ORIGINAL ARTICLE

PREVALENCE OF ILD SUBTYPES ON THE BASIS OF HRCT AT A TERTIARY CARE HOSPITAL

Humaira Anjum,[1] Hussain Ahmad,[1] Mahnoor Rehman,[2] Hina Gul[1]

Department of Radiology, Khyber Teaching Hospital, Peshawar, KPK, Pakistan.
Department of Radiology, Kuwait Teaching Hospital, Pehsawar, KPK, Pakistan.

PJR October - December 2019; 29(4): 234-238

ABSTRACT

BACKGROUND: Interstitial Lung Diseases (ILDs) are a group of respiratory disorders, usually chronic and progressive in nature, primarily affecting the lung parenchyma leading to reduced gas exchange. The frequency of its subtypes is variable in different regions. **OBJECTIVE:** To determine the prevalence of ILD subtypes in our set up on the basis of HRCT. **MATERIALS AND METHODS:** This was a retrospective observational study conducted at Radiology department of Khyber Teaching Hospital Peshawar from 1st July 2014 till 30th June 2019. All HRCTs done during these five years were included for assessment of different subtypes of ILD. Scans with diagnosis other than ILD were excluded. The subtypes of ILD included were idiopathic pulmonary fibrosis (IPF), non specific interstitial pneumonia (NSIP), hypersensitivity pneumonitis (HP), sarcoidosis, connective tissue disease related ILD (CTD-ILD) and others. Patient s age, gender and ILD subtypes were recorded in a proforma. Data was analyzed via spss 19. Results were presented as graphs. **RESULTS:** Of the 632 scans reviewed, 171(27%) met the inclusion criteria. The mean age of patients was 51.5–18.9 years and 89 (56.9%) of the patients were females. The most common Subtype of ILD was IPF 28.16 %(n=49), followed by NSIP 25.29% (n=44), HP 13.79%(n=24), CTD-ILD 9.77%(n=17), and sarcoidosis 7.47%(n=13). Other ILDs collectively constituted 15% of the subtypes. **CONCLUSION:** IPF was found to be the most common ILD, followed by NSIP, HP, CTD-ILD and sarcoidosis. Multidisciplinary approach and larger multicenter studies are required for better understanding of its etiology and management.

Key words: idiopathic pulmonary fibrosis, idiopathic interstitial pneumonia, hypersensitivity pneumonitis, sarcoidosis, connective tissue disease.

Introduction

Interstitial lung diseases or diffuse lung parenchymal lung diseases (DPLDs) are a heterogeneous group of usually chronic and progressive respiratory disorders characterized by difficulty in breathing as a result of reduced gas exchange primarily due to the disease of interstitial compartment of the lung. These disorders may also involve the airspaces, peripheral airways and vascular endothelial linings besides interstitium.[1] These diseases can affect any individual but more commonly the adult age group.

In a UK study (2004-2012), the estimated prevalence of IPF (the worst form of ILD) was 50 cases /100,000 population and a median survival time from diagnosis of approximately 3 years.[2] The causative agent can be identified in fewer than 20% to 30% of patients with ILD.[3] Known causes include genetic factors, autoimmunity, occupational, environmental, and drug exposures.[4]

Clinical presentation of various forms of ILD like idiopathic pulmonary fibrosis (IPF), sarcoidosis, hyper-

Correspondence : Dr. Hussain Ahmad
Department of Radiology,
Khyber Teaching Hospital,
Peshawar, KPK, Pakistan.
Email: dr.hussainahmad79@yahoo.com

Submitted 28 October 2019, Accepted 10 December 2019

sensitivity pneumonitis (HP) and connective tissue disease related ILD (CTD-ILD) may be very similar to each other, hence complete evaluation is required to confirm the diagnosis because the management may vary considerably according to the specific ILD subtype that is diagnosed.[5]

