Original Article

Spectrum of diffuse parenchymal lung diseases with special reference to idiopathic pulmonary fibrosis and connective tissue disease: An eastern India experience

Somenath Kundu, Subhra Mitra[1], Joydeep Ganguly[2], Subhasis Mukherjee[3], Souvik Ray[4], Ritabrata Mitra

Department of Respiratory Medicine, Institute of Postgraduate Medical Education and Research and Seth Sukhlal Karnani Memorial Hospital [1]Calcutta National Medical College and Hospital, [3]College of Medicine and Sagar Dutta Hospital, Kolkata, [2]Murshidabad Medical College and Hospital, Berhampore, [4]Bankura Sammilani Medical College and Hospital, Bankura, West Bengal, India

ABSTRACT

Objective: To evaluate the clinical spectrum of diffuse parenchymal lung diseases (DPLD) encountered in the Indian setting and to compare idiopathic pulmonary fibrosis (IPF) and connective tissue disease associated DPLD (CTD-DPLD), the two commonest aetiologies. **Materials and Methods:** A prospective study of clinical, imaging and laboratory parameters of patients diagnosed as DPLD and followed up in the Pulmonary Medicine Department of a tertiary-care teaching institution in eastern India was conducted over a period of one year. **Results:** 92 patients of DPLD were diagnosed in the study period with IPF (*n* = 35, 38.04%), CTD-DPLD (*n* = 29, 31.5%), hypersensitivity pneumonitis (*n* = 10, 10.9%), sarcoidosis (*n* = 5, 5.4%) and silicosis (*n* = 5, 5.4%) being the common causes. The CTD-DPLD group had a lower mean age (39.5 ± 1.86 vs 56.9 ± 1.12 years), a longer duration of symptoms (3.5 ± 0.27 vs 2.5 ± 0.26 years), more extra pulmonary manifestations, significantly more base line FVC and 6-minute-walk-distance than the IPF patients. 19 patients of IPF (54%) opted for treatment. All the IPF patients had a significant fall in FVC after six months (mean change -0.203 ± 0.01 litres) compared to the CTD-DPLD group (mean change - 0.05 ± 0.04 litres.) **Conclusion:** CTD-DPLD patients belong to a younger age group, with longer duration of symptoms, more extrapulmonary features, better physiological parameters and better response to therapy than IPF patients. Larger prospective epidemiological studies and enrolment in clinical trials are necessary for better understanding of the spectrum of diffuse parenchymal lung disorders and their therapeutic options.

KEY WORDS: Connective tissue disease–associated diffuse parenchymal lung diseases, diffuse parenchymal lung diseases, idiopathic pulmonary fibrosis

Address for correspondence: Dr. Subhra Mitra, 603 'Auroville', 10 Mandeville Gardens, Kolkata - 700 019, West Bengal, India. E-mail: susami2@gmail.com

INTRODUCTION

Diffuse parenchymal lung diseases (DPLD) comprise a wide spectrum of disorders, with varied presentations and prognosis. Foremost among the known causes is the connective tissue disease (CTD), the others being occupational or environmental exposure and drug-induced pneumopathies. Among the disorders of unknown cause, idiopathic pulmonary fibrosis (IPF) has the worst outcome.[1] Most publications in the 1980s and 1990s from this country dealt with CTD-associated DPLD (CTD–DPLD)[2,3] and there were some early reports on fibrosing alveolitis.[4,5] With subsequent characterization of idiopathic interstitial pneumonias (IIPs),[1,6] an increase in the burden of IPF is being reported from various centers in India.[7-9]Although high-resolution computed tomography scan (HRCT) pattern and pathological findings in IIPs are now being applied to CTD–DPLD, there are differences in the treatment and prognosis, making it imperative to differentiate the two conditions.[10]

In this study, we prospectively evaluated the clinical spectrum of DPLDs encountered in the Indian setting and compared the two leading causes of DPLD namely IPF and CTD-DPLD.

Access this article online

Quick Response Code:

Website: www.lungindia.com

DOI: 10.4103/0970-2113.142115

MATERIALS AND METHODS

Study design

A prospective observational study was conducted inthe Pulmonary Medicine Department of a tertiary care teaching institution in eastern India over a period of one year, on cases of diffuse parenchymal lung disease. Written informed consent was taken from all the patients and the study was cleared by the institute's Ethics Committee.

The inclusion criteria were:

1. Patients having clinical features/pulmonary function test suggestive of, and HRCT consistent with DPLD
2. Age 12 years and above, either sex.

The exclusion criteria were:

1. Patients with prior corticosteroid therapy, for more than one month
2. Patients not willing to follow the study protocol
3. DPLD cases diagnosed to have tuberculosis were excluded from the final analysis.

