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Mixed Bag of Interstitial Lung Diseases at Tertiary Care Centre

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Abstract--- Context: *ILD or DPLD is a heterogeneous group of disorders that is characterized by varying degrees of inflammation and fibrosis in the lung parenchyma. This study is being done to analyze the spectrum of ILD, their common clinical presentations, radiological features, and causes so that it may help in a better understanding of the disease in the Indian context.*

Aims: *To study the underlying causes of ILD in Patient diagnosis based on clinical history & HRCT.*

Settings and Design: *We conducted a retrospective study based on the available departmental data records of 41 ILD patients from October 2017 to October 2019 at our tertiary care center.*

Methods and Material: *Patients with chief complaints of dyspnea and cough with a chest radiograph and HRCT thorax suggestive of ILD were collected for the study and statistical analysis was done.*

Statistical analysis used: *SPSS computer software version 20.0.*

Results: *Forty-one patients were enrolled. The mean age of presentation was 55.75 years. There was male predominance seen. Progressive dyspnea (90.24%) and dry cough (63.4%) were the most common symptoms in ILD patients. On examination Velcro crackles, clubbing & restrictive pattern on spirometry were predominantly found. IPF was the most common (46.43%) ILD followed by Non-IPF IIPs, connective tissue disease-related ILD, chronic HP, sarcoidosis & smoking-related ILD were diagnosed in 19.51%, 17.07%, 7.32%, 7.32% & 2.44% of the subjects, respectively.*

Conclusions: *IPF was the most common found IIP followed by NSIP. CTD & chronic HP found as definitive causes in some which changed the treatment & prognosis.*

Keywords--- *ILD, DPLD, Idiopathic Interstitial Pneumonia, HRCT Thorax, IPF, NSIP, CTD-ILD, HP.*

Key Messages: *UIP is the most common pattern seen in ILD. IPF was the most common variety but if CTD & chronic HP found as cause then it changes treatment & has a good prognosis. Therefore in all patients with progressive dyspnea & dry cough, ILD should be considered for early diagnosis.*

I. INTRODUCTION

Interstitial lung diseases (ILDs) or diffuse parenchymal lung diseases (DPLD) are a heterogeneous group of

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disorders that is characterized by varying degrees of inflammation and fibrosis in the lung parenchyma.[1] They are a group of acute and chronic diffuse lung diseases of known and unknown causes.[2]

Various classification of DPLD is described in the literature.[3] About 200 disorders have been implicated in the causation of DPLD.[4] It includes diseases of unknown etiology, such as those secondary to drugs, idiopathic, collagen vascular disease, granulomatous conditions like sarcoidosis, hypersensitivity pneumonitis (HP), occupational exposures, exposure to cigarette smoke, inherited disorders and other forms of ILDs like Lymphangioleiomyomatosis or histiocytosis X.[5][2] A major part of these disorders belongs to the class of idiopathic interstitial pneumonias.[6]

Diagnosis of ILD is made based on history, clinical findings, high-resolution computerized tomogram (HRCT), pulmonary function tests (PFT) and other relevant investigations.[7] It assesses the presence of disease in the lung, type of disease, changes of active lung disease, biopsy site localization, change in disease activity following treatment, characterization of interstitial lung disease (ILD) in an appropriate clinical setting.[8] The understanding of the distinct appearance of the diffuse parenchymal lung diseases in high resolution computed tomography (HRCT) (sensitivity greater than 90%[9]) has greatly reduced the need for biopsy of the condition.[10] Previously a histological diagnosis was the gold standard for ILD diagnosis which now replaced by a multidisciplinary approach.[11] Recent statements and evidence-based guidelines emphasize the need for multidisciplinary discussion (MDD) among expert pulmonologists, radiologists, and pathologists familiar with ILD to facilitate accurate diagnosis of specific idiopathic interstitial pneumonias (IIP), including Idiopathic Pulmonary Fibrosis (IPF).[2]

Treatment of ILD is still a subject of discussion in view of unpredictable responses and a high incidence of adverse effects.[6] Management of ILD includes counselling, pharmacotherapy includes corticosteroids & immunosuppressive therapy. However, with newer studies in IPF, therapy is Pirfenidone & Nintedanib.[12]