The diagnostic work up of ILD is quite dynamic which needs a close liaison between respiratory physician, radiologist and an experienced Histopathologist. HRCT of chest is required in almost all cases of suspected ILD to classify the pattern, stage the disease and plan further investigations.[6] HRCT thorax is an important advance in the management of ILD which may be diagnostic in more than 50% of cases suspected of IPF/UIP. When the classical UIP (usual interstitial pneumonia) pattern is identified on HRCT, a confident diagnosis can be made without proceeding for bronchoscopic or surgical lung biopsy.[7] HRCT chest may also provide clues to non-IPF ILDs for example Hypersensitivity pneumonitis, sarcoidosis and histiocytosis.[8] Small cuts of 1-2 mm are imaged to visualize the lung architecture and two distinct patterns of ground glass haze and reticulation.[9]

The diagnosis of ILD is challenging quite often, because clinicians frequently do not have access to the opinion of pathologists who are experienced in examining lung biopsies from patients with ILD. In addition many patients are either not fit or unwilling for the invasive diagnostic procedures. Limited resources and poor socio-economic conditions also hinder the timely diagnosis of the disease particularly in the developing countries. HRCT and clinical judgement are usually being relied upon to make a probable diagnosis. The incidence and prevalence of different forms of ILD is variable among different countries.[10] We conducted this study in our hospital to know about the pattern of different ILD subtypes determined on the basis of HRCT. This data is expected to help us understand the prevalence of various forms of ILD in our set up where very little is known about the disease pattern. This study may provide the basis for planning further research with a close liaison between radiologist and clinicians.

Objective

To determine the prevalence of ILD subtypes on the basis of HRCT.

Materials and Methods

This was a retrospective observational study conducted at Radiology department of Khyber Teaching Hospital Peshawar from 1st July 2014 till 30th June 2019. The study was duly approved by ethical review board. All HRCTs done during these five years were included for assessment of different subtypes of ILD. Scans with diagnosis other than ILD were excluded. The ILD subtypes included were idiopathic pulmonary fibrosis (IPF), non specific interstitial pneumonia (NSIP), hypersensitivity pneumonitis (HP), sarcoidosis, connective tissue disease related ILD (CTD-ILD) and others.

These variables were defined on the basis of HRCT criteria as follows:

1. **IPF/UIP:**
   a. Bilateral, sub pleural and predominantly basal honeycombing which is heterogeneous, patchy and irregular,
   b. Traction bronchiectasis, and
   c. Minimal or no ground glass haze.
2. **NSIP:**
   a. Extensive ground glass opacification that is bilateral, symmetrical, with apico basilar gradient and immediate sub pleural sparing,
   b. Traction bronchiectasis,
   c. Fine reticular opacities, and
   d. Minimal or no honeycombing.
3. **HP:**
   a. Bilateral Ill-defined centrilobular nodules throughout both lungs,
   b. Ground-glass opacification,
   c. Mosaic attenuation,
   d. Air trapping, and
   e. Appropriate clinical setting (pigeon exposure).
4. **Sarcoidosis:**
   a. Mediastinal/hilar lymphadenopathy,
   b. Perilymphatic micro nodular opacities predominantly along the broncho-vascular bundles and along the fissures,
   c. Confluent nodular opacities with air bronchograms, and
   d. Ground glass haze.
5. **CTD- ILD:** ILD pattern (NSIP or UIP) with the diagnosis of connective tissue disorder.
6. **Others:** ILDs other than mentioned above.

Patient s age, gender and ILD subtypes were recorded in a proforma. Data was analyzed via spss 19. Results were presented in graphs. Mean and standard deviation were calculated for age while frequencies and percentages were calculated for ILD subtypes.

Results

Of the 632 scans reviewed, 171(27%) met the inclusion criteria. The mean age of patients was 51.5 – 18.9 years and 89 (56.9%) of the patients were females (Fig. 1). The most common Subtype of ILD was IPF 28.16 % (n=49), followed by NSIP 25.29% (n=44), HP 13.79% (n=24), CTD-ILD 9.77% (n=17), and sarcoidosis 7.47% (n=13) as shown n (Fig. 2).

