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Pulmonary Medicine

POST COVID LUNG-NOT ALL IS LOST: FOLLOW-UP & ANALYSIS

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ABSTRACT **Background:** The coronavirus disease 2019 (COVID-19) pandemic is an ongoing global healthcare challenge. Up to one-third of hospitalised patients develop severe pulmonary complications and a variety of symptoms affecting other organs. Pulmonary and health outcomes following COVID-19 are unknown. **Methods:** This study is a retrospective observational study investigating pulmonary sequelae of COVID-19. We report the follow-up of cases who suffered from covid-19 and were symptomatic at follow-up. The covid-19 disease severity was classified as mild, moderate and severe according to WHO classification. **Results:** Eighty COVID-19 survivors were included (mild/moderate n=34, severe=46). We confirmed several comorbidities as risk factors for severe disease. Severe disease was associated with impaired pulmonary function. Restrictive abnormality was seen in 53(66.25%) patients. Mean FVC(SD) was 69.87%(16.42%). Mean FEV1 of 72.7% (20.62%). Twenty-eight patients had a baseline (during the covid admission) and on a follow-up HRCT thorax. All patients had changes of COVID-19 with CT severity ranging from 12/25 to 22/25 during the active covid illness. Out of 28, CT was suggestive of near complete radiological resolution of the disease in 17 (61%),while 11 (39%) patients had a partial radiological resolution, none showed progression of the disease. **Conclusions:** The survivors recovered well at follow-up from respiratory aspects. Respiratory sequelae were documented but without much pulmonary disability. A systematic long term follow-up for survivors is needed to assess subsequent long term sequelae if any with regard to the respiratory system.

KEYWORDS : COVID-19, spirometry, pneumonia

INTRODUCTION

The first reported case of coronavirus disease (COVID-19) was on December 31,2019. An outbreak started in Wuhan, China then spread rapidly and turned into a global pandemic [1]. The clinical presentation of COVID-19 ranges from asymptomatic to mild, moderate or severe. Majority of patients presented with coronavirus disease experience mild illness. Covid19 infection not only affects the respiratory system, but also other organs like the kidney, heart, nerves and vessels. In severe cases, the patient can develop various complications including, pneumonia, acute respiratory distress syndrome (ARDS), sepsis, multiple organ failure, prothrombotic state, myocarditis, acute kidney injury, and other viral and bacterial infections that are not unique to coronavirus [2,3]. COVID-19 associated death is usually a result of pneumonia, ARDS and sepsis.The post-coronavirus disease includes persistence of symptoms beyond viral clearance and fresh development of symptoms or exaggeration of chronic diseases within a month after initial clinical and virological cure of the disease[4]. Data is unclear on post COVID sequalae and hence we aimed to determine the incidence, association, and risk factors associated with development of the post-COVID-19 infection and follow up of post COVID-19 patients.

METHODS

A retrospective observational study was conducted with institutional ethic committee permission ECAR/2020/108 dated 20.05.21. One year in the pandemic; we contemplated studying the impact of the covid sequelae, especially on the lung. Consecutive patients following up at the post covid OPD were the database for the study. The follow-up was usually scheduled at 1 month post discharge. However some patients with treatment taken from other centres came referred later. But all patients were assessed within 6 months of recovery from the illness. The patients who were symptomatic from a respiratory point of view were included and assessed with a clinical assessment and spirometry. Primary objective of the study was to assess the lung function in follow-up covid patients .Secondary objective was to assess incidence of comorbidities associated with covid infection and persisting clinical symptoms associated with long covid infection. Spirometry was performed on medgraphics spirometry machine which fulfilled the ATS/ERS spirometry criteria. Spirometry parameters recorded included forced expiratory volume in first second (FEV1) and forced vital capacity (FVC) ratio,FEV1 and FVC absolute values and percentage predicted. Their clinical parameters, presence of comorbidities, if any, spirometry data and investigation details, if available were recorded and analysed. HRCT scan was performed in patients with persistent symptoms and compared to initial CT scan performed during hospitalization. Exclusion criteria included patients not fit to perform pulmonary function test and lost to follow up patients. Qualitative data was reported in percentages and mean. Data was subjected to analysis.