It poses diagnostic and therapeutic challenges to the clinician. Clinicians and patients confronted with ILD are understandably frustrated as there is no cause or cure for most of ILDs. The challenge in diagnosing ILDs in India is confounded by environmental and cultural factors in the midst of infections, especially tuberculosis, bronchitis or heart failure.[13][14]. There is a lack of data on ILD in India, where these diseases are under-estimated and remain under-diagnosed and under-reported for various reasons.[5]

This study is being aimed to analyze the spectrum of ILD, their common clinical presentations, radiological features, and causes so that it may help in a better understanding of the disease in the Indian context. This motivated us to study the clinical profile of interstitial lung disease patients at our institute.

II. SUBJECTS AND METHODS

This study was a retrospective, observational study. The study was conducted in the Department of Respiratory Medicine at our tertiary care center during the period from October 2017 to October 2019. Institutional ethical committee clearance was obtained before data collection. Data was collected from the departmental patient database.

Data of Forty-one patients who had chief complaints of dyspnea and cough with a chest radiograph and HRCT thorax suggestive of interstitial lung disease were collected for the study.

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The case records were retrieved from the departmental database & data was extracted to obtain information. The relevant demographic data like age, sex, occupation, presenting complaints, smoking status, environmental exposures, history of anti-tuberculous treatment, connective tissue diseases, family history, and physical examination findings were collected. HRCT thorax reports were obtained. Spirometry data was collected. The Antinuclear antibody (ANA) profile, Rheumatoid factor (RF), Anti–cyclic citrullinated peptide (Anti-CCP), Antinuclear cytoplasmic antibody (ANCA) and serum Angiotensin-converting enzyme were collected if available as it is not mandatory to perform this particular test in all the patients.

Data were collected, tabulated, coded then analyzed using SPSS computer software version 20.0.

III. RESULTS

Forty-one patients were enrolled in the study. The age distribution of patients ranged from 23 years to 72 years. The majority of patients (48.78%) were having more than 60 years of age. Only one patient presented at the age of 23 years. The mean age of the study population was 55.75 years. There was male predominance seen (58.53%).

Progressive shortness of breath (90.24%) and dry cough (63.4%) were predominant symptoms. Other symptoms seen were chest pain (29.26%), appetite loss (41.46%), weight loss (29.26%), joint pain (19.51%) & fever (17.07%). End inspiratory "Velcro crackles" were the most common examination finding in 35 (85.36%) followed by clubbing in 15 (36.58%). Restrictive pattern (60.97%) was predominant on spirometry while others have mixed patterns. The baseline characteristics of the study subjects are shown in Table 1.

Table 1: Demographic findings, symptomatology & HRCT findings in 41 ILD patients

Mean age	*55.75 years*
Gender	
Male	58.53%
Female	42.47%
Symptoms	
Shortness of breath	90.24%
Dry cough	63.4%
Chest pain	29.26%
Appetite loss	41.46%
Weight loss	29.26%
Joint pain	19.51%
Fever	17.07%
Examination	
Clubbing	36.58%
Crackles	85.36%
Spirometry (restrictive pattern)	60.97%
Radiological abnormalities on HRCT thorax	
Septal thickening with honeycombing	63.41%
ground glass opacity	24.39%
mediastinal lymphadenopathy	7.32%
Bilateral Multifocal patchy consolidation	2.44%
Cystic lesion s/o Smoking-Related ILD	2.44%

The most common abnormality on HRCT chest was septal thickening, subpleural, bibasilar involvement with honeycombing in 26 (63.41%) followed by ground-glass opacity with subpleural sparing in 10 (24.39%),

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mediastinal lymphadenopathy with septal thickening in 3 (7.32%), Multifocal patchy consolidation in B/L lung field in 1 (2.44%) & Cystic lesion s/o Smoking-Related ILD in 1 (2.44%).