Detailed demographical and clinical parameters including age, smoking history, environmental, occupational, and drug exposure, duration and severity of breathlessness, clubbing, end-inspiratory crepitations, and extrapulmonary features (rashes, arthritis, Raynaud's phenomenon, dysphagia, oral ulcers), were assessed. HRCT of the thorax was evaluated for ground-glass opacities, reticular shadows, subpleural involvement, septal thickening, nodular lesions, and honeycombing/traction bronchiectasis. Contrast was given to patients suspected to have mediastinal lymphadenopathy. Spirometry, six-minute walk test (6MWT), according to the ATS guidelines,[11] and echocardiography was done in all cases at the baseline. Tricuspid jet velocity >3.4 m/s and estimated pulmonary artery systolic pressure >50 mmHg[12] were considered to be pulmonary hypertension. The antinuclear antibody (ANA) profile, Rheumatoid factor (RF), anti-cyclic citrullinated peptide (anti-CCP), antinuclear cytoplasmic antiboby (ANCA), and serum angiotensin converting enzyme (SACE) were estimated. Bronchoalveolar lavage (BAL) study, transbronchial lung biopsy (TBLB), and biopsies of lymph node, skin lesions or kidney were done as needed.

Diagnosis

A multidisciplinary approach involving a radiologist, pathologist, and rheumatologist was taken, to ensure accuracy of the diagnosis. A case was labeled as IPF as per the current guidelines of the American Thoracic Society/the European Respiratory Society/the Japanese Respiratory Society/the Latin American Thoracic Association (ATS/ERS/JRS/ALAT),[13] that is, exclusion of known causes and the usual interstitial pneumonia (UIP) pattern on HRCT. Diagnosis of CTD and sarcoidosis was based on their respective diagnostic criteria, while a history of exposure, HRCT patterns, and BAL fluid lymphocytosis, were taken into account for diagnosing hypersensitivity pneumonitis.[14]

Management

Cases of IPF were counseled and those consenting for treatment were prescribed a regimen of oral steroids (prednisolone 0.5 mg/kg/day tapering over three months to 0.125mg/kg/day), azathioprine (2 mg/kg/day to a maximum of 150 mg/day) + N-acetylcysteine (600 mg, orally, thrice a day) with modification, if necessary, due to comorbidities.[6,13,15,]

Scleroderma patients were put on low-dose corticosteroid (10 mg) plus cyclophosphamide (2 mg/kg body weight),[16] rheumatoid arthritis cases on disease modifying drugs including methotrexate and corticosteroids.[17] Symptomatic sarcoidosis patients with stage 2 or 3 disease or disabling extrapulmonary features were prescribed corticosteroids.[18] The vasculitis group was treated with prednisolone (1 mg/kg) and cyclophosphamide (2 mg/kg),[19] the hypersensitivity pneumonitis patients were treated chiefly by environmental management, and in the severely symptomatic patients a short course of corticosteroids was used.[14]

Follow-up

These patients were followed-up at the DPLD clinic based on clinical, spirometry, and 6MWT tests, every six months. Those on immunosuppressives were monitored monthly for hemogram and renal parameters. A patient with a fall in the forced vital capacity (FVC) of 10% or more from the baseline and/or a fall in the oxygen saturation below 88% before or during the 6MWT, with reduction in the six-minute walk distance, at six months, was considered to be with unstable disease.[13]

Statistical analysis

The statistical analysis was performed using the SPSS version 10.0 (SPSS Inc, Chicago, IL) software for MS-Windows. Cases of IPF and CTD–DPLD were compared with respect to the clinical, radiological, and physiological parameters. Descriptive frequencies were expressed in terms of mean ± standard error of mean (SEM). The *P* value was calculated using the Fisher's exact test for categorical variables and a student t-test was used for continuous variables and a $P < 0.05$ was considered to be significant.

RESULTS

Pattern of diagnosis

In this study, a total number of 112 patients with diffuse parenchymal lung diseases were enrolled initially. In 13 patients, a diagnosis of tuberculosis was made, and subsequently in two, lung carcinoma. Another five patients had clinicoradiological features suggestive of idiopathic non-specific interstitial pneumonia (idiopathic-NSIP), but they did not consent to a lung biopsy. These cases were excluded from the study, bringing the final population to 92.

Idiopathic pulmonary fibrosis (IPF) was found to be the most common variety (n = 35, 38.04%) followed by CTD (n = 29, 31.5%) [Table 1]. Of the 29 cases of CTD, systemic sclerosis (n = 17, 58.6%) and rheumatoid arthritis (RA) (n = 8, 27.5%) were the most common followed by systemic lupus erythematosus (SLE) (two cases), polymyositis, and ankylosing spondylitis (one case each). Small vessel vasculitis was diagnosed in four cases, of which two were granulomatous polyangitis, one was Churg-Strauss syndrome, and one microscopic polyangitis.

