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Study of post COVID pulmonary complications in patients with moderate to severe disease at a tertiary hospital

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Abstract

Background: Study of evidence of long-term sequelae and complications of COVID-19 infection is much more relevant since the feasibility for long-term care and follow-up is limited in our country. Present study was aimed to study post COVID pulmonary complications in patients with moderate to severe disease at a tertiary hospital. **Material and Methods:** Present study was retrospective, analytical study, conducted in patients presenting to Pulmonology Out-patient unit or casualty with respiratory complications, with past history of moderate or severe COVID-19 infection. **Results:** Among 50 cases, majority of the study subjects (44%) belonged to the age group 41-60 years. This is followed by 18- 40 (34%) Men comprised 64% of the study subjects and women 36%. Majority of the subjects presented 6-12 months after recovering from COVID Disease Most common complaints were dyspnea, cough and fatigue. CRP, D-dimer and ferritin were slightly higher in men compared to women. However, only the difference in CRP was statistically significant. The difference in D-dimer and ferritin between the two groups was not statistically significant. Majority of the subjects (72%) has moderate disease, while severe disease was reported in 28%. Pulmonary Artery Hypertension was seen in 14% of the study subjects. There is a strong significant association between the PAH and severity of the past disease (P value = 0.005). Normal radiological appearance was noted in 22% of the study subjects. There was reduction in the ground glass opacities and fibrosis in subjects who presented late compared to those who presented early. **Conclusion:** Majority of the subjects were men, from 41-60 years age group, presented with complications 3-6 months after recovery and discharge from COVID. Mild impairment of DLCO was more commonly seen.

Keywords: COVID-19, spirometry, radiological abnormality, Pulmonary artery hypertension

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Introduction

The pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has steadily spread across the world causing huge mortality and morbidity, crippling the health, social and economic systems.[1] While the infection is self-limiting in some people, it may lead to severe pneumonia. Inflammatory burst due to cytokine storm occurring at around one week into the disease has also proved very challenging.[2] Apart from the immediate

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effects, several long-term effects are also likely to occur due to the unique pathological mechanisms that are being played out in case of SARS-CoV.[2,3]

There is a potential for rise in long term complications in the survivors of COVID-19 infection. The respiratory sequelae are likely to be due to residual impairment in lung function owing to the fibrosis of lung tissue. The prothrombotic hypercoagulable state arising due to increased inflammatory agents may also lead to vascular complications affecting the micro as well as macro vasculature of various organs.[4,5]

Study of evidence of long-term sequelae and complications is much more relevant since the feasibility for long-term care and follow-up is limited in our country.[6,7] Present study was aimed to study post COVID pulmonary complications in patients with moderate to severe disease at a tertiary hospital.

Materials And Methods

Present study was retrospective, analytical study, conducted in department of respiratory medicine, at A tertiary care hospital, Eluru, India. Study duration was of 2 years (December 2020 – November 2022). Study approval was obtained from institutional ethical committee.

Inclusion criteria

- Patients presenting to Pulmonology Out-patient unit or casualty with respiratory complications, with past history of moderate or severe COVID-19 infection, Willing to participate in present study

Exclusion criteria

- Subjects who are known cases of COPD, interstitial lung disease, vascular disorders and hypercoagulable disorders before onset of COVD-19 infection.
- Subjects who tested COVID-19 positive at present

Study was explained to patients in local language & written consent was taken for participation & study. After inclusion into the study, detailed history-taking and examination of the study subjects was performed. After detailed history, investigations such as Pulmonary Function test (Spirometry and DLCO), Six Minute Walk Test Echocardiogram, Sputum Sampling for Microbiological Analysis, HRCT Chest, CRP, D-Dimer, Ferritin were done. The relevant findings from the past COVID infection were also noted Severity of Disease was decided as Moderate (Needing admission and oxygen support) & Severe (Needing ICU support). The severity of disease in the past COVID-19 infection was also noted based on the need for admission and oxygen support or ICU support (NIV support).

Data was collected and compiled using Microsoft Excel, analysed using SPSS 23.0 version. Frequency, percentage, means and standard deviations (SD) was calculated for the continuous variables, while ratios and proportions were calculated for the categorical variables. Difference of proportions between qualitative variables were tested using chi-square test or Fisher exact test as applicable. P value less than 0.5 was considered as statistically significant.

