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ORIGINAL ARTICLE

PREVALENCE AND CHARACTERISTICS OF INTERSTITIAL LUNG DISEASES IN AYDER COMPREHENSIVE SPECIALIZED HOSPITAL, MEKELLE, ETHIOPIA

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ABSTRACT

Introduction: *Interstitial lung diseases represent a large number of conditions that involve the parenchyma of the lung, the perivascular and lymphatic tissues. The causes are not known for most patients. Knowledge of local prevalence and characteristics of the case will help to design preventive measures for those who are at high risk. Thus, this study aimed to determine the prevalence and characteristics of interstitial lung disease among patients visiting specialized hospital.*

Methods: *A facility based retrospective cross-sectional study design was employed and 595 patients' charts were reviewed. Patients with interstitial lung disease were employed using consecutive sampling method presented during the study period. Further analysis was done for those individuals presented with the diagnoses of interstitial lung disease. Data were collected using data extraction format by the trained hospital nurse working in the chest clinic. SPSS software version 20 was used analysis*

Results: *The prevalence of interstitial lung disease was 8.4%. The top three causes of morbidity in chest clinic among 595 patients were Asthma, Post Tuberculosis Bronchiectasis and Interstitial Lung Disease respectively. The mean age of patients was 55 years and female patients accounted for 52%.*

Conclusion: *Interstitial Lung Disease is the third common diagnosis in chest clinic. Idiopathic Interstitial Pneumonias are the leading types out of which Nonspecific Interstitial Pneumonitis is the most common. This is an alarm to give due attention to the prevention, diagnose and manage of Interstitial Lung Disease*

Key words: *Interstitial Lung Disease, Ethiopia, lung diseases, Idiopathic Interstitial Pneumonia*

INTRODUCTION

Interstitial Lung Diseases (ILDs) are a large number of conditions that involve the parenchyma of the lung, the alveoli, the alveolar epithelium, the capillary endothelium, and the spaces between those structures—as well as the perivascular and lymphatic tissues (1). The term Interstitial Lung Disease, in general, implies inflammatory-fibrotic infiltration of the alveolar walls (septa) resulting in profound effects on the capillary endothelium and the alveolar epithelial lining cells (2). It is also defined as the presence of cellular proliferation, cellular infiltration, and/or fibrosis of the lung parenchyma not due to infection or neoplasia (3).

The disorders in this heterogeneous group are classified together because of similar clinical, roentgenographic, physiologic, or pathologic manifestations (1). In many of the ILDs, interstitial fibrosis follows injury to the gas-exchanging units. This injury increases alveolar permeability, enabling the serum contents to enter the alveolar spaces. Fibroblastic proliferation and excessive collagen deposition, the histologic hallmarks of ILD, occur either as a direct result of the injury, as a result of an inflammatory cell response that releases pro-inflammatory and pro-fibrotic cytokines, or as a consequence of the regenerative and reparative processes taking place at the epithelial and endothelial surfaces (2).

The term ''Interstitial Lung Disease'' is synonymous with ''Diffuse Parenchymal Lung Disease'' (4). It is classified into four clinically distinct groups: [A] ILD of known association (e.g., Collagen Vascular Disease, Hypersensitivity Pneumonitis (HP) Secondary to exposures), [B] granulomatous ILD (e.g., Sarcoidosis), [C] other rare ILDs (e.g., Lymphangioleiomyomatosis (LAM), Pulmonary Langerhans Cell Histiocytosis (PLCH)), and [D] idiopathic diseases (Idiopathic Interstitial Pneumonias [IIPs] (5). The most recent revision of the classification of IIPs divides these into three categories: [A] major IIPs (includes Idiopathic Pulmonary Fibrosis [IPF]; Idiopathic Non-Specific Interstitial

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Pneumonia [NSIP]; Respiratory Bronchiolitis-Interstitial Lung Disease [RB-ILD]; Desquamative Interstitial Pneumonia [DIP]; Cryptogenic Organising Pneumonia [COP] and Acute Interstitial Pneumonia [AIP]), [B] rare IIPs (includes Idiopathic Lymphoid Interstitial Pneumonia (LIP) and Idiopathic Pleuro-parenchymal Fibroelastosis), and [C] unclassifiable IIPs (6).

The cause of ILD is not known for most of the cases. Some studies found association with history of bacterial and viral infection, genetic background, geographic location, radiation, occupational exposure to chemicals, smoking, gender, age of a patient and drugs (7-12).