Clinical parameters

In contrast to IPF, a majority of patients of CTD–DPLD belonged to a younger age group (n = 25, 86.2% in 20-50 years) [Table 2]. Although there was not much difference in the pulmonary symptoms and signs between IPF and CTD–DPLD [Table 3] among the extrapulmonary features, clubbing was distinctly more common in IPF (92%), while the Raynaud's phenomenon, dysphagia, and digital ulceration were seen in systemic sclerosis in 82, 58, and 35% of the cases, respectively. Joint deformity was noted in seven out of eight patients of RA, skin rashes and oliguria were seen in the SLE- and ANCA-associated vasculitis group, peripheral neuropathy in those with the Churg-Strauss syndrome, and one case of Wegener's granulomatosis.

Clinicophysiological parameters

Compared to CTD–DPLD, IPF patients had significantly less baseline FVC and six-minute walk distance [Table 4]. Pulmonary hypertension was seen in eight cases (47%) of systemic sclerosis (SSc), two cases of RA and one case of polymyositis.

Imaging

All cases of IPF (n = 35, 100%) showed a classical UIP pattern on the HRCT thorax [Table 5]. The HRCT findings differed among the various subgroups of CTD–DPLDs. A majority of RA (n = 8) patients had a UIP pattern with predominant lower lobe (87%) subpleural (75%) involvement, with septal thickening (75%), and a minority had an NSIP pattern (12%). The SSc patients (n = 17) showed an NSIP pattern in 58.8% and a UIP pattern in 47%. One patient with SLE-DPLD showed a lower lobe, subpleural, reticular shadow, with honeycombing, and the other, bilateral diffuse ground-glass opacity, suggestive of diffuse alveolar hemorrhage. Polymyositis-interstitial pneumonia showed an NSIP pattern, while the case of ankylosing spondylitis had bilateral upper lobe fibrosis.

Serum markers

Serum autoantibodies were helpful in differentiating CTD–DPLD from the IPF [Table 6]. In RA, The rheumatoid factor and anti-CCP antibody were found to be positive in 100 and 88% of the cases respectively, while in SSc, the anti Scl-70 and anti-centromere antibodies were positive in 88 and 12% of the cases.

Table 1: Etiological distribution of diffuse parenchymal lung disease cases

Etiological spectrum of DPLD	Number of cases (n=92) with percentages
IPF	35 (38.04)
Connective tissue diseases	29 (31.5)
Hypersensitivity pneumonitis	10 (10.9)
Sarcoidosis	5 (5.4)
Silicosis	5 (5.4)
ANCA-associated vasculitis	4 (4.35)
Pulmonary Langerhans cell histiocytosis	2 (2.2)
Respiratory bronchiolitis associated with ILD	1 (1.1)
Alveolar microlithiasis	1 (1.1)

DPLD: Diffuse parenchymal lung diseases, IPF: Idiopathic pulmonary fibrosis, ANCA: Antinuclear cytoplasmic antiboby, ILD: Interstitial lung disease

Table 2: Demographic parameters

Demography	IPF (n=35)	CTD-DPLD (n=29)	P value
Age>50 years	32 (91%)	3 (10.3%)	0.0001
Mean age	56.9±1.12	39.5±1.86	0.0001
Sex ratio (male:female)	4:3	2:9	
Smoking	15 (42.9%)	2 (6.9%)	0.006

DPLD: Diffuse parenchymal lung diseases, IPF: Idiopathic pulmonary fibrosis, CTD: Connective tissue disease

Table 3: Clinical parameters

Clinical symptoms and signs	IPF (n=35)	CTD-DPLD (n=29)	P value
Mean duration of symptoms (years)	2.5±0.26	3.5±0.27	0.01
Dyspnea	35	28	0.453
Dry cough	35	29	0.4531
Hemoptysis	1	2	0.58
Extrapulmonary manifestations	1	28	0.00001
Clubbing	32	6	0.00001
Joint deformity	0	16	0.0001
Bilateral end-inspiratory crepitations	35	28	0.4531

DPLD: Diffuse parenchymal lung diseases, IPF: Idiopathic pulmonary fibrosis, CTD: Connective tissue disease

Table 4: Physiological parameters

Physiological parameters	IPF (n=35) (%)	CTD-DPLD (n=29) (%)	P value
FVC>1.25 l	15 (43)	21 (72.4)	0.0236
6MWD>300 m	10 (28.5)	25 (86.2)	0.00001
Spo2>88% post exercise	20 (57)	20 (68.9)	0.0417
Pulmonary hypertension	8 (23)	11 (33.3)	0.5874

DPLD: Diffuse parenchymal lung diseases, IPF: Idiopathic pulmonary fibrosis, CTD: Connective tissue disease

Spectrum of diffuse parenchymal lung diseases

Besides IPF and CTD–DPLD, ten cases were diagnosed as hypersensitivity pneumonitis (HP). Nine of these cases had exposure to pigeons and presented with chronic symptoms. Ground-glass opacities in the upper lobes with cystic changes and BAL fluid lymphocytosis (>30% of the total cell count) were seen in all the ten patients of HP.

