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The impact of the COVID-19 pandemic on the profile of interstitial lung disease presenting to the pulmonary medicine department of a tertiary care center in western India

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Abstract

The COVID-19 pandemic impacted the etiological pattern of interstitial lung diseases (ILDs). This study aimed to analyze the profile of ILDs presenting to our department during the pandemic. Specifically, this cross-sectional observational study was conducted with the institute's ethics committee approval in the year 2021-2022. The clinical profile and history of COVID-19 illness in ILDs were noted. Data was analyzed in percentages and means.

Of the 136 cases included, 85 (62.5%) were men and 51 (37.5%) women. The average age was 55.1 ± 12.01 years. Cough and breathlessness were the predominant symptoms. A total of 20 (15%) participants gave a past history of COVID-19, of whom 2 (10%) had mild, 2 (10%) had moderate, and 16 (80%) had severe COVID-19 illness. Among them, 9 (45%) cases had pre-existing ILD. Thus, 11 (55%) had new-onset ILD attributed to severe COVID-19. This contributed to 8% of the ILD caseload. Predominant ILD patterns on high-resolution computed tomography thorax were usual interstitial pneumonia, hypersensitivity pneumonitis (HP), and non-specific interstitial pneumonia. The ILD diagnosis with multidisciplinary discussion was idiopathic interstitial pneumonitis in 44 cases, HP in 36, connective tissue disease-ILD in 35, post-COVID-19 ILD in 11, sarcoidosis in 8, and silicosis in 2.

COVID-19 was attributed to only 8% of the caseload and was the fourth most common cause of ILD. Generally, ILD cases were younger patients and had severe disease.

Key words: post-COVID ILD, pattern of ILD, interstitial fibrosis.

Introduction

Interstitial lung disease is a term that broadly covers a diverse collection of more than 200 lung disorders. These diseases are classified together as they affect the alveolo-capillary basement membrane. Among the ILDs which are broadly classified as due to known causes and idiopathic. The most important are idiopathic pulmonary fibrosis (IPF), sarcoidosis, hypersensitivity pneumonitis (HP), Connective tissue disease (CTD) related ILD, drug induced ILD, and pneumoconiosis. The majorities of these ILDs are idiopathic and include the group of idiopathic interstitial pneumonias (IIPs). Only about one in three cases of ILD have an identifiable cause [1]. The COVID pandemic witnessed a major revolution in the etiological pattern of ILD patients presenting to tertiary institutes in the lockdown and post lockdown era. Post healing of severe COVID infection resulted in fibrosis of the pulmonary parenchyma and interstitium. The patterns of imaging abnormalities coupled with data from prior coronavirus outbreaks suggested that patients with severe COVID-19 pneumonia were likely at an increased risk of progression to interstitial lung disease (ILD) [2]. The UK Interstitial Lung Disease Consortium (UKILD) undertook a longitudinal observational study of patients with suspected ILD following COVID-19, to determine the clinical, genetic, epigenetic and biochemical factors that determine the trajectory of recovery or progression [3]. Interim analysis of this study reported residual lung abnormalities in up to 11% of people discharged after COVID-19–related hospitalization [4]. However, clinically the pulmonologist outpatient clinics diagnosed ILDs as in the pre COVID era with extra vigilance on the history of COVID in their cases of ILD. While most studies followed cases of COVID for development of ILD, there are no major studies who study trends or change in the profile of ILDs in a general pulmonology clinic which actually diagnoses most ILDs as globally medical practice normalized gradually. Hence, we postulated that the patients presenting to the pulmonologists ILD clinic would represent a mixed spectrum of Post COVID ILD (PC-ILD) and other ILDs. On this background we decided to analyze the spectrum, clinical and radiological profile of interstitial lung disease cases presenting to our department in a tertiary care center.