Chest radiography is usually the first method of detecting a diffuse lung process. In up to 10% of cases, the chest radiograph may look normal despite the presence of a diffuse parenchymal lung disease, especially early in the disease course (13). In more established disease, bilateral reticular infiltrates, hazy opacities, and reduced inspiratory lung volumes on chest radiographs should prompt consideration of ILD (14). High Resolution Computerized Tomography (HRCT) of chest is indicated for all except a small proportion of patients for whom a specific diagnosis is strongly suggested by the standard chest radiograph. In some patients, a specific diagnosis can be obtained from the CT appearances alone; a correct first choice diagnosis is made by HRCT in 75–90% of patients with various major ILDs, including sarcoidosis, silicosis, IPF, lymphangitis carcinomatosis, and PLCH (15). A surgical lung biopsy is necessary for a confident clinico-pathologic diagnosis except in cases with a typical clinical–radiological picture of UIP/IPF. Biopsy is not always necessary to make a clinical diagnosis (5).

Much remains unknown or debatable for many of these ILDs, notably issues of prevalence, incidence and mortality rates (15). The information gap is worse in our continent, Africa mainly in the sub-Saharan countries. There is no study done on prevalence of ILD in the current study area. This study aimed to determine the prevalence and characteristics of ILD in Ayder Comprehensive Specialized Hospital (ACSH), chest clinic, which will help to design interventions to prevent the problem and ease of management.

PATIENTS AND METHODS

Facility based retrospective cross-sectional study was conducted among 595 patients' chart at chest clinic of ACSH, Mekelle, Ethiopia. Ayder Referral Hospital is Located in Northern Part of Ethiopia 780 Km far from Addis Ababa.

The hospital renders its service to nearly 10 million population in its catchment areas of the Tigray, Afar and North-eastern parts of the Amhara Regional States. It has a total capacity of about 500 inpatient beds in four major departments and other specialty units. Ayder Referral Hospital is also used as a teaching hospital for the College of Health Sciences, Mekelle University. The institution has undergraduate and postgraduate programs (Residency, fellowship and PhD programs)

The university hospital has specialist and subspecialist Doctors in radiology, internal medicine, surgery, Pediatrics and child health, Gynecology and obstetrics among others. The chest unit started giving service since 2011 with regular follow up of patients. It has now one pulmonologist, one internist, one internal medicine resident and two nurses. The clinic is equipped with bronchoscopy, spirometer, and lung biopsy sets.

Initially, incomplete charts were excluded from review and those charts with complete information were considered for review. All completed charts of patients seen at the outpatient chest clinic of ACSH in two years period from December 1, 2016 to November 30, 2018 were consecutively evaluated and only those subjects with the diagnosis of ILD by chest Computed Tomography were included in the study.

Data were collected by trained nurses using the data extraction format developed after the review of the contents of the patients' chart to avoid missing important variables. Data collectors were nurses who were trained for one day on how to fill the format and how to keep the patient confidentiality. The data collectors were from the chest clinic in ACSH. The collected data didn't contain any patient identifier.

To ensure the quality of data, all ILD patients were diagnosed by chest HRCT scan and Bronchoalveolar lavage (BAL) was done for 3 patients (6%) (Two IPF and one NSIP) and lung biopsy was done for two patients (one NSIP and one Hypersensitivity pneumonitis). Moreover, 5% of the charts were checked for consistency by the principal investigator. HRCT scan reading was conducted by one radiologist, and one pulmonologist and intensive care specialist.

Descriptive analysis was done using SPSS software version 20. Simple descriptive analysis such as mean, median, proportion, percentage, ratios, frequency distribution was used. The results were presented using tables, graphs and texts based on type of data. And the results are narrated and summarized using texts.

These operational definitions are used in this study:
ILD: Inflammatory-fibrotic infiltration of the lung parenchyma evidenced by high-resolution computed tomography (HRCT)

HRCT: A CT technique in which thin-slice chest images are obtained and post-processed in a high-spatial-frequency reconstruction algorithm. This technique obtains images with exquisite lung detail, which are ideal for the assessment of diffuse interstitial lung disease.

Bronchoalveolar Lavage: Is a diagnostic method of the lower respiratory system in which a bronchoscope is passed through the mouth or nose into an appropriate airway in the lungs, with a measured amount of fluid introduced and then collected for examination.
Lung biopsy: Is a procedure for obtaining a small sample of lung tissue for examination. The tissue is usually examined under a microscope, and may be sent to a microbiological laboratory for culture.

Ethical issue was approved by the Institutional Review Board of research and community service, college of health sciences, Mekelle University and permission letter was obtained from the medical director of the hospital. Any patient identifier was not recorded or documented during data collection to ensure confidentiality. Ethical approval was obtained from the Ethical Review Board of Mekelle University College of Health Sciences with the reference number ERC 1579/2019.

RESULTS

There were a total of 595 patients seen at the clinic from December 2016 to November 2019. The commonest diagnoses in the clinic were Asthma followed by post TB Bronchiectasis and ILD. Fifty patients (8.4%) had a diagnosis of ILD by chest Computed Tomography imaging which was commented by radiologists; these were further analyzed. The mean age of patients presented with ILD was 55 years with range of 24 - 80 years old.