RESULTS-

Total 971 patients followed up in the postcovid OPD from Aug 2020 to May 2021. Patients who were symptomatic with respiratory symptoms of cough and/or breathlessness underwent a spirometry. Total 80 patients had persistence of symptoms in post COVID OPD follow up and were included in this study. So, in our set-up, the incidence of long-covid symptoms was 8.2%. Out of the 80, 43(53.75%) were men and 37(46.25%) were women. Mean age was 49.27 (12.14)years. All patients were treated for covid-19 in the past. Covid-19 disease severity was classified as mild, moderate and severe on basis of the WHO COVID-19 disease severity classification. Thirty-four (42.5%) had mild to moderate COVID-19 disease. These were treated in medical ward setup. While 46(57.5%) had severe covid-19. They had covid-19 pneumonia with respiratory distress which needed oxygen, non invasive ventilation, Controlled Mandatory Ventilation with an HDU/ICU stay. Most patients followed up at 1.75 months (range from 1 to 6 months) post discharge from the covid illness.

51 patients had associated comorbidities, of which hypertension accounted for 27(33.75%). Hypertension was the most common comorbidity associated with covid infection followed by diabetes mellitus 16(20.7%),ischemic heart disease in 5(6.25%), bronchial asthma in 4(5.19%), hypothyroidism in 4(5.19%).Breathlessness was the most common symptom which was seen in 56(70%) patients. Other symptoms were cough in 35(43.7%), fatigue in 9(11%) patients, chest pain in 8(10%) patients, chest tightness in 6(7.5%) patients, myalgia in 5(6.25%) patients and headache in 3(3.75%) patients. Spirometry analysis revealed normal lung functions in 24(30%) patients.

Restrictive abnormality was seen in 53(66.25%) patients, while obstructive abnormality was seen in 3(3.75%) patients. Mean FVC was 69.8(16.42) percentage predicted. Mean FEV1 was 72.7(20.62) percentage predicted. Mean FEV1/FVC was 85.78.Thus spirometry

was affected in two thirds of symptomatic patients and normal in one third of these cases.

High resolution computed tomography thorax was done on follow up visits of patients who had history of severe disease and persistent complaints of breathlessness. CT severity data was analysed as complete resolution, partial resolution, deterioration or static. Twenty-eight of the 46 patients had a baseline (during the covid admission) and follow up (during the study period) HRCT thorax. All patients had changes of COVID-19 with CT severity ranging from 12/25 to 22/25 during the active covid illness. Out of 28, CT was suggestive of near complete resolution of the disease in 17 (61%),while 11 (39%) patients had partial radiological resolution. Thus CT showed a favourable response in all.

Table 1. Mean spirometry values

Spirometry	FVC	FEV1	FEV1/FVC
Mean	69.8	72.7	85.78

Normal	Restriction	Obstruction
30.00%	66.25%	3.75%

FVC- Forced Vital Capacity FEV1- Forced expiratory volume in first second FEV1/FVC- Forced Vital Capacity / Forced expiratory volume in first second

DISCUSSION

Since covid 19 is a novel virus, there are limited studies about long term disease progression and long covid effects. Covid infection can cause long term complications in various organs as it affects most of the organ systems, mainly in patients presented with severe initial symptoms[6].In this study mean age was 49.2 years and male predominance of 53.75% was seen which is similar to study conducted by Polese j et al[5]. Even people with mild illness who are not hospitalized can experience prolonged or late symptoms. Recovery period of initial covid infection for mild infection is around 1 to 2 weeks ,however in many patients long term symptoms persisted upto 8 to 10 weeks or longer[6]. In a study conducted by Taquet M et al[7],among COVID-19 survivors (mean age [SD] : 46.3 [19.8], 55.6% female), 57.00% had one or more long-COVID feature recorded during the whole 6-month period , and 36.55% between 3 and 6 months. The incidence of each feature was compared between 1 to 180 day period and 90 to 180 day period. Breathlessness , fatigue , chest pain , headache, abdominal symptoms, myalgia, cognitive symptoms , and anxiety/depression showed a gradual improvement in symptoms, however many patients did not attain complete recovery in 6 month period.

