Clinical Profile and Survival Rate of Interstitial Lung Disease in a Tertiary Care Center of Eastern Nepal

Ghimire RH, Ghimire A, Bimali A, Bista B

Department of Pulmonary, Critical Care and Sleep Medicine

Nobel Medical College Teaching Hospital,

Biratnagar, Nepal.

Corresponding Author

Ram Hari Ghimire

Department of Pulmonary, Critical Care and Sleep Medicine

Nobel Medical College Teaching Hospital,

Biratnagar, Nepal.

E-mail: ramarogya13@gmail.com

Citation

Ghimire RH, Ghimire A, Bimali A, Bista B. Clinical Profile and Survival Rate of Interstitial Lung Disease in a Tertiary Care Center of Eastern, Nepal. *Kathmandu Univ Med J.* 2019;67(3):212-6.

ABSTRACT

Background

The clinical profiles of interstitial lung diseases are reported mainly from developed world. There have been no data from Nepal.

Objective

The objective of this study is to describe clinical profile and survival in Eastern Nepal.

Method

Prospectively collected clinical, radiological and laboratory data of consecutive patients with Interstitial lung disease from an eastern regional tertiary care center were analyzed. The recommended official criteria for diagnosing different types of interstitial lung diseases were followed accordingly.

Result

The study revealed that, 68.0% of the patient's age was of above 60 years with male predominance (66.0%). Idiopathic pulmonary fibrosis (79.5%) was the commonest interstitial lung disease followed by connective tissue disease associated interstitial lung disease. Persistent cough (97.7%) and dyspnea (95.5%) were the commonest presentations. Renal impairment, ischemic Heart Disease and anasarca were significant co morbidities contributing to mortality. Survival rate of the patients was found to be maximum at 5 months (95%) and minimum at 24 months (42%) from the diagnosis of the disease.

Conclusion

Widespread use of High-resolution computed tomography has made early recognition of interstitial lung disease in elderly patients. Well planned large scale multicenter prospective studies are needed to broaden our understanding about this serious pulmonary disorder.

KEY WORDS

Clinical profile, Interstitial lung disease, Survival

INTRODUCTION

Interstitial lung disease (ILD) is a heterogeneous group of acute and chronic inflammatory and fibrotic lung disorders of known and unknown etiologies with variable clinical outcomes.[1] Although uncommon among pulmonary diseases; ILD is a very serious disease and has poor outcome in most of the patients. The clinical profile, incidence and prevalence are reported by many different studies in the world.[2-5] Clinical profile and prognosis may vary depending upon the epidemiological and socio-demographic parameters, diagnostic and treatment facilities.[6] We have to face challenges in diagnosing ILD because of financial, technological, limited human resource and geographical factors. Widespread availability of CT scan of the chest for ILD has made diagnosis easier on the background of clinical judgment and other parameters.[7] Lung biopsy is really impossible in resource limited areas. Therefore most of the time, patients are managed empirically depending upon clinical evidences in countries like ours. The objective of this study is to find the clinical profile and survival of patients with ILD.

METHODS

This was a prospective observational study carried out between 30th January 2017 to 1st February 2019 (Duration 2 years) in the Pulmonary, Critical care and Sleep Medicine department of Nobel Medical College Teaching Hospital, Biratnagar. There were 10894 patients with pulmonary disorders in this department in the last two years, where only 44 (0.40%) were diagnosed as ILD, were included. Census method was used to enroll all 44 consecutive cases purposively. Those patients were included who had only findings of ILD in radiological examination, those with any lesion or finding other than ILD in imaging were not enrolled in the study. Ethical approval was taken from Institutional Review Committee of Nobel Medical College Teaching Hospital, Biratnagar. Verbal and written consent was obtained before collecting the data from each patient. Detail clinical history, physical examination and relevant laboratory and radiological parameters of each patient were reviewed and filled in a preformed structured proforma. As per clinical suspicion the chest X ray, high resolution computed tomography (HRCT) of the thorax, spirometry, serology for autoimmune diseases, serum angiotensin converting enzyme (ACE) levels and serum calcium were investigated. All available data were recorded before start the study.

