

## A Study to Analyze Potential Long-Term Post-COVID Clinical Conditions and Their Management in a Tertiary Care Hospital

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### Abstract

**Background:** Long term Covid is frequently described as clinical features persisting Covid-19 symptoms after three months beyond the initial illness. More research is being carried out into how best to define long Covid, what its symptoms are and how to treat it.

**Aim:** To study the long term persistence of symptoms of COVID-19 and their health-related quality of life (HRQoL) 3 months after the initial COVID-19 disease.

**Objectives:** To classify the systems affected based on the symptoms and treatment in the Hospital.

**Materials:** 86 patients attending the Department of General medicine and ENT with long COVID symptoms were included. Demographic details, clinical symptoms, return to work after active disease discharge, “mMRC” dyspnoea scale scores HRQoL and HRQoL- EQ-5D-5 and EQ-VAS were observed and recorded. Statistical analysis was done using standard methods to know the levels of significance.

**Results:** Out of 2654 COVID-19 patients treated at MGM Hospital 86/2654 (03.24%) patients were included with persistent symptoms as long COVID-19 status. Out of 86 patients 19 (22.09%) were ICU patients and 67 (77.90%) were ward patients. Males were 61 (70.93%) and females were 25 (29.06%) and the male to female ratio was 2.44:1. Patients aged 38 to 57 years constituted to 48/86 (55.8%) of total patients. The mean age was 56.68± 6.20 years in males and 51.45± 4.10 years in females.

**Conclusions:** Patients required hospitalization for persistent COVID-19 disease symptoms like cough, dyspnoea, fatigue, confusion and Mucormycosis. Though overall HRQoL was appreciable, there was notable difference between ward and ICU patients. The overall work performance and return to the job after discharge from COVID-19 was significant. Constant supervision of mental status of COVID-19 patients was necessary during post long COVID-19 period by the health professionals.

**Keywords:** COVID-19, Mental status, fatigue, Mucormycosis and HRQoL

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## Background

By the end of November 2021 the World Health Organization (WHO) had reported nearly 48 million confirmed cases of COVID-19 disease with acute respiratory syndrome all over the world. The number of cases increased rapidly everyday with exponential incidence [1]. Though the death rate was high, many patients recovered from the acute phase of COVID disease. The long-term health consequences of COVID-19 disease was not yet known but already many of them were experiencing long lasting morbidity [2]. Long Covid was the term coined to describe the post Covid-19 disease which may last for weeks to months after the primary illness [3]. Based on the long term clinical features of the diseases like COVID-19, SARS- CoV, ARDS and Q fever, it was assumed hypothetically that the features of long term COVID also would be similar [4,5]. The features were impaired pulmonary functions, lung parenchymal abnormalities, mucormycosis of the eye, nose and paranasal sinuses, fatigability, reduced physical stamina, muscle mass loss, depression, anxiety neurosis, cognitive deficits, mental fatigue, post-traumatic stress disorder [6]. The symptoms enumerated above point out that there was multi organ involvement and which could be explained by the fact that the COVID-19 virus entry was through ACE2 receptors which was present in the tissues of many organs. The entire world showed a growing awareness and reaction to manage the long COVID syndrome [7]. The first workshop on post COVID-19 syndrome was held in U.S.A. by the US National Institute of Allergy and Infectious Diseases [8]. Forty post COVID-19 clinics were opened in UK by the NHS to manage the persistent symptoms and the organization would release the first clinical guidelines in the future [9]. WHO is planning to update its guidance and resources for clinical management of

COVID-19 to include long COVID-19 [10]. However there is much that remains unknown and the response to long COVID is still in its infancy. The present study was an attempt to observe and analyze the long COVID patients reporting with illnesses after 3 months of discharge from the primary COVID disease.

## Materials

86 post COVID-19 patients admitted who were 3 months earlier positive for SARS-CoV-2 RT PCR test from their nasal swabs, and/or cardinal signs of CT Scan chest, X-Ray and admitted in the Government Medical College attached MGM Hospital, Warangal, Telangana were included in the study. An institutional ethics committee approval was obtained and a committee approved proforma, clinical questionnaire and consent forms were used to collect the data. Study Period: June 2020 to November 2020 (6 months).

