EDITORIAL

# A national guideline and ILD PAK Registry Report: Recent landmarks in the understanding of interstitial lung diseases in Pakistan

Mosavir Ansarie

## Introduction to ILD

The Interstitial lung diseases (ILDs) are a heterogeneous group of pulmonary disorders, classified together because of similar clinical, radiological and pathological features.[1] These are often described as diffuse parenchymal lung diseases (DPLD) because the disease process is not limited to the interstitium and may involve alveolar spaces, acini and the bronchioles.[2] Some of the ILDs could be related to particular exposure histories as in the case of Hypersensitivity Pneumonitis (HP) or associated with systemic diseases like Connective tissue disorders (CTD) while a large number of them may not have a proven etiology like Sarcoidosis. The more common and important idiopathic interstitial pneumonias (IIPs) are the Idiopathic Pulmonary Fibrosis (IPF) and Non-specific Interstitial Pneumonitis (NSIP). IPF is the commonest and most dreadful of these with a relentless progression and a prognosis worst than most cancers.

The usual presenting symptoms include difficulty in breathing, especially on exertion and persistent dry cough along with specific auscultatory findings,[3] but these may vary. In addition, systemic extra thoracic clinical features help to guide towards the diagnosis of ILD. Diagnostic investigations include imaging studies such as chest x-ray and High Resolution Computed Tomography (HRCT) of the chest.[4] Each type of ILD manifests a different pattern on the HRCT.[5,6] Pulmonary Function Tests (PFTs) typically show a restrictive pattern of ventilatory defect.[7] However, in cases where diagnosis is ambiguous, a biopsy of the lung tissue is warranted.[8,9] Ideally, the diagnosis of ILD should be based on a multidisciplinary approach involving a pulmonologist, radiologist and histopathologist.[10-12]

Current therapy includes new anti-fibrotic agents aimed at slowing the progression of the disease.[13,14] Many clinical trials are underway and a surge of academic activity raises the hope of having better treatment options in the future for patients with fibrosing ILD.

Consultant Pulmonologist, HealthCare Hospital, Karachi, Pakistan.
**Correspondence:** Email: mosaviransarie@hotmail.com

## ILD National Guideline 2016

A resource group consisting of prominent pulmonologists from different parts of the country with a known interest in ILDs, recently deliberated over relevant literature and local experience on the subject. The objective was to prepare a guideline document on the diagnosis and management of ILD in Pakistan as a concise edition of updated knowledge. These deliberations were documented after consensus of the committee members and non-committee peer review and endorsed by the Pakistan Chest Society which is a singular professional body of pulmonologists in Pakistan. As a result of this process the first edition of a national Guideline Document on Diagnosis and Management of ILDs in Pakistan was published in April 2016.[15]

The ILD Guideline is a forty eight page illustrated handbook pertaining to definitions, pathophysiology, epidemiology, classification, clinical manifestations and diagnostic workup of ILDs as a whole to give the reader a broad picture of the disease spectrum. It includes a section to understand the HRCT scan which is indispensible to identifying, managing and monitoring ILD. It then deals with IPF specifically and in its entirety, encompassing the diagnostic algorithms in current use as well as updated management strategies. The Guideline noted evidence of online national registries in this subcontinent which would soon enable us to use local data in refining our knowledge on the profile of disease in our part of the world.[16,17] It reiterated the importance of multi-city entry into a national ILD Registry and strongly encouraged pulmonologists across the country to cooperate with regional centers in this regard.

## Development of ILDPAK Registry

Given that a registry is a comprehensive document that records data and keeps track of a specific sub

population of patients with a specific condition within stipulated time boundaries, it facilitates in a variety of ways. It can collect epidemiologic and clinical information regarding individuals with diseases, treatments and outcomes. Importantly, it can help register people for prospective participation in future clinical trials and analyses.

Historically, a population based registry differentiating between various types of ILDs established in New Mexico in 1994 was a landmark study in this respect.[18] Later in 2001, a comparison of registries established in Belgium, Germany and Italy highlighted the similarities and dissimilarities between their data.[19]

Considering that this data emanated from European countries alone with possible geographical differences, a local registry was set up in 2008 in Karachi, Pakistan by the name of ILD PAK Registry.[20] Since 2011, however, after the consensus document from ERS/ATS/JRS/ALAT, a greater recognition of the need of registries has led to the establishment of new registries at a national level in various countries like Spain, Greece, Germany, India and Australia, in that order.[21-25] At this point of time, ILD PAK was converted into a web based electronic national registry which over the course of time provided data entry access to various pulmonology centers across the country.

