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A Study to Evaluate Post Acute Sequelae of SARS-CoV-2 Infection (PASC) Conducted in a Tertiary Health Care Centre in India (A Retrospective Cohort Study)

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Abstract: ***Introduction: Long-COVID refers to a variety of symptoms affecting different organs reported by people following Coronavirus Disease 2019 (COVID-19). The epidemiological, clinical characteristics, pathogenesis, and complications of patients with COVID-19 at acute phase have been explicitly described, but the long-term consequences of the illness remain largely unclear. This study aims to investigate and characterize the manifestations which appear after eradication of the acute corona virus infection and its relationship to age, sex, co-morbidities, duration of hospital stay and the degree of hypoxia. Methods: 150 patients admitted to General Medicine ward of Dr. R.N. Cooper Hospital during the period from 1st March 2021 to 31st May 2021 were followed up for 3 months post discharge. Results: The individuals reported fever (19.3%), dyspnea (18%) and cough (18%) which were the highly reported symptoms. The persistence of symptoms was significantly more in those with severe disease at onset. Conclusion: At 3 months after acute infection, COVID-19 survivors were mainly troubled with fever, dyspnea and cough.***

Keywords: Covid-19 infection, post covid symptoms. covid complications

1. Introduction

SARS-CoV-2 infection (COVID-19) is a major pandemic resulting in substantial mortality and morbidity worldwide. Of the individuals affected, about 80% had mild to moderate disease and among those with severe disease, 5% develop critical illness [1]

The total number of SARS COVID-19 cases in India (as of 30th June 2023) is 44.994 million with 98.81% cases recovering from acute infection. However, they are not completely asymptomatic, but have new symptoms arising and persisting beyond the usual expected recovery time from this acute “flu like illness".

It is therefore necessary to perform comprehensive follow up, to assess the health of these pandemic survivors at regular intervals and provide appropriate assistance to not only their physical health but also their psychological condition.

However, the information regarding the persistence of these symptoms in patients who were discharged from hospital after recovery from COVID-19 is still lacking.

These symptoms that arise after recovery lasts for weeks to months and this is called “LONG COVID”, “LONG HAULERS” or “POST COVID SYNDROME”. The term long COVID was first used by Perego in social media to denote persistence of symptoms weeks or months after initial SARS-CoV-2 infection and the term ‘long haulers’ was used by Watson and by Yong. **[9],[10],[11].** Post covid syndrome is persistent of symptoms beyond 3 weeks after infection with SARS-COV-2 [**7]**

2. Aims and Objectives

1) To find out the persistent symptoms in patients after Covid-19.
2) To find out the occurrence of new symptoms in discharged patients after Covid-19 infection.
3) To find out the severity of COVID-19 infection and co-morbidities associated with post-covid symptoms.

3. Methods

150 patients admitted to General Medicine ward of Dr. R.N. Cooper Hospital during the period from 1st March 2021 to 31st May 2021 were followed up for 3 months post discharge.

Inclusion criteria:
All patients who were RTPCR positive or CBNAAT positive or RAT positive and admitted in the Government Medical College and Hospital and were successfully discharged as per World Health Organization criteria i.e.

1) No fever for 3 consecutive days,
2) Improvement in pre-admission symptoms,
3) Willing to give consent.

Patients were offered a comprehensive medical assessment with detailed history and physical examination. The data included demographic details, clinical signs and symptoms, associated co-morbidities and pharmacological history which was collected in an organized electronic data collection system.

Specifically, data on particular symptoms potentially co-related with COVID-19 were obtained using a standardized questionnaire administered at the time of enrollment. Patients were asked to retrospectively recollect the presence of symptoms during the illness and if they persisted for 3 months post COVID-19. Additionally, they were asked if there was onset of any new symptom system wise including the systems getting potentially involved in post COVID-19 period.

This study was approved by the Institutional Ethics Committee.

Verbal consent was obtained from all the participants.

4. Results

150 eligible patients were included in this study done during the period from 1st March 2021 to 31st May 2021.

1) **Age:** Youngest patient was 13 years old and eldest being 88 years, Average of 52.56 years. The age distribution in the study is as follows. There were 14.75% individuals below 30 years of age, while highest proportion of individuals (50%) belonged to the age group ranging from 30 to 60 years. Additionally, 35.3% patients were a part of more than 60 years age group.