Among the patients presented with ILD, eleven types of ILDs were diagnosed. The leading type ILD was NSIP accounting 44% followed by IPF (30%) and %) RA-ILD (6%). LIP and HP each accounted about 4% while LAM, COP, PLCH, Sarcoidosis, Silicosis and Bysinosis each contributed 2% to the burden of ILD. The ILD types NSIP and RA were higher among females compared to male patients accounting for about 59.1% and 66.7% respectively.

In contrast, IPF was higher among male patients compared to females accounting for nearly 3/4th of the cases (Figure 1).

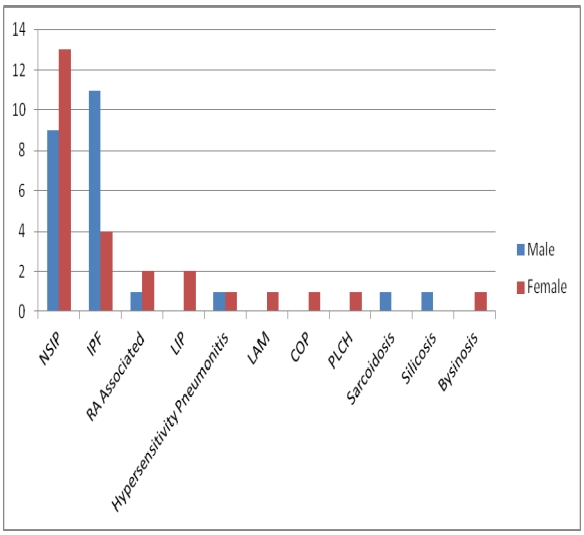

Figure 1: Gender variation in interstitial lung disease subtypes, chest clinic, Ayder Comprehensive Specialized Hospital, Mekelle. December 2016 to November 2019.

NSIP: Non Specific Interstitial Pneumonitis, IPF: Idiopathic Pulmonary Fibrosis, RA: Rheumatoid Arthritis, LAM: Lymphangioleiomyomatosis, COP: Cryptogenic Organizing Pneumonia, PLCH: Pulmonary Langerhans Cell Histiocytosis.

NSIP was found more in patients between 51-60 years old accounting 36.4% followed by those 31-40 years old and patients above 70 years old in equal frequency accounting 18.2% of NSIP. IPF was more common in patients whose age was above 61 years accounting 66.6% of IPF. All three patients with the diagnosis of RA associated ILD were between 41 to50 years. Both LIP patients and a patient with Silicosis were between 31 to 40 years. The age of LAM and Bysinosis patients was in the range of 51-60 years. Patients with Hypersensitivity Pneumonitis and PLCH were between 41-50 years of age. The age of the patient with Silicosis was between 31-40 years while the one with Sarcoidosis was between 20-30 years.

Among the patients presented with ILD, three cases were smokers. Of these, 2 had IPF type and 1 had PLCH type. About 29 patients (58%) reported previous history of tuberculosis. Of these, 41.4% were presented with NSIP and 31% with IPF. History of pneumonia was seen among 43 (86%) ILD patients where most of them were NSIP (41.9%) followed by IPF (34.9%).

Farmers and House wives have equal frequency in having ILD each accounting 22 patients (44%). (Table 2) From those who have NSIP, 10 patients (45.5%) were house wives and 9 patients (40.9%) were farmers while 2 (9.1%) were students and 1 (4.5%) was driver. Among patients who had IPF, 10 patients (66.7%) were farmers and 4 patients were house wives while one patient (6.7%) was working in Mill. Two of the RA associated ILD patients (66.7%) were House wives and one patient (33.3%) was a farmer.

One of the LIP patients (50%) was house wife and the other one was secretary. Patients diagnosed with LAM, COP, Bysinosis, PLCH and one of the Hypersensitivity pneumonitis patients were house wives. The other Hypersensitivity Pneumonitis patient and a patient with Sarcoidosis are farmers. The patient diagnosed with Silicosis works in deep rock excavation.

Table 1: Sociodemographic characteristics among ILD patients: chest clinic, Ayder Comprehensive Specialized Hospital, Mekelle. December 2016 to November 2019

		Total number	Percent
Age (Years)	21-30	4	8.0%
	31-40	7	14.0%
	41-50	10	20.0%
	51-60	12	24.0%
	61-70	7	14.0%
	>=71	10	20.0%
Gender	Male	24	48.0%
	Female	26	52.0%
Retroviral infection Status	Non-reactive	46	92.0%
	Reactive	4	8.0%
History of Tuberculosis Treatment	No	21	42.0%
	Yes	29	58.0%
History of Pneumonia Treatment	No	7	14.0%
	Yes	43	86.0%
Place of residence	Urban	17	34.0%
	Rural	33	66.0%

Table 2: Distribution of occupation among ILD patients: chest clinic, Ayder Comprehensive Specialized Hospital, Mekelle. December 2016 to November 2019

OCCUPATION	Total number	Percent (%)
Farmer	22	44.0%
House wife	22	44.0%
Driver	1	2.0%
Student	2	4.0%
Secretary	1	2.0%
Mill	1	2.0%
Deep Rock Excavation	1	2.0%

DISCUSSION

Totally there were 11 types of ILDs diagnosed in the clinic. The predominant types were IIPs, the most common type being NSIP followed by IPF. The mean age of ILD patients was 55 years. Female patients were predominant. The prevalence of ILD was 8.4%.

