVID. To understand long term effects of COVID infection further studies with much longer follow up and clinical examination along with necessary investigations need to be carried out.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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DISCLAIMERS

The opinions expressed in this article are the authors' personal views and do not represent that of their affiliated organizations, employers or associations.

DATA AVAILABILITY STATEMENT

Not Applicable

HIGHLIGHTS OF THE STUDY

- Knowledge regarding long covid is still incomplete, present study is a step in that direction

- In our study participants were more than 3 months post COVID, majority of literature regarding long COVID is less than 3 months later
- Almost one third participants complained of post COVID symptoms with weakness being most common followed by fatigue and joint pains in 5-6% only
- Age, comorbidity, socioeconomic status and severity of primary disease are significant predictors of long COVID in unadjusted analysis
- We didn't find any difference regarding gender

AUTHOR CONTRIBUTIONS

AG conceived the review idea. MM conducted the literature search. AG and MP prepared the first draft of the manuscript. SG and HS reviewed, edited and revised the manuscript substantially on the key intellectual content. AG and AT finalized and approved the current version agreed to be accountable for accuracy and integrity and decided to submit the manuscript to Trends in Medical Research.

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