Serum ACE was elevated in all the five patients of sarcoidosis (mean value of 98 U/L). The serum calcium and 24-hour urine calcium were elevated in three patients. The Mantoux test was negative with 10 TU in all five cases.

The chest X-ray showed Stage 2 disease in three and Stage 3 disease in two. HRCT showed upper lobar involvement, with peribronchovascular thickening (100%), centrilobular nodules (60%), septal thickening, and ground-glass opacities (40%). Transbronchial lung biopsy (TBLB) showed non-caseating granuloma consistent with sarcoidosis in four cases. Cervical lymph nodes biopsy demonstrated non-caseating granuloma in the other case.

All five cases of silicosis were of workers involved in sandblasting, with upper zone involvement and mediastinal adenopathy (80%) including egg-shell calcification in one case. A case of pulmonary Langerhans cell histiocytosis (PLCH) presented with pneumothorax and characteristic HRCT features [Figure 1], while the case of alveolar microlithiasis had its unique imaging features [Figure 2].

Follow up

All cases were counseled for treatment options and followed up in the DPLD clinic.Nineteen out of 35 patients in the IPF group voluntarily agreed to treatment with the standardized triple drug regimen. Cases of CTD–DPLDs were put on appropriate therapy. Although 47% of the patients in the IPF group receiving the therapy experienced subjective improvement of dyspnea, on spirometry, all cases showed more than a 10% fall in FVC at six months [Table 7]. Eighty-four percent of the treated patients developed systemic hypertension, 63% diabetes, and 52% had at least one exacerbation (mainly infection) requiring hospitalization. Of the remaining 16 patients of IPF, who did not opt for triple drug therapy, after six months, 75% of them expressed subjective improvement of dyspnea, but all had a significant fall in FVC and an oxygen desaturation of <88% after the six-minute walk test. Improvement in the 6MWD, after six months, was seen in three patients (15.7%) in the treatment group and in seven patients (43.7%), who did not receive the triple drug therapy. Therefore, the triple drug therapy for the IPF group did not show any positive outcome. Two patients (on therapy) died within six months due to respiratory failure during exacerbation. Both patients had advanced disease, with a baseline dyspnea of grade 4 MMRC, FVC <1.25 liters, post six-minute walk test, and oxygen saturation <88%. On the contrary, in the CTD–DPLD group, 62.1% of the patients showed subjective improvement of dyspnea, 13 (44.8%) patients showed improvement in 6MWD, with 31% of the cases showing 6MWD of more than 300 m. Mean (± SEM) value of 6MWD and FVC after six months of treatment were 209.14 ± 9.72 m and 1.01 ± 0.03 l in the IPF group, and 267.5 ± 12.7 m and 1.17 ± 0.05 l, respectively, in the CTD–DPLD group.

Table 5: High-resolution computed tomography thorax

Patterns on HRCT	IPF (*n*=35)	CTD-DPLD (*n*=29)	*P* value
Upper lobe	0	4	0.0001
Middle lobe	0	9	
Lower lobe	35	23	0.0063
Subpleural	35	13	0.0001
Peribronchovascular	0	2	0.2014
Reticular	32	21	0.05
Nodular	0	2	0.2014
Ground-glass	2	13	0.0003
Honeycombing	35	19	0.0001

DPLD: Diffuse parenchymal lung diseases, IPF: Idiopathic pulmonary fibrosis, CTD: Connective tissue disease, HRCT: High-resolution computed tomography

Table 6: Serum markers

Immunological markers	IPF (*n*=35)	CTD DPLD (*n*=29)	*P* value
Serum ANA (hep-2)	3 (8.57%) (< 1:80)	17 (58.6%) (> 1:160)	0.0001
RA factor	1 (2.85%)	9 (31%)	0.0037
Anti-jo antibody	0	1 (3.4%)	0.4531
Anti-scl 70	0	15 (51.7%)	0.0001

DPLD: Diffuse parenchymal lung diseases, IPF: Idiopathic pulmonary fibrosis, CTD: Connective tissue disease