**Inclusion Criteria:** Patients aged above 18 years and below 67 years were included. Patients of both genders were included. Patients with COVID positive RT PCR test at the time of admission 3 months earlier were included. Patients with positive radiological evidence of COVID-19 lung disease were included. Patients with general symptoms and attending the OPD of General Medicine were included. Patients with nasal symptoms and attending the ENT department were included. Patients directly admitted into ICUs and the designated COVID wards were included.

**Exclusion Criteria:** Patients below 18 years and above 70 years were excluded. Patients who were not previously positive for COVID-19 and those who were positive within 3 months were excluded. Patients without being hospitalized in this Hospital were excluded. Patients under treatment for

co-morbid diseases such as diabetes mellitus, hypertension, bronchial Asthma and chronic Kidney disease were excluded. Patients with immune deficiency disorders, on Onco-chemotherapy were excluded. All the patients were elicited of their symptoms in detail. Demographic data was collected at the time of the admission. The clinical questionnaire consisted of queries regarding: 1. post COVID-19 disease symptoms which developed 3 months after discharge. 2. Modified Medical Research Council (mMRC) dyspnoea scale scores: Score 0: Dyspnoea on heavy exercise. Score 1: Dyspnoea developing while climbing stairs. Score 2: Walking pace was not same as his colleagues of his age Score 3: After walking for 100 yards, stops for breath (91 m) or after a few minutes. Score 4: Too dyspnoic to leave house or breathless when dressing. 3. Professional activities; like job doing now and before. 4. Daily physical activities. 5. Memory. 6. Attention to the family members, friends and colleagues. 7. Sleep disorders. 8. Panic attacks, anxiety neurosis. The Health related quality of life (HRQoL) was assessed with the help of EQ-5D-5 L questionnaire, [11]: Health status expressed by the patients themselves as: from 1 to 5 rating; in five domains of mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Visual analogue scale (VAS) used ranged from: 0- worst possible health” to 100- the best possible health; EQ-VAS was used. From the obtained VAS scale the EQ-5D- index was calculated: ranging from states worse than dead to most healthy status. ( $p < 0.05$ ). Patients complaining of facial pain, facial numbness, facial or nasal ulceration, soft tissue swelling of the face, chemosis of the eyes, purulent discharge from the nose, black colored crust formation from nose, loss of sense of smell were admitted to the ENT ward. To identify and confirm Mucormycosis in patients, nasal smear

examination was done to identify the fungus, nasal endoscopy to observe the paranasal sinuses drainage areas. Wherever necessary debridement of Mucormycosis black charred tissues were removed.

### Statistical Analysis

The study data was analyzed by simple statistical methods: mean, standard deviation, percentage. The data was analyzed: for quantitative variables t-tests used; for qualitative variables: Chi-square test was used. (tests were two-sided),  $p$ -value  $< 0.05$  was taken as statistically significant.

### Results

This study was conducted in the departments of General Medicine and ENT of MGM Hospital attached to the Kakatiya Medical College, Warangal between June 2020 and November 2020 (6 months). Totally 2654 patients were admitted to the MGM Hospital during the same period for treatment of COVID-19 disease with positive RT PCR test. In the present study 86/2654 (03.24%) patients reported back with persistent symptoms after having affected by COVID-19, 3 months ago. This included the patients who were directly admitted to the ICUs and those to the ward. Among these patients 3 months later 86 post COVID-19 patients reported back to the departments with various complaints related to medical problems and ENT complaints. Among these 86 patients 19 (22.09%) had been admitted to the ICUs and the remaining 67 (77.90%) patients were admitted to the COVID wards 3 months ago. There were 61 (70.93%) male patients and 25 (29.06%) female patients with a male to female ratio of 2.44:1. The patients belonging to the age groups of 38 years to 57 together constituted to 48/86 (55.8%) of the total patients. The mean age was  $56.68 \pm 6.20$  years in males and  $51.45 \pm 4.10$  years in females. This number when compared with other age

groups in the study was significantly higher. (p value was more than 0.05), (Table 1). The higher incidence among the male patients was also significant statistically with a p value 0.031. The number of patients admitted in the ICUs was higher than the ward patients. p value was 0.011; hence significant. The incidence of patients with

BMI values were tabulated in the Table1 and there was significant correlation between the patients of BMI less than 30 Kg/m<sup>2</sup> with those patients with BMI more than 30 Kg/m<sup>2</sup> ( p value less than 0.05e than 0.05), (Table 1). However there was no correlation among the co-morbidities observed in the study.