Results

Among 50 cases, majority of the study subjects (44%) belonged to the age group 41-60 years. This is followed by 18- 40 (34%) Men comprised 64% of the study subjects and women 36%. Majority of the subjects presented 6-12 months after recovering from COVID Disease

ISSN: 0975-3583,0976-2833 VOL14, ISSUE 08, 2023

Table 1: General characteristics

	No. of patients (Percentage)
Age groups (in years)	
18-40	17 (34)
41-60	22 (44)
>60	11 (22)
Gender	32 (64)
Male	18 (36)
Duration Since Past COVID Disease	
3 – 6 months	12 (24)
6 – 12 months	29 (58)
More than 12 months	9 (18)

Most common complaints were dyspnea, cough and fatigue.

Table 2: Presenting Complaints of Study Subjects

Complaints	**No. of patients (Percentage)**
Dyspnea on Exertion	33 (66)
Dyspnea on Rest	7 (14)
Cough	24 (48)
Expectoration	8 (16)
Fatigue	18 (36)

CRP, D-dimer and ferritin were slightly higher in men compared to women. However, only the difference in CRP was statistically significant. The difference in D-dimer and ferritin between the two groups was not statistically significant.

Table 3: Inflammatory Markers in the Study Subjects According to Gender

Marker	**Mean + SD (mg/L)**	**Male (mg/L)**	**Female (mg/L)**	**p-value**
CRP	3.7 + 0.3	3.9 + 0.8	3.1 + 0.6	0.04
D-Dimer	0.26 + 0.07	0.27 + 0.08	0.24 + 0.05	0.07
Ferritin	0.13 + 0.04	0.16 + 0.04	0.12 + 0.02	0.11

Majority of the subjects (72%) has moderate disease, while severe disease was reported in 28%. Pulmonary Artery Hypertension was seen in 14% of the study subjects. There is a strong significant association between the PAH and severity of the past disease (P value = 0.005).

Table 4: Pulmonary Artery Hypertension & Severity of Past COVID Infection

Pattern	**Moderate Disease**	**Severe Disease**	**Total**
PAH	2 (4)	5 (10)	7 (14)
No PAH	34 (68)	9 (18)	43 (86)
Total	36 (72)	14 (28)	

Majority of the study subjects had mild impairment in the DLCO. Moderate impairment was seen in 22% and severe impairment in 12% of the study subjects.

Table 5: DLCO in the Study Subjects

DLCO	**No. of patients (Percentage)**
Normal (>75%)	15 (30)
Mild Impairment (60-75%)	18 (36)

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Moderate Impairment (40-60%)	11 (22)
Severe Impairment (<40%)	6 (12)
Total	50 (100)

Subjects with history of severe infection have higher markers compared to those who had moderate infection. However, this difference was not statistically significant.

Table 6: Inflammatory Markers & Severity of Past COVID Infection

Marker	Moderate Disease (Mean + SD)	Severe Disease (Mean + SD)	p-value
CRP	3.6 + 0.7	3.9 + 0.9	0.08
D-Dimer	0.22 + 0.08	0.24 + 0.04	0.62
Ferritin	0.12 + 0.05	0.16 + 0.04	0.07

Normal spirometry pattern was seen in 48% of the study subjects. Obstructive pattern was seen in 12% and restrictive pattern in 10%. Mixed pattern was noticed in 30% of the study subjects. The subjects with severe infection had significantly higher impairment in spirometry compared to those who had moderate disease in the past (P value = 0.04).

Table 7: Spirometry Pattern & Severity of Past COVID Infection

Pattern	Moderate Disease	Severe Disease	Total
Normal	19 (38)	5 (10)	24 (48)
Obstructive	3 (6)	3 (6)	6 (12)
Restrictive	2 (4)	4 (8)	5 (10)
Mixed	13 (26)	2 (4)	15 (30)

Fibrosis was seen in majority of the study subjects. This was followed by ground glass opacities in 16% and pleural thickening in 12%. Normal radiological appearance was noted in 22% of the study subjects. There was reduction in the ground glass opacities and fibrosis in subjects who presented late compared to those who presented early. This difference was found to be statistically significant (P value < 0.001).

Table 8: Radiological Findings in Study Subjects according to Duration since past COVID.

Radiological Findings	3-6 months N (%)	6-12 months N (%)	>12 months N (%)	Total
Normal	7 (14)	2 (4)	2 (4)	11 (22)
Ground Glass Opacities	5 (10)	2 (4)	1 (2)	8 (16)
Fibrosis	1 (2)	21 (42)	7 (14)	29 (58)
Pleural Thickening	1 (2)	2 (4)	3 (6)	6 (12)
Other Abnormalities	1 (2)	1 (2)	2 (4)	4 (8)

The proportions of radiological abnormalities are higher in those who had history of severe disease. P value = 0.50

Table 9: Radiological Findings & Severity of Past COVID Infection

Radiological Findings	Moderate Disease N (%)	Severe Disease N (%)
Normal (11)	8 (16)	3 (6)
Ground Glass Opacities (8)	5 (10)	3 (6)
Fibrosis (29)	17 (34)	12 (24)
Pleural Thickening (6)	2 (4)	4 (8)

ISSN: 0975-3583,0976-2833 VOL14, ISSUE 08, 2023

Other Abnormalities (4)	1 (2)	2 (4)

Discussion

While the clinical course of SARS-CoV-2 is being well established, there is another alarming concern regarding this disease – the long-term sequelae. Due to its profound clinical as well as public health impact, there is a need to study the long-term sequelae of this disease and their correlation with disease severity.