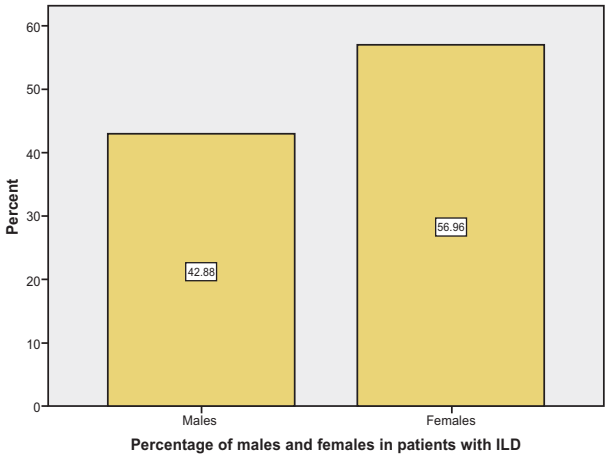
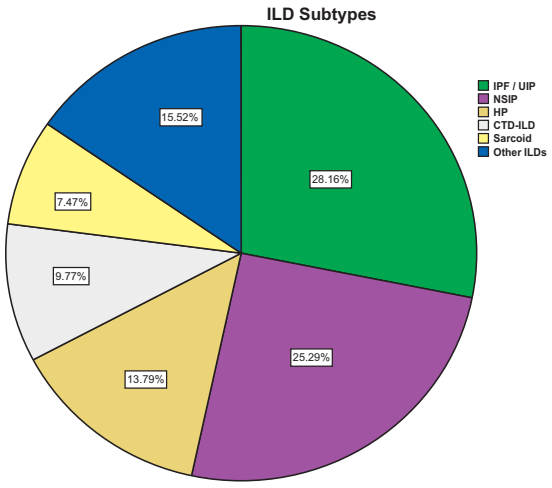


Figure 1: Gender of patients with interstitial lung disease



(ILD: Interstitial lung disease, IPF: Idiopathic pulmonary fibrosis, NSIP: Nonspecific interstitial pneumonia, HP: Hypersensitivity pneumonitis, CTD-ILD: Connective tissue disease related ILD).

Figure 2: Percentages of various common ILD sub types.

Other ILDs including Cryptogenic organizing pneumonia (COP), Desquamative interstitial pneumonia (DIP), Lymphangioleiomyomatosis (LAM), Lymphocytic interstitial pneumonia (LIP), drug induced ILD, Pulmonary alveolar proteinosis (PAP) and Pneumoconiosis collectively constituted 15% of the subtypes

Discussion

We found that ILDs were predominantly more common in females. This finding is consistent with the results published by an Indian ILD registry[11] and ILDPAK registry[12] while contrasting results have been reported from Belgium and New Mexico stating that males are more commonly affected, most probably due to occupational exposures.[13]

Idiopathic pulmonary fibrosis is the worst form of ILD predominantly affecting the advanced age group and the diagnosis is usually made on the basis of clinical evaluation and typical HRCT findings rarely supported by lung biopsy.[14] Based on the data from systemic review of 15 studies, with differences in study population, case definition and diagnostic criteria, IPF accounts for 17 37% of all ILD diagnoses.[15]

IPF was the commonest ILD subtype (28.16%) among our study population which is in accordance with the result of ILD Pak registry (32.9%),[12] studies from Germany (32%) and Italy (37%) with some differences in percentages.[10] According to studies from Saudi Arabia and Greece, the prevalence of IPF was lower (23.3% and 20% respectively).[16,17] Smoking habits, ethnic and genetic differences among populations may be responsible for this variability. Moreover, a multicenter study from India reported HP to be the commonest ILD (47.3%) and the prevalence of IPF was only 13%.[18] This contrasting result from India may be explained by the fact that 48% of patients were exposed to air coolers where mold growth may be the inciting agent besides geographical and environmental differences.

The second most common ILD was NSIP (25.29%) in our set up. A study from Karachi has reported its prevalence as 19.7%.[19] Its exact incidence is unknown, with different reports ranging from 14 to 36 % of all idiopathic interstitial pneumonias (IIPs).[20] The lack of uniform diagnostic criteria and the overlap of HRCT features could explain the discrepancy in prevalence. MacDonald et al has confirmed that the HRCT pattern

of UIP and NSIP (fibrotic variant) have a significant overlap.[21] NSIP has a wide list of etiologies and this type of ILD needs detailed work up to reach a definite diagnosis.