**Table 1: Showed the demographic data in the study (n-86).**

Variable	Number	Percentage	p- value
Age			
18 to 27	07	08.13	0.027
28 to 37	18	20.93	
38 to 47	25	29.06	
48 to 57	23	26.74	
58 to 67	13	15.11	
Gender			
Male	61	70.93	0.031
Female	25	29.06	
Admission during active COVID			
ICUs	19	29.06	0.011
COVID wards	67	70.93	
Co-morbidities			
Diabetes	09	10.46	0.644
Hypertension	22	25.58	
Bronchial Asthma	13	15.11	
chronic Kidney disease	06	06.97	
BMI- Kg/m <sup>2</sup>			
Less than 30	57	66.27	0.012
More than 30	29	33.72	

Out of 86 patients who were positive for COVID-19, 3 months after getting discharged from the Hospital were readmitted with new complaints of cough in 79 (91.86%) patients, Dyspnoea in 68 (79.06%) patients, Myalgia in 41 (47.67%) patients, Fatigue in 39 (45.34%) patients, Confusion in 34 (39.53%) patients, Pain in the chest in 35 (40.69%) patients, Swelling on the face in 18 (20.93%) patients, Nasal discharge in 14 (16.27%) patients, Black discoloration of nose in 07 (08.13%) patients, Chemosis of eyes in 05 (05.81%) patients, Black discharge in 07 (08.13%) patients, Anosmia in 09 (10.46%) patients, Facial pain in 08 (09.30%) patients, facial numbness in 08 (09.30%) patients was noted. (Table 2) Comparing the patients of COVID-19 disease in ICUs with symptoms and dyspnoea scores, it was observed that 25/67 (37.31%) patients had mMRC grade 2, among the ward patients and 05/19 (26.31%) among the ICU patients. (Table 2) There was no statistically significant difference between ward and ICU groups. (p value was more than 0.05). Among the ward patients 42/67 (62.68%) returned to work and 13 (68.42%) of the ICU patients returned to work. (Table 2) This data was observed to be significant between ward and ICUs group of patients with less than 0.05 p values. Both the groups had similar

dimensions of the EQ-5D HRQoL in terms of mobility, self-care, pain, anxiety or depression, usual activity. But here was slight difference in pain scores of the ICU group, but not statistically significant. The mean EQ-VAS was 72.51% among the ward patients and 70.14% in ICU patients. (Table 2) The mean EQ-5D index was 0.88 for total patients 0.76 forward patients and 0.79.4 for the ICU patients; the values were similar between ICU and ward patients (p value was 0.422;  $p > 0.05$ - not significant). Among the patients who developed mucormycosis with earlier admission to the wards and ICUs were compared for incidence and found that there was statistical significance (p value 0.038), (Table 2)

**Table 2: Showed the post COVID presenting symptoms, persistent symptoms mMRC Dyspnoea score and HRQoL- EQ-5D-5 score (n-86), (mMRC- Modified Medical Research Council, HRQoL- Health related quality of life and index:EQ-5D-5)**

Variables	Total Number-86	Percentages	Wards-67	ICUs-19	p-value
Symptoms on Admission					
Cough	79	91.86	41	10	0.211
Dyspnoea	68	79.06	40	11	
Myalgia	41	59.30	37	08	
Fatigue	39	45.34	36	09	
Confusion	34	39.53	31	07	
Pain in the chest	35	40.69	28	11	
Swelling on the face	18	20.93	12	05	
Nasal discharge	14	16.27	10	04	
Black discoloration of nose	07	08.13	03	03	
Chemosis of eyes	05	05.81	02	04	
Black discharge	07	08.13	05	02	
Anosmia	09	10.46	04	04	
Facial pain	08	09.30	03	01	
Facial numbness	08	09.30	02	02	
Hair loss in women	08	09.30	04	04	
Persistent symptoms					
Cough	14	16.77	10	03	0.358
Fatigue	11	12.79	03	04	
Attention disorder	09	10.46	02	02	
Memory loss	07	08.13	05	04	
Dyspnoea	11	12.79	04	01	
Sleep disorder	08	09.30	03	02	
Anxiety	09	10.46	02	04	
Panic attacks	02	02.32	01	02	
mMRC Dyspnoea score					
Grade 0	21	24.41	16	02	0.361
Grade 1	28	32.55	16	12	
Grade 2	21	24.41	25	05	
Grade 3	15	17.44	10	00	
Going to Job Returned to work	55	63.95	42	13	0.001