Table 1: Shows relation between frequency and age of patients

Age in Years	*Frequency (n=150)*	*Percentage (%)*
<30	22	14.7
30 to 60	75	50.0
>60	53	35.3
Total	150	100.0

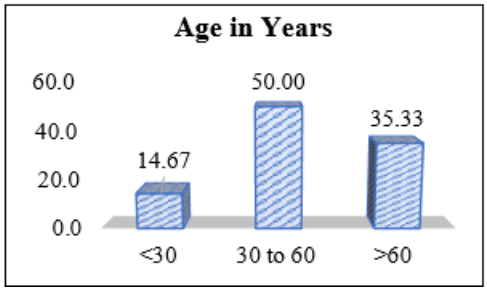

Figure 1: Demonstrates relation between age and frequency of patients

2) **Gender distribution:** Among the 150 patients screened, larger fraction of individuals were found to be males. According to the study and as shown in the table and fig, 78 patients were males which is 52% and the remaining 72 were females which accounted as 48%.

Table 2: Shows relation of number of patients and gender

Gender	*Frequency (n=150)*	*Percentage (%)*
Male	78	52.0
Female	72	48.0
Total	150	100.0

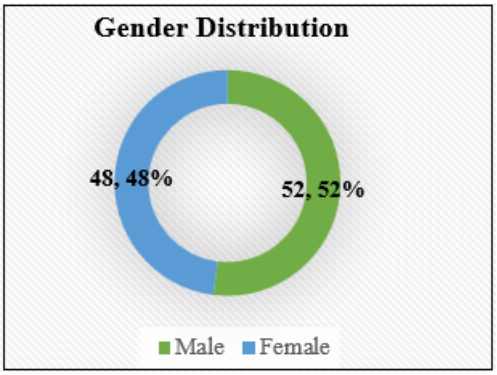

Figure 2: Demonstrates relation between number of patients and gender

3) **Comorbidities:**

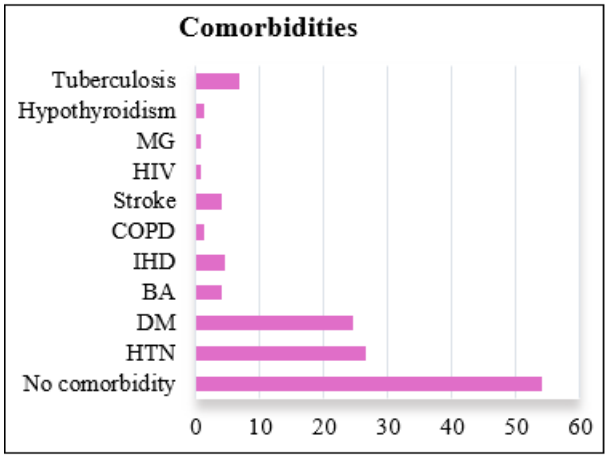

Figure 3: Shows relation between number of patients and co-morbidities

As per Figure 3, the majority of (54%) patients did not have any comorbidity of the 150 enrolled. In contrast, 69 (46%) patients had multifarious co-morbidities.

150 patients, 40 patients (26.6%) had Hypertension, 37 (24.6%) had Diabetes Mellitus. 6 patients had Bronchial asthma, 7 had ischemic heart disease and another 6 patients had stroke. This indicates Diabetes and hypertension were the most common co-morbidities which lead to increased prevalence of SARS-CoV2 in these patients.

2 patients had COPD, 1 was PLHIV, 1 had Myasthenia Gravis.

4) Duration of hospital stay:

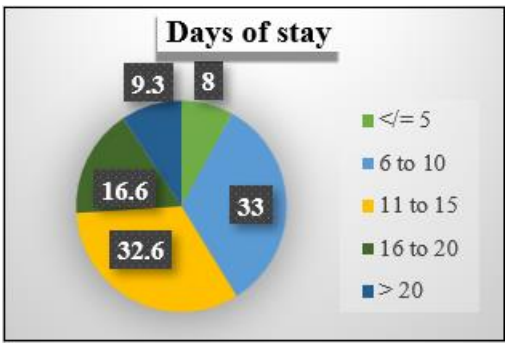

Figure 4: demonstrates duration of hospitalization of patients Out of 150 patients, 12(8%) had hospital stay less than or equal to 5 days, 50(33%) were in the hospital for 6-10 days, 49(32.66%) had hospital stay of 11-15 days, 25(16.6%) patients had stay of 16-20 days, 14(9.3%) patients were in the hospital for more than 20 days.