Materials and Methods

This cross-sectional observational study was conducted in our pulmonary medicine unit of tertiary care center with IEC approval (PG Academic number ECARP/2021/05). All adult patients with diagnosis of ILD referred to the department of pulmonary medicine in the year 2021-2022 were included in the study. ILD was diagnosed with multidisciplinary discussion (MDD) i.e. clinical and radiological correlation in most patients. Patients less than 18 years of age and unwilling to

give consent were excluded from the study. One hundred and thirty six patients were included in the study. The clinical history, general and systemic examination, pulse oximetry, post exercise desaturation, six-minute walk test (6MWT), hematological, bio-chemical laboratory investigations, chest radiograph, spirometry, high resolution computed tomography (HRCT) thorax, two dimension echocardiography (2D-ECHO) findings were noted at the time of visit. In every case a detailed history regarding past history of COVID-19 disease was elicited. If diagnosed previously with COVID-19 then the severity of the symptoms, investigations and treatment given was obtained. The severity of COVID illness was as per the WHO COVID-19 disease severity classification to mild, moderate, severe disease [2,3]. The need for oxygen and ventilation was enquired and listed from the discharge summary of the cases. Data was analyzed and presented in percentages and mean.

Results

Demographic data

Study population consisted of 136 cases. Of these, 85 (62.5%) were men and 51 (37.5%) were women. Male : female ratio was 1.6:1. While the youngest patient with ILD was 24 years old; oldest was 80 years old. The average age was 55.1 (± 12.01) years. Further most patients (54%) were in age group between 41-60 years (Table 1).

Clinical symptomatology

The most common presenting symptom was cough, seen in 133 patients (97.8%). Dyspnea on exertion was present in 131 patients (96.3%). None of the cases were asymptomatic. Ninety-six patients (71%) had 12-60 months of symptoms before the diagnosis of ILD was made, 34(25%) presented with less than 12 months of symptoms and 6 (4%) had more than 60 months. The average duration of symptoms was 26.1 (± 14.53) months. Among the 136 patients; 83 (61%) were new cases and 53 (39%) were follow-up cases. The common comorbid conditions seen in ILD patients were Diabetes Mellitus in 54 (40%), hypertension in 43 (32%) and hypothyroidism in 17 (13%) cases.

Past history of covid illness

Of 136 patients; 20 (15%) gave past history of COVID, while 116 (85%) did not give any history of covid in the past. Amongst the 20 patients, 2(10%) patients had mild COVID disease, 2(10%) patients had moderate COVID and 16(80%) patients had severe COVID illness. Of these; 2 mild,

2 moderate and 5 cases with severe COVID had pre-existing ILD already. Hence the total new cases of ILD were 11 and these were attributed to severe COVID-19. This contributed to only 8.1% of total ILDs caseload, however consisted of 55% of subgroup with past history of COVID-19. Table 2 gives the distribution of covid history in various ILD patients.

Clinical examination and bed side tests

On clinical examination, clubbing was present in 93 patients (68%). Post exercise desaturation was observed in 134 patients (99%) and crackles were heard on auscultation in all patients (100%). Arterial blood gas analysis of 136 patients was noted. The A-a gradient was increased in 131 patients (96.3%) with mean of $42.99(\pm 25.2)$. Out of these 131 patients; 55 (40.6%) had type 1 respiratory failure, 2 (1.4%) patients had type 2 respiratory failure. Mean PaO₂ was $66.41(\pm 14.53)$. Mean Pco₂ was $35.95 (\pm 6.86)$ mm Hg. Six-minute walk distance (6MWD) of all patients were noted. The mean 6MWD was $243.2(\pm 69.95)$ meters. Most patients had 6MWD between 200-299 meters i.e 70 (51%). Of the rest, 24 (18%) patients walked between 100-199 meters, 40 (29%) patients had between 300-399 meters, and 2 (2%) patients walked more than 399 meters. Spirometry data of all 136 patients was available. Normal lung function was documented in 7 patients (5%), restrictive abnormality in 129 patients (95%) and none had mixed pattern or obstructive abnormality. The mean forced vital capacity (FVC) was 49.64% (1.42L) of predicted & SD of 15.21%(0.57L). Restrictive abnormality was classified as mild restriction in 43 (32%), moderate restriction in 54(40%), and severe restriction was in 32(25%) (Table 3). Most common abnormality noted on 2D-ECHO was presence of pulmonary hypertension with mean value of PASP of 37.7mmHg & SD of 7.11. The severity of pulmonary hypertension was mild in 115 patients (84.5%), moderate degree in 4 patients (2.9%), severe degree in 5 patients (3.6%) and normal in 12 patients (8.8%).

HRCT findings

Most common pattern of ILD on HRCT thorax was usual interstitial pneumonia (UIP) pattern seen in 47 patients, accounting for 35%. This was followed by HP pattern seen in 36 patients (26%), non-specific interstitial pneumonia (NSIP) in 32 patients (24%), Post COVID ILD pattern in 11(8%), sarcoidosis in 8(6%) and organizing pneumonia (OP) pattern seen in 2(1%) patients (Figure 1).