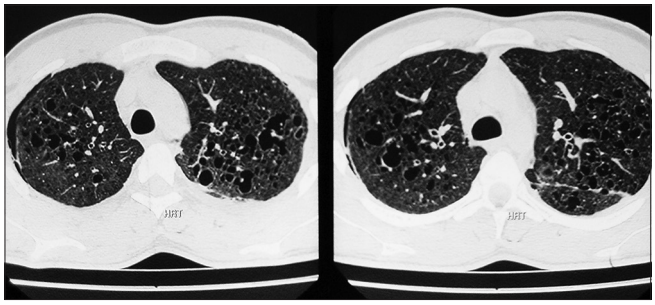

Figure 1: Pulmonary Langerhans cell histiocytosis presenting with pneumothorax

DISCUSSION

Our study showed that IPF was the most common entity (38.04%) among DPLD cases [Table 1] followed by CTD–DPLD (31.5%), hypersensitivity pneumonitis (10.9%), sarcoidosis (5.4%), and silicosis (5.4%). The frequency of IPF varied from 28.6 to 46% in two studies from north India[4,5] and from 43 to 45% in two studies from the south,[7,9] while CTD–DPLD ranged from 18 to 50.8%.[5,7]

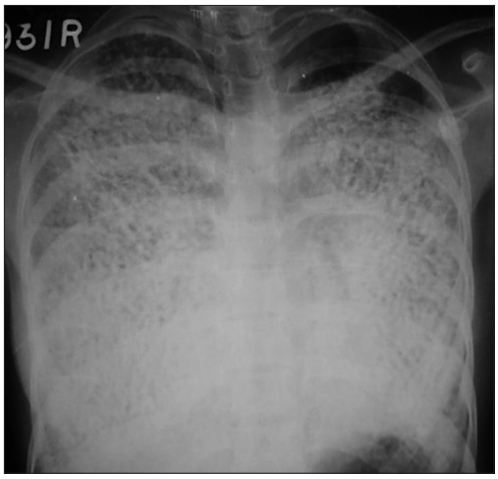

Figure 2: Alveolar microlithiasis

Table 7: Treatment outcome after six months

Outcome of treatment	IPF (*n*=19)	CTD-DPLD (*n*=29)	*P* value
Improvement of dyspnea	9	18	0.038
Mean change in 6MWD after six months (in meter)	−43.088±14.58	−16.06±15.44	0.23
Mean change in FVC after six months (in liters)	−0.203±0.01	−0.05±0.04	0.0038
Number of patients with 6MWD<300 m after six months of treatment	19 (100%)	20 (68.9%)	0.0073
Number of patients showing>10% fall in FVC after six months of treatment	19 (100%)	18 (62.1%)	0.0017

DPLD: Diffuse parenchymal lung diseases, IPF: Idiopathic pulmonary fibrosis, CTD: Connective tissue disease, FVC: Forced vital capacity

Sarcoidosis presenting with DPLD was reported in 9.6 and 22% among the DPLD cases.[7,9]

On account of high prevalence of tuberculosis in India, many patients with interstitial lung disorders are misdiagnosed to be with tuberculosis, and receive antitubercular drugs (ATDs).[20] In our study, 64 patients had a prior history of intake of ATDs for more than one month, although none had tuberculosis. Ten percent of the cases of cryptogenic organizing pneumonia[21] and 37% of sarcoid patients[22] from Mumbai were initially diagnosed with TB and received ATDs. On the contrary, tuberculosis may mimic DPLDs, as 13 cases in our study, initially suspected to be DPLD, were subsequently found to be suffering from tuberculosis with the help of a BAL/TBLB study. This was also the finding of others.[7] Awareness about a varied DPLD spectrum and differentiation from tuberculosis is a very important issue in the Indian context.

The mean age of IPF cases [Table 2] in our series was 56.8 ± 8.3 years, similar to other Indian studies (53 ± 10[9] and 50.6 ± 11.9 years[8]), but less than that quoted in western literature (two-third of the cases over 60 and mean age at diagnosis of 66 years).[6] The preponderance of males and smokers in the IPF group in this study is similar to the Indian and western literature.[6,13] The median time between the onset of symptoms and diagnosis in the IPF group, studied by Johnston *et al.*,[23] was 12 months. Mean duration of illness before diagnosis was 2.5 years in our IPF group and 2.25 years in the group studied by Subhash *et al.*[9] Low awareness of the disease, over-reliance on the chest radiograph,[7] and high TB burden is probably responsible for the delayed diagnosis compared to western literature.