For the diagnosis of IPF, the ATS/ERS/Japanese Respiratory Society/Latin American Thoracic Association guidelines were followed.[8] for the diagnosis of other IIPs; the ATS/ERS Multidisciplinary Consensus Classification of the IIPs was followed.[9,10] Diagnosis of sarcoidosis was made on the basis of consistent clinical and radiological findings. Diagnosis of hypersensitivity pneumonitis (HP) was made based on a history of exposure to organic dusts, typical HRCT appearance including any combination of ground glass opacities, centrilobular nodules, septal thickening and mosaic attenuation and honeycombing. Diagnosis of a connective tissue (CTD) associated ILD was made in the presence of a CTD like rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), systemic sclerosis (SS) and the presence of ILD on HRCT of the chest. The diagnosis of CTD was made based on standard criteria. A diagnosis of interstitial pneumonia with autoimmune features (IPAF) was made using the ATS/ERS research statement. Although drug induced pulmonary fibrosis is a very rare entity and diagnosis of exclusion, we excluded all patients who were on drugs causing pulmonary fibrosis. The final diagnosis was made on the basis of clinical details, laboratory investigations and HRCT findings. Those patients who were getting immune suppressives were labeled as on Specific Treatment and those on symptomatic management were regarded as on Conservative Treatment in this study.

Collected data were entered in Micro Soft Excel 2007 and converted it into Statistical Package for Social Science (SPSS) 11.5 version for statistical analysis. For descriptive statistics percentage, mean, standard deviation, median and inter quartile range were calculated along with graphical and tabular presentation.

RESULTS

During the period between 30th January 2017 to 1st February 2019 (total duration 2 years) there were 10894 patients with pulmonary disorders in our Chest Clinic, of them 44 (0.40%) were ILD patients. The average age of ILD patients was 62±14.9 years. Sixty-eight percent patients were above 60 years and 56.8% of the patients were smokers while 66% patients had history of indoor air pollution. Because of various reasons like patients poor general condition, poor effort, financial problem, poorly interpretable spirometry even when performed, only 20 patients spirometric tests were interpretable. Half of them had restriction abnormality and 68.2% patients had diffuse involvement of lung parenchyma in HRCT. Seventy percent patients had grade I-II dyspnea in mMRC scale and 68.2% patients were on conservative management and rest were on specific treatment. Those who were treated outside especially in India were on specific treatment. Cough (97.7%) was the commonest presenting symptom followed by dyspnea (95.5%). Seventy percent patients had clubbing followed by basal velcro crepitations (52.3%). Commonest ILD was idiopathic pulmonary fibrosis (IPF) (79.5%) followed by connective tissue associated ILDs (13%). Gastro-esophageal reflux disease (GERD) (45.4%) was commonest co-morbidity followed by diabetes mellitus (15.9%) and hypertension (15.9%). The survival rate of the patients from the diagnosis of the disease at 5, 12 and 24 months were 0.95±0.03, 0.84±0.1 and 0.42±0.21 respectively as shown in Table no.7.

Table 1. Baseline characteristics of the study subjects (n = 44).

Characteristics	Value (n%)
Age (yrs.)	62.1±14.9
Male	29 (65.9)
Body mass index (kg/m^2)	22.9±4.2
Smokers	25 (56.8)
Indoor air pollution	29 (65.9)
Duration of diagnosis (months)	5.7±4.0
Spirometric abnormality (n=20)	
Normal	6 (30)
Obstruction	4 (20)
Restriction	10 (50)
HRCT Chest abnormality distribution	
Diffuse involvement	30 (68.2)
Lower lobe predominant	10 (22.8)
Upper/middle lobe predominant	4 (9.1)
Oxygen saturation at rest %	94±5
MMRC Scale	
Grade I	19 (43.2)
Grade II	12(27.3)
Grade III	7(15.9)
Grade IV	6(13.6)
Management	
Conservative	30 (68.2)
Steroid	5(11.4)
Pirfenidone plus steroids	4(9.1)
Other immunosuppressives	5(11.4)

Table 2. Distribution of ILD patients in different age group (n=44).

Characteristics	Categories	N(%)
Age Group (yrs.)	< 40	4(9.1)
	40-59	10(22.7)
	60-69	13(29.5)
	> 70	17(38.6)

Table 3. Symptoms of ILD patients during presentation (n=44).

Characteristics	N(%)
Fever	15(34.1)
Cough	43(97.7)
Dyspnea	42(95.5)
Sputum	6(13.6)
Chest Pain	13(29.5)
Orthopnea	4(9.09)
Hemoptysis	2(4.5)

Table 4. Signs of ILD patients during presentation (n=44).