ILD diagnosis with MDD

The subtype of ILD in clinical and radiological correlation was as follows; 44 (32.3%) patients had Idiopathic Interstitial Pneumonitis (IIPs), Chronic HP in 36 (26.5%), CTD-ILD in 35(25.7%), Post COVID ILD in 11 (8.1%), sarcoidosis in 8 (5.9%), and silicosis in 2(1.5%). Of the IIPs; 28(63.6%) were IPF, 14(31.8%) were iNSIP, 2(4.6%) were COP. Table 4 gives the distribution of all ILDs. Table 2 also gives a detailed covid history status in individual ILD subtypes. COVID-19 cases had statistically higher risk of development of post COVID ILD. COVID-19 did not impact other ILDs. Amongst the total ILDs post COVID ILD was forth common cause after IIPs (32.3%), Chronic HP (26.5%) and CTDs (25.7%).

Discussion

ILD is an important chronic respiratory disease with a heterogenous spectrum. Some exposures are known to cause ILD. In the COVID pandemic we witnessed a new cause for ILD formed due to COVID sequelae in seriously ill cases. The process in course of the COVID infection resulted in fibrosis of the pulmonary parenchyma and interstitium. The patients with severe COVID-19 pneumonia were the most affected. The high prevalence of respiratory failure and the need for mechanical ventilation in patients with severe manifestations of the disease were the suspected causes for post COVID ILD. The spectrum of patients presenting to the ILD clinic in post COVID era represented a mixed spectrum of Post covid ILD and other ILDs. Data on patients with pre-existing ILD who were affected with COVID was limited. This study thus profiled the ILD spectrum at the tertiary care center in the post COVID era. In addition, we also compared this cohort with the previous study reported a decade back from our center to see the change in clinical characteristics [5].

We have 136 patients over two year's duration. The previous study from this center which recruited patients from 2012 to 2015 included 140 cases. Thus, this shows an increasing awareness and trend in the diagnosis of ILDs over the last decade [5]. Whether this impact was due to COVID is unclear. Among the 136 patients, the male-to-female ratio was 1.6:1. Hence a male predominance was noted concurrent to previous studies [5,6]. While the youngest patient with ILD who was 24 years old; oldest was 80 with average age in the sixth decade. This was in concordance with other studies [7,8]. Even our center reported an average age of 54 years a decade ago [5]. There was no major change in the demographic distribution over the decade at our center. In the current study most patients were in age group between 41-60 years, whereas a decade ago, our ILD patients were majorly in the age group of 50-69 years. This could be due to

the COVID pandemic which impacted younger individuals in the second wave. The most common presenting symptoms were cough and dyspnea and signs were crackles and clubbing. These trends are consistent with ILD presentation in most studies [5,8-10].

Our present study had a mean A-a gradient of 42.99(25.2) versus 29.25(13.16) in our previous study. This was statistically significant (t test, $p < 0.0001$). Current mean PaO₂ was 66.41(14.53) versus 72.22(12.16). This difference was statistically significant (t test, $p < 0.0001$). This could be as an impact of COVID on the profile of ILD or late referral due to the lockdown in the pandemic. In our study Type I respiratory failure was common. This was consistent with other studies where hypoxemic (type 1) respiratory failure was more common in interstitial lung diseases patients [11]. The six minute walk distance data was concurrent with other studies [11]. The mean 6MWD was 243.2(69.95) versus 320.64(98.68) meters in our previous study [5]. This difference was statistically significant (t test, $p < 0.0001$). Spirometry wise most patients 129 (95%) showed a restrictive abnormality with mild restriction in 32%, moderate in 40% and severe in 25%. This concurred with most studies [12-15]. The mean FVC was 1.42(0.57) versus 1.58(0.76) in our previous study. This difference was statistically significant (t-test, $p = 0.049$). Thus ABG, 6MWT and PFT characteristics of current study population were worse than those reported in ILD a decade ago by our center [5]. The CT features of ILD are in concordance with other studies on ILD wherein UIP pattern is most common HRCT pattern in ILD [13]. Table 5 details the differences of the clinical profile in the pre and post COVID era.