Table 4: Shows the duration of hospitalization

Duration of Hospitalization	*Frequency (n=150)*	*Percentage (%)*
0 to 5 Days	12	8.0
5 to 10 Days	50	33.3
10 to 15 Days	49	32.7
15 to 20 Days	25	16.7
> 20 Days	14	9.3
Total	150	100.0

5) Relation between duration of hospitalization and presence of post covid symptoms:

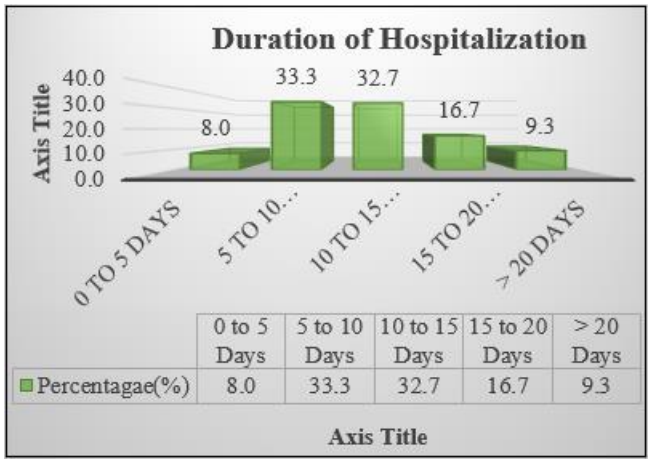

Figure 5: Demonstrates the relation between duration of hospitalization and presence of post covid symptoms.

Table 5: shows the relation between duration of hospitalization and presence of post covid symptoms.

Duration of Hospitalization in days	*Post-Covid Symptoms*			
	Present		Absent	
	Frequency (n=150)	Percentage (%)	Frequency (n=150)	Percentage (%)
0 to 5	1	0.7	11	7.3
5 to 10	7	4.7	43	28.7
10 to 15	13	8.7	36	24.0
15 to 20	10	6.7	15	10.0
> 20	6	4.0	8	5.3
Total	37	24.7	113	75.3
Chi Sq. Value= 10.53		P value= 0.03236		

6) Hypoxia – Out of 150 patients, 94 patients required Oxygen supplementation, 56 did not. 10 required NIV, 38 required O2 by mask, 44 required O2 by Nasal canula, 56 did not require O2, 1 patient required intubation, 1 patient required HFNO.

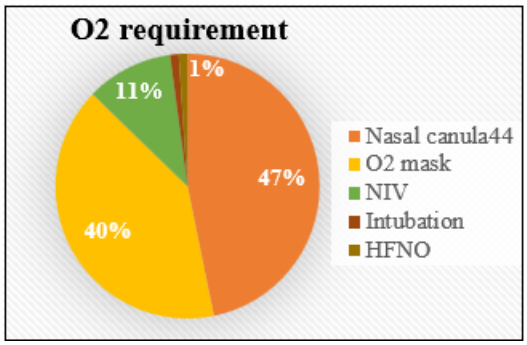

Figure 6: demonstrates the mode of oxygen delivery administered to patients.

Table 6: Shows the relation between mode of oxygen delivery and presence of post covid symptoms.

O2 Requirement	*Post-Covid Symptoms*			
	Present		Absent	
	Frequency (n=150)	Percentage (%)	Frequency (n=150)	Percentage (%)
Nasal Canula	8	5.3	33	22
NIV	1	0.7	10	6.7
NRBM	14	9.3	20	13.3
Intubation	1	0.7	0	0
HFNO	1	0.7	0	0
O2 Mask	2	1.3	4	2.7
No O2 Required	10	6.7	36	24
Chi Sq. Value= 12.75		P value=0.04723		

7) Symptoms on admission: There was a wide variety of symptoms observed at the time of admission of these COVID-19 positive patients. The highest proportion of individuals reported fever as their most common presenting symptom. In 110(73%) patients, followed by cough 102(68%). Among other common symptoms reports by patients on admission was dyspnea 88(58.6%) and weakness/fatigue 47(31.3%). Other symptoms which patients complained on admission were body ache 17 (11.3%), anosmia 6(4%), ageusia 1 (0.1%).