IPF was the most common (46.43%) ILD followed by Non-IPF IIPs, connective tissue disease-related ILD, chronic HP, sarcoidosis & smoking-related ILD were diagnosed in 19.51%, 17.07%, 7.32%, 7.32% & 2.44% of the subjects, respectively. (Table 2) Idiopathic nonspecific interstitial pneumonia was the most common non-IPF IIP encountered followed by cryptogenic organizing pneumonia. The connective tissue disease-associated ILD comprised of seven patients of whom four had rheumatoid arthritis, one had systemic sclerosis, one had mixed connective tissue disease & one had dermatomyositis. Among them, four had UIP pattern & three had NSIP on HRCT thorax.

Table 2: Clinical Spectrum of ILD in 41 Patients

Type of ILD	***No. of patients (%)***
IPF	19 (46.34%)
Idiopathic NSIP	7 (17.07%)
Chronic HP	3 (7.31%)
CTD-ILD	7 (17.07%)
COP	1 (2.43%)
Sarcoidosis	3 (7.31%)
Smoking-related ILD	1 (2.43%)

IV. DISCUSSION

As India being a country with great diversity where dresses, diets & emotions vary drastically all around, many chronic diseases with identical presentations have important regional differences.[11] But still, there is limited data from India on the presentation and diagnosis of DPLD patients. The main issues that are important in diagnosis are differentiation from other illnesses having similar presentations and establishing the etiology of pulmonary fibrosis.[15] Now a need of the gold standard histological diagnosis was changed to a multidisciplinary approach which includes clinical, radiological & histological diagnosis.[11]

The mean age of presentation was 55.75 years in our study which was similar to data from the result of a prospective registry of ILD in India 2017 (55.3 years). There was male predominance (58.53%), similar to Das et al.[6] (54%) but contradictory to this Indian ILD registry[2] & Udwadia et al.[15] had shown female predominance. The commonest presenting symptoms were breathlessness and dry cough in the present study and the same has been observed in other Indian studies.[2][10][6] The most characteristic examination findings in ILDs are clubbing & fine end-inspiratory Velcro crackles. Studies have shown that clubbing may be seen in 25%-50% patients and 'velcro' crackles may be present in more than 80% patients.[16][17] Similarly in our study Velcro crepitations and clubbing were seen in 85.36% & 36.58% respectively. These findings were similar to Jindal et al.[4], Das et al.[6] & Mahashur et. al.[14]. The restrictive pattern was most common on spirometry.

Idiopathic pulmonary fibrosis (IPF), a diagnosis of exclusion[18] is a progressive and fatal disease that lacks an effective treatment. The median survival time for IPF patients is just three years.[19] A study in the United States stated that the incidence and prevalence of IPF, corrected for positive predictive value, were 14.6 per 100,000 person-years and 58.7 per 100,000 persons, respectively. These estimates indicate that, in the BRIC (Brazil, Russia,

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India, and China) region which is a large, populated area, there may be approximately two million people living with IPF. So particularly in an era when effective and safe drugs for IPF are finally available, it is a good challenge to diagnose IPF.[20] In our study, IPF was the most common ILD found in 46.34% of total patients, which was similar in previous studies like Udwadia et al.[15], Subhas et al.[3] and Kundu et al.[21] respectively 43%, 45% & 38.04%. In contrast to this, Indian ILD registry 2017 which is the largest and first prospective study to describe the pattern of ILD among patients with new-onset ILD from multiple centers had showed IPF in only 13.7%[2], while most common ILD found in this registry was Hypersensitivity Pneumonitis(47.3%)[22] attributing to air-cooler exposure in Northern India in 48.1%[2] because more centers being from north India. Although prior registries have suggested an incidence and prevalence of 3–13% for HP[23][21] which is similar to our study (7.31%).

CTDs are cause for endless of pulmonary complications, including bronchiolitis, bronchiectasis, pleuritis, pulmonary hypertension, and ILD, all called CTD-ILD.[24] Different disease subtypes have varied prevalence of ILD; like in up to 90% of patients with systemic sclerosis (SSc) ILD is noted, whereas it is less prevalent in rheumatoid arthritis (4–68%), mixed connective tissue disease (20–85%), and the inflammatory myopathies polymyositis and dermatomyositis (15–70%), still this reported numbers can vary.[25] Connective tissue disease-related ILD was found in 17.07% of the patients in our study which correlate with Udwadia et al.[15] & Indian ILD registry[2]. European countries' registry also suggested the incidence of CTD-ILD is 2-9%.[23] Interstitial lung disease (ILD) is the primary pulmonary involvement in RA with prevalence ranging from 4% to 68% mostly in the age group of 50 to 60 years.[26] RA-ILD was most common in our study & among them, 3 had UIP & 1 had NSIP pattern on HRCT which supports the finding from Badarkhe-Patil, et al.[9] UIP was more common than NSIP, and both were more common than OP in RA.[27] Rheumatoid arthritis was the most common specific CTD (38.4%) followed by scleroderma (22.5%)[2]