Types	N(%)
Clubbing	31(70.45)
Cyanosis	3(6.8)
Anasarca	2(4.54)
Limb Swellings	10(22.7)
Velcro Crepitations	23(52.3)
Cachexia	10(22.7)

Table 5. Spectrum of ILD

Types	N(%)
Idiopathic pulmonary fibrosis	36(79.5)
Rhematoid Arthritis	3(6.8)
Systemic sclerosis	2(4.5)
Systemic lupus erythematosus	1(2.3)
Cryptogenic organizing pneumonia	1(2.3)
Lymphangioleiomyomatosis	1(2.3)

Table 6. Co-morbidities of ILD patients (n=44)

Characteristics	N(%)
Gastro-esophageal reflux disease	20 (45.4)
Diabetes Mellitus	7 (15.9)
Hypertension	7 (15.9)
Cor Pulmonale	6(13.63)
Renal Impairment	5 (11.4)
Ischemic heart disease	4 (9.1)
Obstructive Sleep Apnoea	2 (4.5)
Pulmonary Tuberculosis	2 (4.6)
Hypothyroidism	1 (2.3)

Table 7. Survival rate in months

Duration in Month	Survival rate ± S.D.
5	0.95±0.03
12	0.84±0.1
24	0.42±0.21

DISCUSSION

Although ILD is a rare pulmonary disease, its incidence is increasing and mostly occurs in elderly. We found that the average age was 62±14.2 years of our ILD patients. The peak age of incidence was above 70 years (38.6%). Other similar Indian study shows peak age below 70 years.[13] The mean age reported by Lim et al. was 60 years Gayatri et al. reported 66 years.[12,13] Our finding more or less corroborates with these studies. High index of suspicion is needed in elderly for ILD because persistent cough and dyspnea may be confused with asthma and COPD in elderly. Our finding suggests that elderly with persistent cough

should undergo HRCT chest if ILD is suspected. IPF was the commonest (79.5%) ILD in our studies followed by CTD associated ILD. In India some earlier studies reported IPF as the commonest (43%) ILD and recent studies reported sarcoidosis (42.2%) as the commonest ILD followed by IPF (21.2%), CTD associated (12.7%).[14,15] Different earlier studies especially in Indian ones, IPF were the commonest ILD like ours but recently the spectrum has changed to sarcoidosis, hypersensitivity pneumonitis (HP). Number of IPF patients in present study is high probably because of exposure to indoor air pollution and smoking in our country. We are surprised that in our study there were no patients of Sarcoidosis and HP ILD. It may be because of less number of cases we studied, diseases are uncommon and less suspicion, less expertise and experience on the part of pulmonologists and radiologists. Our diagnosis of sarcoidosis was based on the clinico-radiological grounds. HP was not found which may be because of lack of risk factors like air cooling systems and harboring pigeons. Most of the patients were diagnosed within six months of symptoms probably because of severe cough that did not respond to ordinary medication and availability of HRCT chest in most of the urban setting. Most of our patients were males and smokers. But other studies showed female preponderance.[15,16] It may be because males have high mobility and have early and easy access to health care facilities that caused more diagnosis. But this is the matter of further exploration. During presentation most of the patients have cough and dyspnea. In many patients dry cough was so troublesome that it occurred during any time and position especially in supine and night. It persisted even with best treatment and cough was very severe and intractable in patients with renal impairment. During renal impairment especially when infection is present, clinical or subclinical, there is volume overload leading to lung congestion and intractable cough mainly in supine position. Dyspnea in few patients was refractory with best possible management. These findings are similar with other recent study.[13] Our experience is very frustrating and discouraging in treating cough and dyspnea in ILD patients when they were admitted for exacerbation of symptoms. Two patients had hemoptysis and very cachectic later on they were found to have sputum positive pulmonary tuberculosis. This opens our eye in that even with ILD patient's hemoptysis may point towards tuberculosis. Most of our patients had digital clubbing and probably it makes us to suspect IPF in proper clinical setting. We are surprised many ILD patients had comorbidities. Dyspepsia, Renal impairment, DM, IHD, OSA and Cor pulmonale were important comorbidities affecting patient's quality of life in many different ways. Two patients with OSA had very severe intractable cough. Most of our patients were on conservative management either diagnosed in our hospital or outside. Few were on steroids and immunosuppressive. The reason behind that may be IPF has no effective specific management, difficult access to drugs, fear of adverse effects, financial problems, level of understanding about disease and drugs. Unfortunately 5 patients died during study period, three males and 2 females. Almost three males had IHD and renal impairment died despite adequate recommended treatment. Two females who died had renal impairment with moderate anasarca. The survival rate was found to be maximum at 5 months and minimum at 24 months in patients diagnosed with ILD. These findings need large prospective studies with many patients to verify. Almost all patients with immunosuppressive had gastrointestinal adverse events hampering quality of life.