Pulmonary symptoms and signs among CTD–DPLD were similar to that of IPF, except clubbing, which was uncommon in this group. The observations of Rajasekaran *et al.*[24] were similar. Pulmonary hypertension was demonstrated in 22% of our IPF cases and 34.5% of the CTD-DPLD cases [Table 4]. It had been reported in 30% among DPLD cases by Subhash *et al.*[9] and in a third of the patients with advanced IPF (right heart catheterization) in western literature.[25] The prevalence of isolated pulmonary arterial hypertension and pulmonary hypertension with interstitial lung disease in systemic sclerosis were similar and ranged between 18 and 22% in various studies.[26]

Previously the diagnosis of IPF was based on fulfilling the major and minor criteria in the absence of surgical lung biopsy (SLB).[6] According to the current guidelines, a classical UIP pattern on HRCT, in an appropriate clinical setting, is sufficient to make a diagnosis of IPF.[13]

The HRCT patterns in patients with CTD–DPLD mostly correlate with the lung pathology.[27] Of the four usual patterns described in RA-associated DPLD[17] our cases predominantly showed UIP followed by NSIP, but none had an organizing pneumonia or bronchiolitis pattern. Although, as with western literature, NSIP was the most common radiographic subtype among SSc-associated DPLD,[17] there was also a significant number of our SSc patients with a UIP pattern. Therefore, in our series, CTD associated DPLD had more of a UIP pattern (n = 16, 55.2%) than NSIP (n = 12, 41.4%), although traditionally NSIP was known to be more frequent.

Decline in the FVC of 10% or more at six months and decreased 6MWD with desaturation have been shown to be measure of disease progression and surrogate markers of mortality.[13,28-29,30] In our study, 54% (n = 19) of the cases of IPF, who opted for the standardized triple drug regimen, with prednisolone, azathioprine, and acetylcysteine, showed no benefit (in fact, there were more drug side effects) compared to the 46% (n = 16) who opted for only supportive treatment. The triple therapy (prednisolone, azathioprine, and NAC) arm had to be discontinued due to excess morbidity and mortality compared to the placebo arm and the NAC arm in PANTHER-IPF study.[31,32]

The SSc-associated DPLD patients treated with oral cyclophosphamidewere found to have less change in FVC and functional ability compared to the placebo-treated patients in the North American Scleroderma Lung study.[16] However, a recent meta-analysis found no significant improvement of pulmonary function with cyclophosphamide treatment.[36] Unlike in the IIPs, there appears to be no difference in survival between those with an NSIP and those with a UIP pattern.[37]

Treatment of RA-DPLD is essentially empirical in the absence of randomized controlled trials, and the best response has been reported with RA-associated organizing pneumonia.[17] In their study, Rajasekaran *et al.*,[24] found patients with RA-DPLD to have a better prognosis than those with IPF, with median survival rate of 60 months versus 27 months, respectively. However, no distinction regarding prognosis was made between the UIP and NSIP patterns in their RA-DPLD group.

Park *et al.*[35] reported a better prognosis of the CTD-DPLD group, not only due to the higher prevalence of NSIP in this group, but also due to a better prognosis of CTD–DPLD patients, even those with a histological pattern of UIP,

compared with patients with IPF. However, some studies quote a poor prognosis and similar mortality rates between the two groups.[33,34]

In this study, as a whole, the CTD–DPLD group fared better than the IPF group (both the treated and observation arms) at six months of therapy [Table 7].

Our study is probably one of the few studies from India that has looked at the spectrum of DPLD prospectively and has attempted a comparison between two of its largest contributors. However, the study has certain limitations, in that, the diffusing capacity of the lung could not be done for monitoring the disease progress; triple drug therapy versus supportive therapy in the IPF group was not randomized, the CTD–DPLD groups were not age- or sex-matched, and surgical biopsy was not feasible.

To conclude, the picture of diffuse parenchymal lung disease revealed in our study is similar to some of the retrospective studies from India. IPF seems to have presented a decade earlier in our country compared to the West. Both the burden of tuberculosis and its role as a 'mimicker' of DPLD caused a significant delay in the diagnosis of IPF in our country. Compared to IPF, the CTD–DPLD patients belonged to a younger age group, with a longer duration of symptoms, more extrapulmonary features, better physiological parameters, a mix of NSIP and UIP patterns on HRCT, and a better response to therapy. Larger prospective epidemiological studies and enrollment in clinical trials are necessary for a better understanding of the spectrum of diffuse parenchymal lung disorders and their therapeutic options.