In our study sarcoidosis was seen in 7.31% similar to the ILD India registry[2] & Kundu et al.[21] respectively 7.8% & 5.4%. Non-IPF IIPs were found in 19.51%, among them, 17.07% had idiopathic NSIP. Similarly in the Indian ILD registry[2] 8.5% had idiopathic NSIP. In similarity to the ILD registry[2], our study 2.43% had cryptogenic organizing pneumonia.

Patients with CTD-ILD can be treated with steroid and immunosuppressive drugs.[28] HP patients also had a good response to steroids. While IPF can be managed with antifibrotic like pirfenidone & Nintedanib.[29]

Patients with connective tissue disease and interstitial lung disease have a better long-term prognosis than patients with IPF.[30] IPF is a fatal disease that requires early diagnosis & for that raising awareness and educating health-care professionals and the general population is needed.[31] Other groups like CTD associated ILD, sarcoidosis, hypersensitivity pneumonitis had an excellent response to the therapy. So increased awareness would serve to provide early diagnosis and this may impact on the high mortality rate of this disease.

Our study is limited by the analysis of patients from a single tertiary care center, which may not be generalizable to community centers or other academic institutions. Our study was also limited by sample size for some comparisons. Furthermore, it may be possible that some of the observed associations are false-positive findings, as we did not correct for multiple comparisons. The retrospective nature of our study resulted in missing or inadequate

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data, including post-exercise saturation & DLCO. Some high-cost investigations like bronchoscopic lung cryobiopsy, VATS guided biopsy are not possible at our center. Despite these limitations, this is one of the few studies to assess the pattern of ILD on HRCT & clinical history at a tertiary care center.

V. CONCLUSION

In patients with progressive breathlessness & dry cough, ILD should be ruled out as these are being the most common complaints of ILD patients & HRCT thorax is a choice of non-invasive investigation in clinically suspected cases. Our study suggests that ILDs are not uncommon in India but lack of diagnostic facilities explains the reason for few studies. We concluded that the UIP pattern was the most common ILD pattern followed by the NSIP pattern. CTD & chronic HP found as definitive causes in some which changed the line of treatment & prognosis. This suggests that HRCT with clinical data & other relevant laboratory investigations helps in diagnosing ILDs.

REFERENCES

[1] Dhooria S, Agarwal R, Sehgal IS, Prasad KT, Garg M, Bal A, et al. (2018) Spectrum of interstitial lung diseases at a tertiary center in a developing country: A study of 803 subjects. *PLoS ONE* 13(2): e0191938

[2] Singh S, Collins BF, Sharma BB, Joshi JM, Talwar D, Katiyar S, Singh N, Ho L, Samaria JK, Bhattacharya P, Gupta R. Interstitial lung disease in India. Results of a prospective registry. *American journal of respiratory and critical care medicine.* 2017 Mar 15; 195(6):801-13.

[3] Subhash HS, Ashwin I, Solomon SK, David T, Cherian AM, Thomas K. A comparative study on idiopathic pulmonary fibrosis and secondary diffuse parenchymal lung disease. *Indian J Med Sci.* 2004; 58(95): 186–8.

[4] Maheshwari U, Gupta D, Aggarwal AN, Jindal SK. Spectrum and diagnosis of idiopathic pulmonary fibrosis. *Indian Journal of Chest Diseases and Allied Sciences*. 2004 Jan 1; 46(1):23-6.

[5] Sen T, Udwadia ZF. Retrospective study of interstitial lung disease in a tertiary care centre in India. The *Indian journal of chest diseases & allied sciences.* 2010 Oct; 52(4): 207.