The subtype of ILD in clinical and radiological correlation was as follows; 44 (32.3%) patients had Idiopathic Interstitial Pneumonitis (IIPs), Chronic HP in 36 (26.5%), CTD-ILD in 35(25.7%), Post COVID ILD in 11 (8.1%), sarcoidosis in 8 (5.9%), and silicosis in 2(1.5%). This data is contrastingly different than a decade ago at our center. A decade back we reported a cohort of 140 cases of which 83 were IIPs, 22 were CTD ILD, 12 were HP, 12 were sarcoidosis and 11 others. Figure 2 compare the differences in the subtypes of ILD in pre and post COVID era. There was a trend towards decreasing numbers of IIPs and increasing chronic HP and CTD-ILDs and a small but significant proportion of post COVID ILD. The trend of HP as the most common new onset ILD was evident from the ILD India registry results and consistent with the same. In our study, COVID-19 was statistically significantly associated with 55% increased risk of developing a Post COVID ILD. This is consistent with global reports [16,17].

Our study was limited due to referral bias and selection bias as the hospital is a tertiary care center and was a dedicated covid hospital in the pandemic. We tried to overcome the same by including all cases of ILD as feasible.

Conclusions

To conclude our study highlighted the profound impact of the COVID pandemic on the spectrum and profile of ILD when compared with global and local data through the general ILD database. ILD cases were younger with more severe disease as compared to the trends a decade back. This serves as learning points towards increasing awareness and identification of ILD in general population to seek the impact of global epidemics/pandemics of respiratory diseases.

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Table 1. Age-wise distribution of interstitial lung disease.

Age Distribution (years)	Number of patients (N)	Percentage
0-20	0	0
21-40	17	12
41-60	73	54
61-80	46	34
>80	0	0

Table 2. Distribution of COVID-19 history in various interstitial lung diseases.

ILD (N)	Subtype	Total Number	History of Covid	No past history of covid
IIP (44)	IPF	28	3	25
	NSIP	14	1	13
	COP	02	0	2
Chronic HP (36)		36	1	35
Sarcoidosis (08)		08	1	7
CTD- ILD (35)	RA associated	10	0	10
	Scleroderma associated	06	1	5
	SLE associated	01	0	1
	MCTD associated	03	0	3
	Other	15	2	13
Silicosis (02)		02	0	2
Post COVID ILD (11)		11	11	0

Table 3. Spirometry findings in interstitial lung disease.

Spirometry	Number of patients	Percentage
Normal	7	5
Mild restriction	43	32
Moderate restriction	54	40
Severe restriction	32	23

Table 4. Etiology of interstitial lung disease.

ILD (N)	Subtype	Number
IIP (44)	IPF	28
	NSIP	14
	COP	02
Chronic HP (36)		36
CTD- ILD (35)	RA associated	10
	Scleroderma associated	06
	SLE associated	01
	MCTD associated	03
	Other	15
Sarcoidosis (08)		08
Silicosis (02)		02
Post COVID ILD (11)		11

Table 5. Comparison of interstitial lung disease cases in pre and post-COVID era.

Variable	Pre-COVID	Post-COVID	p
Study Duration	2012 to 2015	2021-2022	NA
No of years	Three	Two	NA
No of cases	140	136	NA
Mean Age	54	55	NA
Predominant age group	50-69 years	41-60 years	NA
M:F		1.6:1	NA
Mean A-a gradient	29.25	42.99	<0.0001
Mean PaO2	72.22	66.41	<0.0001
Mean 6 MWD	320.64	243.2	<0.0001
Mean FVC	1.58	1.42	0.049
Commonest CT patten	UIP	UIP	NA
ILD subtype as per MDD	83 IIP 12 HP 22 CTD-ILD 12 sarcoidosis 11 others	44 IIP 36 HP 32 CTD-ILD 8 sarcoidosis 2 others 11 Post COVID ILD	NA