Lung disease is the most common long term complication associated with severe covid 19 infection[6]. Even though most of the patients with mild and moderate forms of disease return to normal health completely, certain number of patients who had severe infection tends to have excessive lung damage and even developed pulmonary fibrosis. Thus severe covid lung infection increases the likelihood of long term complications and chronic lung disease. In this study, dyspnea (70%) and cough (43%) were the most frequently seen symptoms which show similarity to study by Polese J et al[5]. After the autopsy results of the patients with postviral infection, it was confirmed that COVID-19 is a disease has a systemic characteristic. It is verified that comorbidities like old age, diabetes, hypertension, cardiovascular diseases are associated with chronic endothelial dysfunction, thus severe or critically ill covid 19 patients frequently presents with such underlying conditions. 63% of patients had comorbidities, in which hypertension is the most common risk factor consisting of 35%. Other major risk factors were diabetes Mellitus, hypothyroidism, bronchial asthma and coronary vascular Disease, this is similar to study done by Cesar Fernandez et al[10].

Fatigue is one of the most common symptoms in patients presenting with covid 19 infection. Persistent fatigue lasting 6 months or longer without an alternate explanation is termed as chronic fatigue syndrome[11]. Interestingly, fatigue was not associated with initial disease severity, and there were no detectable differences in pro-inflammatory markers or blood investigations. Fatigue was seen more in male 7(71%) predominance in this study which is varied from study conducted by Townsend et al.[12] showing 52% of female predominance.

Skeletal muscle, after regular physical activity, is responsible for the production of myokines that signal a state of physiological muscle inflammation, which, in the presence of the SARS-CoV-2, can be significantly increased. Myokine production also stimulates a prolonged muscular inflammation, with high levels of IL-6. The SARS-CoV-2 infection there is increasing the rate of proinflammatory macrophages and stimulating an increase in inflammatory cytokines . Atrophy of muscle fibres, with sporadic necrosis, focal infiltrations of muscle fibres and infiltration of immune cells contributed to muscle weakness and fatigue [13]. Muscle pain was seen 17% in postcovid follow up patients by Polese J et al[5] which more than our study showing 5%.

Follow-up chest CT scans obtained in covid patients showed lung fibrotic like changes in one third of patients who survived severe covid 19 infection. It remain uncertain that fibrotic changes seen in the CT scans represents true fibrotic changes observed[14]. Out of 28, CT was suggestive of near complete resolution of the disease in 17 (61%),while 11 (39%) patients had partial radiological resolution. Thus CT showed a favourable response in all.

Spirometric studies conducted in post covid patients 66% showed restrictive abnormality, which is similar to study conducted by Sonn weber et al[15].Spirometry analysis revealed normal lung functions in 24(30%) patients. Restrictive abnormality was seen in 53(66.25%) patients, while obstructive abnormality was seen in 3(3.75%) patients. Mean (SD) FVC was 69.87%(16.42%). Mean FEV1 of 72.7% (20.62%). In a study conducted by Alessia et al[16],baseline pulmonary function tests was seen 55.7 ± 15.6 for FEV1%, 68.6 ± 16.0 for FVC%. Compared to baseline values, patients experienced a more significant improvement after 6 and 12 months in FEV1% (95.4±13.7 and 107.2±16.5), FVC% (91.3±14.5, and 105.9±15.6), and FEV1/FVC% values (1.04±0.04, and 1.01±0.05), demonstrate that there is gradual improvement in lung functions after a period of infection.

The study however, has some limitation. Most of the patients included in the study was healthcare workers which were younger and healthy compared to normal population, this led to selection bias. Referral bias happened due to referrals from primary care physicians to tertiary care centre hospital. Hence the representation was not in an uniform and unbiased way.

As, severe form of COVID-19 may cause a respiratory sequalae, it is mandatory to monitor the health status of the recovered patients. This disease appears to affect most of the organs, long term effects of organ involvement is still unknown. In order to determine the actual consequences and effects of the condition, it is essential to maintain follow-up studies on patients, and it will help to determine long term effects of covid infection. Severe COVID-19 disease was associated with functional and radiological abnormalities, potentially due to interstitial pneumonia and lung parenchymal involvement. However, the survivors recovered well at follow-up from respiratory aspects. Respiratory sequelae was documented but without much pulmonary disability. A systematic long term follow-up for survivors is needed to assess subsequent long-term sequelae if any with regards to the respiratory system.

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