[6] Das V, Desai U, Joshi JM. Clinical profile of interstitial lung disease at a tertiary care centre, India. *Pneumon.* 2017 Jan 1; 30(1):17-23.

[7] Muhammed Shafeeq K, Anithakumari K, Fathahudeen A, Jayaprakash B, Ronaid Win B, Sreekala RS, Sanjeev Nair MM. Aetiology and clinic-radiological profile of interstitial lung disease in a tertiary care centre. *Cough.* 2011; 63: 90-0.

[8] Agrawal MK, Kumar A, Agrawal R, Rana R. To study the significance of HRCT over Chest x-ray in the diagnosis of interstitial lung diseases. *Journal of Evolution of Medical and Dental Sciences.* 2019 Jan 14; 8(2): 94-9.

[9] Badarkhe-Patil P, Kawade D, Titare P, Rote-Kaginalkar V. HRCT Assessment of Interstitial Lung Diseases. *Int J Contemp Med Res.* 2016; 3(8): 2426–30.

[10] Devi HJG, Halappa S, Davis D, Jain A. Interstitial Lung Disease : A Tertiary Care Center Experience. *IOSR J Dent Med Sci.* 2016; 15(1): 5–8.

[11] Singh V, Sharma BB. Laying the ground for research of interstitial lung disease in our country: ILD India registry. *Lung India: official organ of Indian Chest Society.* 2014 Oct; 31(4):320.

[12] Je M, Hogg JC, Mcdonough JE, Columbia B, Cooper JD, Gefter WB, et al. Fishman's pulmonary disease & disorders. 5th editio. 1697 p.

[13] Raghu G, Mehta S. Interstitial lung disease (ILD) in India: Insights and lessons from the prospective, landmark ILD-India registry. Lung India: official organ of Indian Chest Society. 2016 Nov; 33(6):589.

[14] Agarwal, Vikas, et al. "Clinical profile of headache from a tertiary care center in eastern India." *International journal of general medicine and pharmacy (IJGMP)* 2.3 (2013): 9-14.

[15] Mahashur AA, Dave KM, Kinare SG, Kamat SR, Shetye VM, Kolhatkar VP. Diffuse fibrosing alveolitis-an Indian experience. *Lung India.* 1983 Aug 1; 1(5):171.

[16] Sen T, Udwadia ZF. Retrospective study of interstitial lung disease in a tertiary care centre in India. *The Indian journal of chest diseases & allied sciences.* 2010 Oct; 52(4):207.

DOI: 10.37200/IJPR/V24I5/PR2020676
Received: 16 Apr 2020 | Revised: 22 Apr 2020 | Accepted: 12 May 2020

[17] Nagai S, Kitaichi M, Itoh H, Nishimura K, Izumi T, Colby TV. Idiopathic nonspecific interstitial pneumonia/fibrosis: comparison with idiopathic pulmonary fibrosis and BOOP. *European Respiratory Journal.* 1998 Nov 1; 12(5):1010-9.

[18] Chandrika, K.B. "Need and intervention of social workers in public health care services and social development." *International Journal of Humanities and Social Sciences* 4.1 (2015): 57-62.

[19] Johnston ID, Prescott RJ, Chalmers JC, Rudd RM. British Thoracic Society study of cryptogenic fibrosing alveolitis: current presentation and initial management. Fibrosing Alveolitis Subcommittee of the Research Committee of the British Thoracic Society. Thorax. 1997 Jan 1; 52(1):38-44.

[20] Raghu G, Remy-Jardin M, Myers JL, Richeldi L, Ryerson CJ, Lederer DJ, Behr J, Cottin V, Danoff SK, Morell F, Flaherty KR. Diagnosis of idiopathic pulmonary fibrosis. An official ATS/ERS/JRS/ALAT clinical practice guideline. *American journal of respiratory and critical care medicine.* 2018 Sep 1; 198(5): e44-68.

[21] Huang H, Dai HP, Kang J, Chen BY, Sun TY, Xu ZJ. Double-blind randomized trial of pirfenidone in Chinese idiopathic pulmonary fibrosis patients. *Medicine.* 2015 Oct; 94(42).