Not returned to work	31	36.04	26	05	
HRQoL- EQ-5D-5 \EQ-VAS					
EQ-VAS (%)	72.5	--	69.1	70.14	0.422
EQ-D index	0.88	--	0.76	0.71	
Mucormycosis of the nose and PNS					
Nasal cavity	07	08.13	04	03	
Paranasal sinuses	05	05.81	02	03	0.038
Cheek	04	04.65	01	03	
Orbital involvement	03	03.48	01	02	

## Discussion

In the present study 86/2654 (03.24%) patients reported back with persistent symptoms after having affected by COVID-19, 3 months ago. The symptoms for which they reported were especially dyspnoea, cough, nasal discharge, swelling of the face. However the HRQoL was much better as 55/86 (63.95%) of the patients had returned to their jobs after discharge; p value was less than 0.05, hence significant (Table 2). Except to the incidence of mucormycosis there was no significant difference in other symptoms between ward patients versus ICU patients. (Table 2)

There was also no significant difference in the HRQoL- EQ-5D-5 and EQ-VAS index between the ward patients and ICU patients in this study. (Table 2) The trend showed that many of the patients treated in ICUS were also given proper care during the COVID-19 active stage. However the study consisted of a small group of subjects and from only a single center, hence a differential bias was possible. In addition many patients were unable to reach the center due to travel restrictions and taken treatment at the local hospitals. The present study correlated well with other larger studies which included more severe ICU patients. <sup>(12)</sup> 8/86 (09.30) women patients complained of spontaneous hair loss during the 3 months after the discharge. The hair

loss was explained by few authors as due to telogen effluvium; followed by viral infections and/or a stress generated by the hospitalization and the disease [13]. In the present study Myalgia was noted in 41 (47.67%) patients and Fatigue in 39 (45.34%) patients. This could be due to the severity of respiratory insufficiency and relatively long hospital stay of the patients during active COVID-19 disease in them. In addition the ICU patients on mechanical ventilation with critical disease had suffered a decreased physical capacity leading to reduced muscle mass, as reported by Kress JP, Hall JB *et al.* [14].

Such a hypothesis was recently published in the Italian COVID-19 cohort study, showing low physical functioning at the time of discharge [15]. This study showed confusion in 34 (39.53%) patients, attention disorder in 09 (10.46%) and loss of memory in 07 (08.13%) patients. In a similar cohort study by van den Borst B, Peters JB *et al* [16]. One-third of their patients showed below normal mental status and/or cognitive function, 3 months after COVID-19 disease. They suggested that such findings should make all healthcare professionals alert in treating post COVID-19 disease as post-traumatic stress syndrome generally developed after 3 months; Mazza MG, De Lorenzo R *et al.* [17] suggested studies on

patho-physiological role of inflammation underlying psychological and psychiatric symptoms after COVID-19. The mental status of the patients of COVID wards and ICUs in this study was similar. In a similar study the patients with critical disease who had cytokine storm during the acute disease state were affected by psychological symptoms [18]. Hence to detect the multifactorial cause of these phenomena required more investigation. Longer follow-up studies should be conducted to explain the natural course of the post COVID-19 disease and its recovery; also to find the predictors of post COVID-19 symptoms and their long-term effects. The studies should also develop effective strategies to minimize the long-term COVID-19 morbidity.

### Conclusions

Patients required hospitalization for long COVID-19 disease for the persistent symptoms like cough, dyspnoea, fatigue, confusion and mucormycosis. Though overall HRQoL was appreciable, there was significant difference between ward and ICU patients. The overall work performance and return to the job after discharge from COVID-19 was significant. Constant monitoring of the mental status was essential during long COVID period by the health professionals. Our findings must be confirmed in larger cohorts, including more severe patients.

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