The defined objectives of ILD PAK registry are to record the epidemiology of ILD in Pakistan in terms of incidence, prevalence, survival and mortality. It would also determine the relative frequencies of various ILDs with demographic features such as age, gender, ethnicity, location, occupation, exposure and smoking status, along with the clinical features, associated risk factors and co-morbidities in this population. An important aspect of the registry is to mandatorily record exposure histories and relate identifiable causes of ILDs in local environment.[26]

The registry could provide a data bank of clinical profiles of Pakistani ILD patients who may be available for research and clinical trials in future. Provision of access to comprehensive information of patients available to respective investigators for publication individually and jointly with other investigators is possible. This data will enable them to determine differences in disease behavior in different regions of the country and harmonize the management on a national scale enabling a periodic review of the national guidelines.

## Registry Methodology

Participating clinicians are requested to obtain approval from his respective institutional Ethics Review Board. The coordinating pulmonologist is designated as one of the Principal Investigators (PI) who ensures recording of patient details into the online database according to the guidelines and the inclusion criteria, after obtaining written informed consent from the patient. A record of supporting documents (such as PFT reports, HRCT scans, Echocardiogram and so on) should be maintained with the PI. The participating centers will be responsible to update the registry on patient's follow up and reported deaths of patients.

## ILDPAK Registry Report

ILD PAK Registry Report is a forty six page document covering six years registry data (2010-2015) published by the Pakistan Chest Society with date line June 2016. It consists of 22 pages of graphic illustration with explanations of the results and provides evidence based understanding of the local profile of interstitial lung disease and its risks in Pakistan.

## Results and Interpretation

The most common frequent type of ILD was Idiopathic Pulmonary Fibrosis (32.90%), followed by Sarcoidosis (18.50%), Collagen Vascular Associated Lung Disease, Non Specific Interstitial Pneumonia, Hypersensitivity Pneumonitis and miscellaneous class of ILDs comprised of rarer entities.

The data highlights the significance of age in characterization of IPF and Sarcoidosis. In Sarcoidosis a large majority of patients (73%) were under 60 years of age. Contrarily in IPF the majority of patients (52%) were above the age of 60 years. There was also a sizeable number of patients between ages 41 and 60 years suggesting that IPF in our population may also be considered in the age group less than 60 years. The overall age distribution in ILD differentials suggests that these are less common in the younger age group and that their prevalence increases with age. All the differentials of ILD greatly burdened the female gender more than the males except in IPF, which occurred almost equally among both genders. A family history of affected first degree relatives was also seen in IPF more than in any other type (7.5%). In describing risk factors that may predict the clinical outcome and have importance in preventive strategies, a significant association of Pulmonary Hypertension PH (41%) and Gastro Esophageal

Reflux Disease GERD (33%) with IPF was noted. The data shows that almost a quarter of IPF patients presented with smoking history of greater than 25 pack years.

Persistent dry cough was found very commonly among all the ILDs. Although exertional dyspnoea was universal among all patients, there was a substantial number who had dyspnoea at rest and others who desaturated significantly on or less than six minutes' walk, majority belonging to the IPF group. Clubbing was found most commonly among IPF followed by HP. Crepitations were heard in almost all the ILDs although Sarcoidosis was one type with relatively less than others. The mean Forced Vital Capacity was maximally reduced in IPF (53.7%±19% predicted) but relatively less in Sarcoidosis (69.5%±22% predicted). The most frequently occurring co-morbidity with ILD was Hypertension followed by Diabetes, though these numbers may merely reflect their prevalence in the general population. Among all the causes of ILD, highest mortality was found among the IPF cases (22.4%) and least among Sarcoidosis (6.7%).The median survival in mortality cases of IPF was 2 years (Range 1-5 years) and in Sarcoidosis was 5 years (Range 3-6 years).

## Conclusion

To our knowledge, this is the first multicentre registry that attempts to provide an epidemiologic update of ILD trends in recent years, in a population segment of patients in Pakistan. The forte of this registry is its mandatory recording of HRCT and PFT investigations and the recording of exposure history and clinical manifestations without which no case was included. The electronic database support and direct data entry access to principal investigators across the country, along with the recently published PCS ILD National Guideline and this six year registry report from a few centers of one large city will gather impetus towards the production and publication of further regional reports periodically. This Report proves that the PCS-ILD PAK Registry nexus can thus function on a national scale as a standardized recording and tracking mechanism in trends of presentation, incidence, prevalence, morbidity, mortality and treatment evaluation in the future.

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