[22] Afolabi, Adeola Folashade, Adeniyi Olanipekun Fasanu, and Adewale Samson Adeyemi. "Comparison of ELISA and rapid screening tests for the diagnosis of HIV in high risk individuals." *infection* 1 (2014): 3.

[23] Richeldi L, Rubin AS, Avdeev S, Udwadia ZF, Xu ZJ. Idiopathic pulmonary fibrosis in BRIC countries: the cases of Brazil, Russia, India, and China. *BMC medicine.* 2015 Dec; 13(1):237.

[24] 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: official organ of Indian Chest Society.* 2014 Oct; 31(4): 354.

[25] Jasim, Wisam Abdullah, and Hussein Imran Mousa. "Neurosurgical Congenital Anomalies in Basrah Sociodemographic Review." *International Journal of Medicine and Pharmaceutical Science (IJMPS)* 8. 2, Apr 2018, 33-38

[26] Singh S, Collins BF, Sharma BB, Joshi JM, Talwar D, Katiyar S, Singh N, Ho L, Samaria JK, Bhattacharya P, Chaudhari S. Hypersensitivity pneumonitis: Clinical manifestations–Prospective data from the interstitial lung disease-India registry. Lung India: official organ of Indian Chest Society. 2019 Nov; 36(6):476.

[27] Thomeer MJ, Costabel U, Rizzato G, Poletti V, Demedts M. Comparison of registries of interstitial lung diseases in three European countries. European Respiratory Journal. 2001 Jul 1; 18(32 suppl):114s-8s.

[28] Owonikoko, Kola M., et al. "Assessment of Blood Transfusion Practices at Caesarean Section in a Teaching Hospital in South-western Nigeria." *International Journal of Medicine and Pharmaceutical Sciences* 4.6 (2014): 69-76.

[29] Levi Y, Israeli-Shani L, Kuchuk M, Shochet GE, Koslow M, Shitrit D. Rheumatological assessment is important for interstitial lung disease diagnosis. The Journal of rheumatology. 2018 Nov 1; 45(11):1509-14.

[30] Chan C, Ryerson CJ, Dunne JV, Wilcox PG. Demographic and clinical predictors of progression and mortality in connective tissue disease-associated interstitial lung disease: a retrospective cohort study. BMC pulmonary medicine. 2019 Dec 1; 19(1):192.

[31] Das, P.C., et al. "Dementia care in India: Issues & prospects." *Int J Med Pharm Sci* 4 (2014): 29-36.

[32] Agrawal A, Thyagarajan B, Ceniza S, Hasan Yusuf S. Interstitial Lung Disease of the UIP Variant as the Only Presenting Symptom of Rheumatoid Arthritis. *Case reports in pulmonology.* 2015.

[33] Zamora-Legoff JA, Krause ML, Crowson CS, Ryu JH, Matteson EL. Patterns of interstitial lung disease and mortality in rheumatoid arthritis. *Rheumatology. 2*017 Mar 1; 56(3):344-50.

[34] Singh P, Thakur B, Mohapatra AK, Padhan P. Clinical features and outcome of acute exacerbation in connective tissue disease- associated interstitial lung disease: A single- center study from India. *International journal of rheumatic diseases.* 2019 Sep; 22(9): 1741-5.

[35] Raghu G, Rochwerg B, Zhang Y, Garcia CA, Azuma A, Behr J, Brozek JL, Collard HR, Cunningham W, Homma S, Johkoh T. An official ATS/ERS/JRS/ALAT clinical practice guideline: treatment of idiopathic pulmonary fibrosis. An update of the 2011 clinical practice guideline. *American journal of respiratory and critical care medicine.* 2015 Jul 15; 192(2): e3-19.

[36] Cottin V. Interstitial lung disease. *Eur Respir Rev.* 2013; 229(127): 26-32

[37] María Molina-Molina, Myriam Aburto, Orlando Acosta, Julio Ancochea, José Antonio Rodríguez-Portal, Jaume Sauleda, Carlos Lines & Antoni Xaubet (2018) Importance of early diagnosis and treatment in idiopathic pulmonary fibrosis, *Expert Review of Respiratory Medicine*, 12:7, 537-539.

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