This was a small, single centre prospective observational study. Bronchial, transbronchial lung biopsy (TBLB) and Open lung biopsy could not be performed.

CONCLUSION

Widespread use of HRCT in diagnosing lung diseases has helped us to pick up more ILD cases. Diagnosis of ILD is a multidisciplinary approach including physician, radiologist, thoracic surgeon and pathologist. If possible we have to involve all in teamwork. This provides us with much information regarding clinical profile of ILD patients. To more elaborate above findings of this study, large well planned longitudinal studies are needed.

REFERENCES

1. Troy L, Corte T. Interstitial lung disease in 2015: where are we now? *Australian family physician.* 2015 Aug; 44(8):546.
2. Tinelli C, De AS, Richeldi L, Oggionni T. The Italian register for diffuse infiltrative lung disorders (RIPID): a four-year report. *Sarcoidosis, vasculitis, and diffuse lung diseases: official journal of WASOG.* 2005 Dec;22:S4-8.
3. Xaubet A, Ancochea J, Morell F, Rodriguez-Arias JM, Villena V, Blanquer R, et al. Report on the incidence of interstitial lung diseases in Spain. *Sarcoidosis Vasc Diffuse Lung Dis*. 2004; 21(1):64-70.
4. Coultas DB, Zumwalt RE, Black WC, Sobonya RE. The epidemiology of interstitial lung diseases. *Am J Respir Crit Care Med.* 1994; 150(4): 967-72.
5. Thomeer M, Demedts M, Vandeurzen K. Registration of interstitial lung diseases by 20 centres of respiratory medicine in Flanders. *Acta Clin Belg.* 2001; 56(3):163-72.
6. 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. *Bio Med research international.* 2015;2015.
7. Gotway MB, Freemer MM, King, Jr TE. Challenges in pulmonary fibrosis: Use of high resolution CT scanning of the lung for the evaluation of patients with idiopathic interstitial pneumonias. *Thorax.* 2007 Jun; 62(6): 546-53.

8. Raghu G, Collard HR, Egan JJ, Martinez FJ, Behr J, Brown KK, et al. 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(6):788-824.

9. 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(2): 277-304.

10. Travis WD, Costabel U, Hansell DM, King TE Jr., Lynch DA, Nicholson AG, et al. An official American Thoracic Society/European Respiratory Society statement: Update of the international multidisciplinary classification of the idiopathic interstitial pneumonias. *Am J Respir Crit Care Med.* 2013; 188(6):733-48.

11. Fischer A, Antoniou KM, Brown KK, Cadranel J, Corte TJ, du Bois RM, et al. An official European Respiratory Society/American Thoracic Society research statement: interstitial pneumonia with autoimmune features. *Eur Respir J.* 2015; 46(4):976-87.

12. Lim GI, Lee KH, Jeong SW, Uh ST, Jin SY, Lee DH, et al. Clinical features of interstitial lung diseases. *The Korean journal of internal medicine*. 1996 Jun; 11(2):113.

13. Devi HJG, Halappa S, Davis D, Jain A. Interstitial Lung Disease: A Tertiary Care Center Experience. J Dent Med Sci. 2016; 15(1):05-08.

14. 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.

15. Dhooria S, Agarwal R, Sehgal IS, Prasad KT, Garg M, Bal A, et al. Spectrum of interstitial lung diseases at a tertiary center in a developing country: A study of 803 subjects. *PloS one.* 2018 Feb 8;13(2):e0191938.

16. Jindal SK. Fibrosing alveolitis- a report of 61 cases seen over past 5 years. *Ind J Chest Dis Allied Sci.* 1979;21:174.