Table 7: Shows the presence of symptoms on admission

Symptoms on admission and frequency	
Fever	109
Cough	102
Dyspnea	88
Weakness/Fatigue	47
Body Ache	17
Anosmia/Ageusia	6/1

Patient receiving Steroids during hospital stay – Out of 150 patients, 116 (77.34%) received steroids.

Table 8: Shows the relation between presence of post covid symptoms and steroids administered.

Steroids Given to treat COVID	*Post-Covid Symptoms*			
	Present		Absent	
	Frequency (n=150)	Percentage (%)	Frequency (n=150)	Percentage (%)
Yes	33	22.0	83	55.3
No	4	2.7	30	20.0
Total	37	24.7	113	75.3
Chi Sq. Value= 3.93		P value=0.04720		

8) Post Covid symptoms: Researchers identified two main patterns of symptoms in people with long COVID: they are 1) fatigue, headache and upper respiratory complaints (shortness of breath, sore throat, persistent cough and loss of smell) and 2) multi-system complaints including ongoing fever and gastroenterological symptoms [13]

Out of 150 patients, 37 patients (24.7%) reported symptoms post 3 months of discharge from the hospital.

Out of the 37 patients, multiple symptoms were reported by patients on follow up, of which cutaneous and respiratory system involvement was most pronounced followed by musculoskeletal system and generalized weakness.

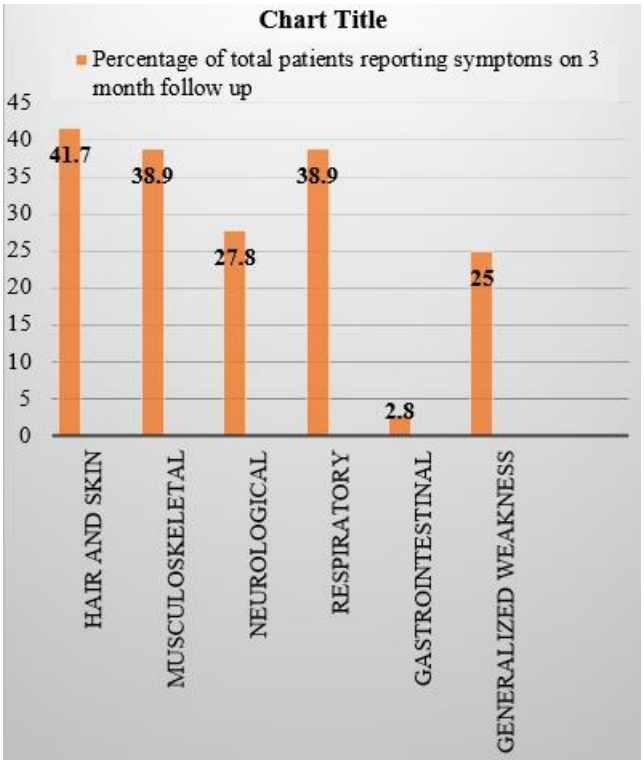

Figure 7: Demonstrates the percentage of patients reporting with post covid symptoms based on systems.

9) Individual symptom as reported by patients on 3 month follow up:

Respiratory system – Out of 15 patients who reported respiratory symptoms, 4 had dry cough, 4 had cough with expectoration. 8 out of 15 patients reported dyspnea on exertion, atypical chest pain by 1.

Neuropsychiatric symptoms – Total of 11 patients reported neuropsychiatric symptoms. 4 patients found it difficult to concentrate on their task in hand, 2 compliant of memory issues in form of increased forgetfulness. Out of 11 patients, 7 had anger issues, 5 developed anxiety. 2 patients reported to have depressed mood and 1 reported insomnia.