REFERENCES

1. American Thoracic Society; European Respiratory Society.American Thoracic Society/European Respiratory Society International Multidisciplinary Consensus Classification of the Idiopathic Interstitial Pneumonias. This joint statement of the American Thoracic Society (ATS), and the European Respiratory Society (ERS) was adopted by the ATS board of directors, June 2001 and by the ERS Executive Committee, June 2001.Am J Respir Crit Care Med 2002;165:277-304.
2. Thiruvengadam KV, Chandrasekaran AN, Kulandaivelu V, Inbavazhvu MN, Venkatramani K. Pleuro pulmonary manifestations of rheumatoid arthritis. Indian J Chest Dis Allied Sci 1979;21:35-43.
3. Guleria JS, Pande JN, Malik SK, Bhutani LK. Lungs in progressive systemic sclerosis. Br J Dis Chest 1970;64:150-60.
4. Sharma SK, Pande JN, Guleria JS. Diffuse interstitial pulmonary fibrosis. Indian J Chest Dis Allied Sci 1984;26:214-9.
5. Jindal SK, Malik SK, Deodhar SD, Sharma BK. Fibrosingalveolitis: A report of 61 cases seen over thepast five years. Indian J Chest Dis Allied Sci 1979;21:174-9.
6. American Thoracic Society. Idiopathic pulmonary fibrosis: Diagnosis and treatment.International consensus statement. American Thoracic Society (ATS), and the European Respiratory Society (ERS).Am J Respir Crit Care Med 2000;161:646-64.
7. Sen T, Udwadia ZF.Retrospective study of interstitial lung disease in a tertiary care centre in India.Indian J Chest Dis Allied Sci 2010;52:207-11.
8. Maheshwai U, Gupta D, Aggarwal AN, Jindal SK. Spectrum and diagnosis of idiopathic pulmonary fibrosis.Indian J Chest Dis Allied Sci 2004;46:23-6.
9. Subhash HS, Ashwin I, Solomon SK, David T, Cherian AM, Thomas K. A comparative study on idiopathic pulmonary fibrosisand secondary diffuse parenchymal lung disease. Indian J Med Sci 2004;58:185-90.
10. Vij R, Strek ME. Diagnosis and treatment of connective tissue disease-associated interstitial lung disease. Chest 2013;143:814-24.
11. ATS Committee on Proficiency Standards for Clinical Pulmonary Function Laboratories. ATS statement: Guidelines for the six-minute walk test. Am J Respir Crit Care Med 2002;166:111-7.
12. Galiè N, Hoeper MM, Humbert M, Torbicki A, Vachiery JL, Barbera JA, *et al*. ESCCommittee for Practice Guidelines (CPG). Guidelines for the diagnosis and treatment of pulmonary hypertension: The Task Force for the Diagnosis and Treatment of Pulmonary Hypertension of the European Society of Cardiology (ESC) and the European Respiratory Society (ERS), endorsed by the International Society of Heart and Lung Transplantation (ISHLT). Eur Heart J 2009;30:2493-537.
13. Raghu G, Collard HR, Egan JJ, Martinez FJ, Behr J, Brown KK, *et al*. ATS/ERS/JRS/ALAT Committee on Idiopathic Pulmonary Fibrosis. An official ATS/ERS/JRS/ALAT statement: Idiopathic Pulmonary Fibrosis: Evidence-based guidelines for diagnosis and management. Am J Respir Crit Care Med 2011;183:788-824.
14. Costable U, Bonella F, Guzman J. Chronic hypersensitivity pneumonitis. Clin Chest Med 2012;33:151-63.
15. Demedts M, Behr J, Buhl R, Costabel U, Dekhuijzen R, Jansen HM, *et al*. IFIGENIA Study Group. High-dose acetylcysteine in idiopathic pulmonary fibrosis. N Engl J Med 2005;353:2229-42.
16. Tashkin DP, Elashoff R, Clements PJ, Goldin J, Roth MD, Furst DE, *et al*. Scleroderma Lung Study Research Group. Cyclophosphamide versus placebo in scleroderma lung disease. N Engl J Med 2006;354:2655-66.
17. Antoniou KM, Margaritopoulos G, Economidou F, Siafakas NM. Pivotal clinical dilemmas in collagen vascular diseases associated with interstitial lung involvement. Eur Respir J 2009;33:882-96.
18. Statement on sarcoidosis. Joint Statement of the American Thoracic Society (ATS), the European Respiratory Society (ERS) and the World Association of Sarcoidosis and Other Granulomatous Disorders (WASOG) adopted by the ATS Board of Directors and by the ERS Executive Committee, February 1999. Am J Respir Crit Care Med 1999;160:736-55.
19. Fauci AS, Haynes BF, Katz P, Wolff SM. Wegener's granulomatosis: Prospective clinical and therapeutic experience with 85 patients for 21 years.Ann Intern Med 1983;98:76-85.
20. Udwadia ZF, Sen T, Jindal SK. Interstitial lung diseases in a resource-limited setting: The case of India. Eur Respir Mon 2009;46:357-74.
21. Sen T, Udwadia ZF. Cryptogenic organizing pneumonia: Clinical profile in a series of 34 admitted patients in a hospital in India. J Assoc Physicians India 2008;56:229-32.
22. Doshi AV, Udwadia ZF. A profile of sarcoidosis from a private hospital in Bombay. Chest 2002;122:146S-7S.
23. Johnston ID, Prescott RJ, Chalmers JC, Rudd RM. British Thoracic Society study of cryptogenic fibrosingalveolitis: Current presentation and initial management. Fibrosing Alveolitis Subcommittee of the Research Committee of the British Thoracic Society. Thorax 1997;52:38-44.
24. Rajasekaran BA, Shovlin D, Lord P, Kelly CA. Interstitial lung disease in patients with rheumatoid arthritis: A comparison with cryptogenic fibrosingalveolitis. Rheumatology (Oxford) 2001;40:1022-5.
25. Lettieri CJ, Nathan SD, Barnett SD, Ahmad S, Shorr AF. Prevalence and outcomes of pulmonary arterial hypertension in advanced idiopathic pulmonary fibrosis. Chest 2006;129:746-52.
26. Solomon JJ, Olson AL, Fischer A, Bull T, Brown KK, Raghu G. Scleroderma lung disease. Eur Respir Rev 2013;22:6-19.
27. Kim EA, Lee KS, Johkoh T, Kim TS, Suh GY, Kwon OJ, *et al*. Interstitial lung diseases associated with collagen vascular diseases: Radiologic and histopathologic findings. Radiographics 2002;22:S151-65.
28. du Bois RM, Weycker D, Albera C, Bradford WZ, Costabel U, Kartashov A, *et al*. Forced Vital Capacity in Patients with Idiopathic Pulmonary Fibrosis. Am J Respir Crit Care Med 2011;184:1382-89.
29. du Bois RM, Weycker D, Albera C, Bradford WZ, Costabel U, Kartashov A, *et al*. Six-minute-walk test in idiopathic pulmonary fibrosis: Test validation and minimal clinically important difference. Am J Respir Crit Care Med 2011;183:1231-7.
30. Caminati A, Bianchi A, Cassandro R, Mirenda MR, Harari S, *et al*. Walking distance on 6-MWT is a prognostic factor in idiopathic pulmonary fibrosis. Respir Med 2009;103:117-23.
31. Demedts M, Behr J, Buhl R, Costabel U, Dekhuijzen R, Jansen HM, *et al*. IFIGENIA Study Group. High-dose acetylcysteine in idiopathic pulmonary fibrosis. N Engl J Med 2005;353:2229-42.
32. Wells AU, Behr J, Costabel U, Cottin V, Poletti V. Triple therapy in idiopathic pulmonary fibrosis: An alarming press release. Eur Respir J 2012;39:805-6.