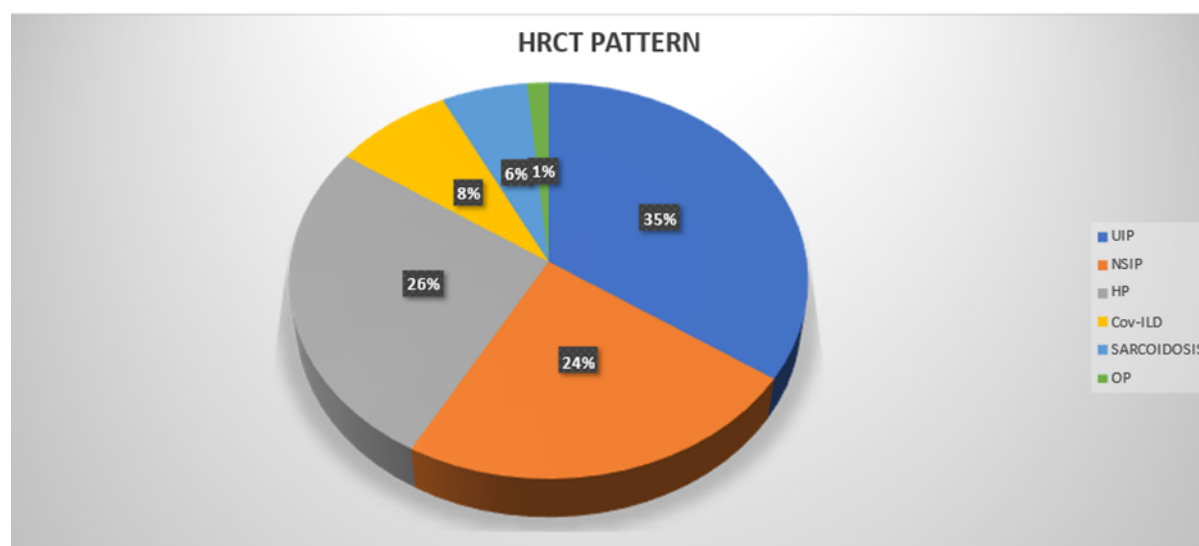


Figure 1. High-resolution computed tomography pattern of the interstitial lung disease cases in the post-COVID era.

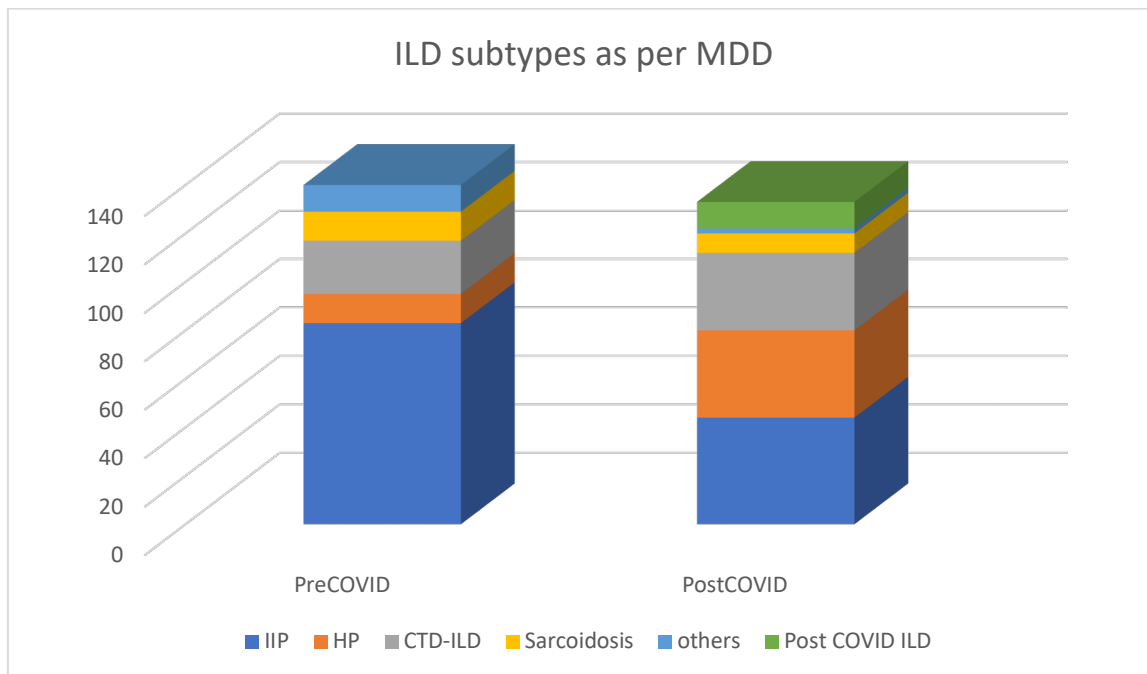


Figure 2. Interstitial lung disease subtypes as per multidisciplinary discussion in the pre-COVID and post-COVID eras.