Gastrointestinal symptoms – Only 1 patient complaint of intermittent abdominal pain since discharge from hospital with initial evaluation not pointing to a specific cause.

Cutaneous Manifestations – Amongst the cutaneous manifestations, hair fall was reported by 14 patients of follow up.

Musculoskeletal symptoms- 15 patients reported to have diffuse generalized muscle aches and pains.

Table 9: Shows the number of patients presenting with each post covid symptoms mentioned in the table.

Symptoms	*Post-Covid Symptoms*			
	Present		Absent	
	Frequency (n=150)	Percentage (%)	Frequency (n=150)	Percentage (%)
Cough	27	18.0	73	48.7
Fever	29	19.3	79	52.7
s	6	4.0	11	7.3
Body ache	2	1.3	15	10.0
Dyspnea	27	18.0	4	2.7
Anosmia	3	2.0	3	2.0
Diarrhea	1	0.7	2	1.3
Headache	0	0.0	10	6.7
Chi Sq. Value= 54.09		P value=0.0000001		

5. Discussion

The coronavirus disease 2019 (COVID-19) pandemic has resulted in millions of patients infected worldwide. From its first case in Wuhan, China in December 2019, to the first case in Kerala, India in January 2020; the infection has spread far and wide. A robust scientific and medical literature quickly emerged which provided information on patients vulnerable to the infection. This aided in prevention of the diseases and formulation of therapeutic modalities. Recent evidences suggest that SARS-CoV-2 indirectly affects several other organ systems resulting in disruption of daily activities of the diseased. COVID-19 appears to be associated with long-term effects that are common and diverse.

The scientific community and health care professionals are dealt with understanding the pathophysiology of COVID-19 in the human body as well as its long-term complications. Although the virus does not replicate in the body but it results in effects that were not present prior to COVID-19 infection. These "Long haulers" of COVID-19 have persistent symptoms beyond the average duration of recovery. [2] It is also called "post-COVID syndrome". It can be continuous or relapsing and remitting in nature [12] Long- term outcomes have been reported with similar diseases from other coronaviruses, namely Middle East Respiratory Syndrome (MERS) and Severe Acute Respiratory Syndrome (SARS).

The scientific community and health care professionals are dealt with not only understanding he multifaceted ways in which COVID-19 affects the human body but also its long-lasting effects. Even though the virus may not be actively

replicating in the body, it shows effects that were not present prior to COVID-19 infection. These "Long-haulers" of COVID-19 have persistent symptoms well beyond the average course of 1 recovery.

The Italian COVID sequelae followup up included 179 patients, and it was completed on average 60.3 days following the start of the first COVID 19 symptom. Only 18% were fully free of sequelae, according to the study. The most frequent symptoms mentioned included fatigue (53.1%), dyspnea (43.4%), and chest pain (21.7%), while 44.1% of patients experienced a general deterioration in quality of life. The additional symptoms were diarrhoea, 'pins and needles' sensation, headache, palpitations, cough, and skin rashes. In addition to experiencing mental health conditions such anxiety, sadness, and post-traumatic stress disorder [3]

Long haulers/chronic COVID 2 syndrome (CCS) may be caused by factors such viral load, which may get eradicated or persist due to tissue binding. [3] The term "Long-COVID" or "COVID long haulers" refers to people whose symptoms persist for more than 28 days following diagnosis, whether laboratory- or clinically-confirmed. [4], [6]

In Wuhan, China, a 3-month longitudinal follow-up study including 538 covid survivors was conducted. The median patient age was 52 years old, and time from discharge to follow-up was 97 days.

Similar to our study, it was discovered that 13% of patients had cardiovascular symptoms like chest discomfort and 49.6% of patients had persistent respiratory symptoms such cough and dyspnea during routine activity. Acute COVID infection severity and post-discharge persistence in 6 symptoms, both in terms of duration and severity, were significantly correlated. [7]

6. Conclusion

Persistence of various symptoms in people who recovered from COVID-19 (collectively called Long COVID) is a major health issue worldwide. It could be due to various mechanisms such as post-intensive care syndrome, post-viral fatigue syndrome, permanent organ damage or others. Proper clinical evaluation will help identify the etiology, and to customize treatment. As the disease is new, it is too early to know the true long-term outlook.

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