33. Kocheril SV, Appleton BE, Somers EC, Kazerooni EA, Flaherty KR, Martinez FJ, *et al*. Comparison of disease progression and mortality of connective tissue disease-related interstitial lung disease and idiopathic interstitial pneumonia. Arthritis Rheum 2005;53:549-57.
34. Hubbard R, Venn A. The impact of coexisting connective tissue disease on survival in patients with fibrosingalveolitis. Rheumatology (Oxford) 2002;41:676-9.
35. Park JH, Kim DS, Park IN, Jang SJ, Kitaichi M, Nicholson AG, *et al*. Prognosis of fibrotic interstitial pneumonia: Idiopathic versus collagen vascular disease-related subtypes. Am J Respir Crit Care Med 2007;175:705-11.
36. Nannini C, West CP, Erwin PJ, Matteson EL. Effects of cyclophosphamide on pulmonary function in patients with scleroderma and interstitial lung disease: A systematic review and meta-analysis of randomized controlled trials and observational prospective cohort studies. Arthritis Res Ther 2008;10:R124.
37. Bouros D, Wells AU, Nicholson AG, Colby TV, Polychronopoulos V, Pantelidis P, *et al*. Histopathologic subsets of fibrosingalveolitis in patients with systemic sclerosis and their relationship to outcome. Am J Respir Crit Care Med 2002;165:1581-6.

How to cite this article: Kundu S, Mitra S, Ganguly J, Mukherjee S, Ray S, Mitra R. Spectrum of diffuse parenchymal lung diseases with special reference to idiopathic pulmonary fibrosis and connective tissue disease: An eastern India experience. Lung India 2014;31:354-60.

Source of Support: Nil, **Conflict of Interest:** None declared.