The third most common type of ILD was HP (13.79%). Literature shows different percentages of its prevalence ranging from as low as 4.3%, 5.1% and 13% in European countries 10 to as high as 47.35% in India.[18] Local customs, exposure to birds, seasonal, environmental and geographical variations and smoking habits could contribute to this wide spread variation in prevalence of HP among different countries.[22]

Finally, CTD related ILD and sarcoidosis contributed for 17% and 7.47% of all ILDs respectively in our study. The prevalence of CTD related ILDs is variable among studies ranging from 7.5-19%.[23] The overall incidence of ILD in connective tissue diseases is about 15%, being more prevalent in females and has a better prognosis than idiopathic interstitial pneumonias.[24] The prevalence of ILD secondary to sarcoidosis as reported by various studies generally range from 12-35%.[23] An epidemiological study from Turkey including 2245 patients from 31 centres, reported sarcoidosis as the commonest ILD subtype (37%).[25] Our study showed a much lower prevalence of sarcoidosis most probably because it is close mimicker of a more common diseases like tuberculosis in our set up and it may be taken as TB. Moreover, genetic, racial and geographic differences may also contribute to the disease variations besides the stage of disease at diagnosis and the availability of diagnostic tools.

To summarize, comparing different study results, it is clear that these five diagnoses constitute 85% of ILD subtypes, with significant similarities and discrepancies in prevalence. Due to the non-uniform study designs, inclusion criteria, and availability of diagnostic facilities it is not clear whether these differences are real or partly due to selection bias.

Limitations: The most important limitation of our study was that the diagnosis was based on HRCT features and the available clinical record with no confirmation by histopathology. Moreover, this was a single centre study so the results may not be generalizable.

Recommendations:

Multidisciplinary approach involving pulmonologist, radiologist, thoracic surgeon and histopathologist could be the best way of exploring the etiology of ILDs and diagnostic work up.

Conclusion

IPF was found to be the most common ILD, followed by NSIP, HP, CTD-ILD, and sarcoidosis. Multidisciplinary approach and larger multicenter studies are required for better understanding of its etiology and management.

Conflict of Interest: Author mentioned no financial or institutional conflict of interest.

References

1. Cushley MJ, Davison AG, duBois RM, Egan J, Flower CD, Gibson GJ, et al. The diagnosis, assessment and treatment of diffuse parenchymal lung disease in adults. Thorax 1999; **54:** S1S30.

2. Snell N, Strachan D, Hubbard R, Gibson J, Maher T, Jarrod I. Epidemiology of idiopathic pulmonary fibrosis in the UK: findings from the British lung foundation s respiratory health of the nation project. BMJ 2016; **71:** 209-33.

3. King TE, Pardo A, Selman M. Idiopathic pulmonary fibrosis. Lancet (London, Engl). 2011; **378(9807):** 1949-61.

4. Hubbard R, Venn A, Smith C, Cooper M, Johnston I, Britton J. Exposure to commonly prescribed drugs and the etiology of cryptogenic fibrosing alveolitis: a case-control study. Am J Respir Crit Care Med. 1998; **157:** 743-47.

5. Meyer KC, Raghu G. Patient evaluation. In: Baughman RP, Du Bois RM, editors. Interstitial Lung Disease: A Practical Approach. Second. New York: Springer; 2011: 3-16.

6. Kanne JP. Interstitial lung disease (ILD): imaging finding, and the role of imaging in evaluating the patient with known or suspected ILD. Semin Roentgenol. 2010; **45:** 3.

7. Hunninghake GW, Zimmerman MB, Schwartz DA, King TE, Lynch J, Hegele R, et al. Utility of a lung biopsy for the diagnosis of idiopathic pulmonary fibrosis. Am J Respir Crit Care Med. Jul 2001; **164(2):** 193-6

8. Honda O, Johkoh T, Ichikado K, Yoshida S, Mihara N, Higashi M, et al. Comparison of high resolution CT findings of sarcoidosis, lymphoma, and lymphangitic carcinoma: is there any difference of involved interstitium? J Comput Assist Tomogr. May-Jun 1999; **23(3):** 374-9.