The present study showed a male preponderance of study subjects. Majority of them were men compared to women. In a study by Zhao et al.,[8] male (59 %) preponderance was noticed. Men comprised 59% of the study subjects. Similar gender preponderance was not reported by Ngai et al.,[9] (men 34.5%) & Hui et al.,[10] (female 59 %).

Lewis et al.,[11] reported a much older mean age of 59.2 years. The studies in Western countries reported a higher mean age compared to studies in Asian countries. In Asian countries the middle age groups had higher incidence of post-COVID complications. This could be because their survival of initial infection and follow-up rate was higher compared to older age groups.

In study by Goel et al,[12] fatigue (65 %) was the most common symptom, followed by breathlessness (60 %), cough (45 %) & chest pain (28.5 %). Similar findings noted in present study. This indicates the presence of clinical features indicative of COVID infection that are persistent even after the patient otherwise recovers from the disease.

In the present study, 72% of the study subjects had moderate COVID disease in the past & 28 % had severe disease in the past needing ICU admission. A much higher proportion of past severe illness was reported as Ngai et al.,[10] (36 %), Hui et al.,[9] (31.5 %), Lewis et al.,[11] (31.2 %).

In present study, presence of lung function abnormality was significantly higher in those with history of severe infection than those with history of moderate infection. The difference was statistically significant. In study by Zhao et al.,[8] lung function abnormality in spirometry was observed in 25.45% of the study subjects. Anomalies in Total Lung Capacity was reported in 7.27%. Anomalies in Forced Expiratory Volume (FEV1) were reported in 10.91% of the study subjects and anomalies in FVC were reported in another 10.91% of the study subjects. Ngai et al.,[10] reported a significant difference between patients with history of severe disease and those with history of moderate disease. The two difference in the two groups is more significant with respect to Total Lung Capacity and Vital Capacity. Thus, the findings of the present study were corroborated by those of the previous studies.

Zhao et al.,[8] reported abnormal DLCO in 16% of the study subjects with history of COVID disease. Ngai et al reported that the intubated group showed significantly lower DLCO compared to the moderate illness group. These findings were corroborated in the present study.

In the present study, a total of 7% of the study subjects developed pulmonary artery hypertension. There was a highly significant association between severity of past COVID disease and present occurrence of pulmonary artery hypertension. Aul et al.,[13] reported that 1.3% had Left Ventricular Dysfunction and 2.3% of the study subjects had developed pulmonary hypertension. So, the occurrence of pulmonary artery hypertension in present study was higher compared to the previously reported studies.

Goel et al.,[12] reported abnormal radiological presentation in 34.2% of the study subjects. On HRCT chest, the most common presentation was diffuse reticulations which were seen in 52.9% of the study subjects. This was followed by ground glass opacities in 35.2% of the study subjects. The reason for higher reporting of radiological abnormalities in this study could probably be the relatively shorter time of follow-up reported, compared to other studies.

ISSN: 0975-3583,0976-2833 VOL14, ISSUE 08, 2023

The present study did not show any significant difference in the laboratory parameters between the two groups. Though the markers in severe disease group were slightly higher, the difference was not statistically significant. This may be due to the duration of follow-up, and since these markers are acute inflammatory parkers, they do not persist for long after recovery.

Zhao et al.,[8] reported that there was significant difference in coagulation markers and D-dimer between the subjects with history of moderate disease and those with history of severe disease.

Present study recommends that, high index of suspicion is needed for complication in patients recovered from COVID-19. Regular screening should be done for pro-inflammatory and prothrombotic sequelae. Special long-term care for patients who recovered from severe disease. More research into treatment regimen that will mitigate the long-tern microvascular side effects.

Conclusion

Majority of the subjects were men, from 41-60 years age group, presented with complications 3-6 months after recovery and discharge from COVID. Mild impairment of DLCO was more commonly seen. On spirometry, obstructive pattern was seen in 12% and restrictive in 10% and mixed in 30%. Fibrosis was the most common radiological abnormality, followed by ground glass appearance and pleural thickening. Pulmonary artery hypertension was significantly associated with severity of the past COVID disease.

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