9. Bonelli FS, Hartman TE, Swensen SJ, Sherrick A .Accuracy of high-resolution CT in diagnosing lung diseases. Am J Roentgenol. Jun 1998; **170(6):** 1507-12.

10. Thomeer MJ, Costabe U, Rizzato G, Poletti V, Demedts M. Comparison of registries of interstitial lung diseases in three European countries. Eur Resp J. 2001; **32:** 114s-8s.

11. Singh V, Sharma BB. Laying the ground for research of interstitial lung disease in our country: ILD India registry. Lung India 2014; **31:** 320-2)

12. Ansari M, Naseem A, Ahmed R, Azeemuddin M. Profile of interstitial lung diseases in Pakistan, Karachi pulmonology clinics registry data 2008 - 11. Eur Respir J. 2012; **40(56).**

13. Coultas DB, Zumwalt RE, Black WC, Sobonya RE. The epidemiology of interstitial lung diseases. Am J Respir Crit Care Med.1994; **150:** 967-72.

14. Behr J, Kreuter M, Hoeper MH. Management of patients with idiopathic pulmonary fibrosis in clinical practice: INSIGHTS-IPF registry. The Eur Respir J. 2015; **46(1):** 186-96.

15. Nalysnyk L, Cid-Ruzafa J, Rotella P, Esser D. Incidence and prevalence of idiopathic pulmonary fibrosis: review of the literature. European Respiratory Review 2012; **21:** 355-61.

16. Esam H. Alhamad. Interstitial lung diseases in Saudi Arabia: A single-center study. Ann Thorac Med. Jan-Mar 2013; **8(1):** 33-7.

17. Karakatsani A, Papakosta D, Rapti A, Antoniou KM, Dimadi M, Markopoulou A, et al. Epidemiology of interstitial lung diseases in Greece. Respir Med. 2009; **103(8):** 1122-9.

18. Singh S, Collins BF, Sharma BB, Joshi JM, Talwar D, Katiyar S, et al. Interstitial Lung Disease in India. Results of a Prospective Registry. Am J Respir Crit Care Med. 2017; **195(6):** 801-13.

19. Sarwar Zubairi AB, Hassan M, Shahzad T, Sarwar S, Abbas A, Ahmad H, et al. Spectrum of interstitial lung disease from a tertiary care hospital in Karachi. J Pak Med Assoc. 2017 Jul; **67(7):** 1065-69.

20. Kim DS, Collard HR, King TE. Classification and natural history of idiopathic interstitial pneumonias. Proc Am Thorac Soc. 2006; **3(4):** 285-92.

21. MacDonald SL, Rubens MB, Hansell DM. NSIP and UIP: Comparative appearances at and diagnostic accuracy of thin-section CT. Radiology 2001; **221:** 600-5.

22. Jindal SK and Gupta D. Incidence and recognition of interstitial pulmonary fibrosis in developing countries. Curr Opin Pulm Med. 1997; **3(5):** 378-83.

23. Kreuter M, Herth FJ, Wacker M, Leidl R, Hellmann A, Pfeifer M, et al. Exploring Clinical and Epidemiological Characteristics of Interstitial Lung Diseases: Rationale, Aims, and Design of a Nationwide Prospective Registry--The EXCITING-ILD Registry. BioMed research international 2015; **12:** 38-76.

24. Antoniou KM, Margaritopoulos G, Economidou F, Siafakas NM. Pivotal clinical dilemmas in collagen vascular diseases associated with interstitial lung involvement. Eur Respir J. Apr 2009; **33(4):** 882-96.

25. Musellim B, Okumus G, Uzaslan E, Akgun M, Cetinkaya E, Turan O, et al. Epidemiology and distribution of interstitial lung diseases in Turkey. Clin Respir J. 2014; **8(1):** 55-62.