The commonest types were IIPs accounting up to 80% (NSIP (44%), IPF (30%), LIP (4%) and COP (2%) followed by CTD related ILD (RA-associated ILD (6%). NSIP is predominant from IIPs which is different from studies done in India, Paris and Italy where IPF was Predominant(6, 16).

The difference could be due to age variation of the study population or difference in genetics and geographical distribution of diseases. Sarcoidosis is a least cause of ILD in this study unlike the European studies where it was the commonest diagnosis (16-21). It may be associated with the difference in race of the study populations (22,23).

In our study RA associated ILD is one of the predominant types next to IIPs which is in line with French, Saudi Arabia, New Mexico and recent Spanish studies (16,24,25). It might be even under diagnosed because some patients may have subclinical ILD that is masked by the co-existent peripheral symptoms, and are not necessarily referred to a pulmonologist. Regard to this, an international guideline on IIPs have raised awareness of the need to search carefully for connective tissue disease signs and perform autoimmune serologies in patients with ILDs (26).

The mean age of our patients found to be 55 years which was between the findings from Greece study (mean age 58.6 years) and Indian study done in tertiary center (mean age 50.6 years) (17,18). This can be explained by the effect of commonest diagnoses in the studies because there is expected age variation in distribution of ILDs. It could also be due to the difference in the nature of the studies because most of them were population-based studies. Two third our ILD patients (64%) are beyond 40 years old. This is similar with the finding on a study done in India (6). Two third of IPF patients were above 60 years old which is in line with findings from Paris done on 2012 (16).

Female predominance was seen in our study which is consistent with studies from India, Turkey and Greece while in contrary to studies from United States of America and Spain (17,18,20,24,25). This difference in predominance of different gender could be due to the difference in predominant diseases, where male predominance was seen in studies with IPF as a predominant ILD. In our study Females are predominant (59.1%) in NSIP patients but male patients predominate in IPF accounting 73.3%. Since we found more NSIP patients than IPF, this could affect the general female predominance.

The prevalence of ILD is found to be 8.4%. It was only preceded by Asthma and post Tuberculosis bronchiectasis. We couldn't compare with other studies because the epidemiological studies done to find the prevalence of ILD were population-based studies and we couldn't get similar studies from African countries.

This study provides baseline information for further researches on respiratory diseases in the nation and other African nations. One of the limitations of the study is the nature of the study being a retrospective chart review. The other limitation is being a tertiary care referral hospital based retrospective cross-sectional study which may not be representative of the general population.

Conclusion

Interstitial Lung Disease is the third diagnoses following asthma and post tuberculosis complications. IIPs are the commonest types of ILDs, from which NSIP is the leading type. This is an alarm to give due attention to the prevention, diagnosis and management of ILD.

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Competing Interest:

The authors declare that this manuscript was approved by all authors in its current form and that no competing interest exists.

REFERENCES

1. Kasper DL, Fauci AS, hauser SL, et al. Harrison's principles of Internal Medicine. 19th ed ed. New York McGraw-Hill Education; 2015.
2. Mason RJ, Broaddus VC, Martin TR, et al. Murray & Nadel's textbook of respiratory medicine. 5th ed ed. Philadelphia: Saunders Elsevier 2010.
3. Rosas IO, Dellaripa PF, Lederer DJ, et al. Interstitial lung disease: NHLBI Workshop on the Primary Prevention of Chronic Lung Diseases. Ann Am Thorac Soc 2014;11:S169-S77.
4. Wells AY, Hirani N, Bradley B, et al. Interstitial lung disease guideline: the British Thoracic Society in collaboration with the Thoracic Society of Australia and New Zealand and the Irish Thoracic Society. Thorax 008;63:1–58.
5. Travis WD, Batman ED, King TE, et al. American Thoracic Society/European Respiratory Society International Multidisciplinary Consensus Classification of the Idiopathic Interstitial Pneumonias. Am J Respir Crit Care Med 2002;165(2):277-304.
6. Singh V, Bhushan SB. A Novel Tool for Epidemiological Surveillance of Interstitial Lung Disease in India. Indian J Chest Dis Allied Sci 2013; 55:197-9.
7. Dauti S, Kim HJ, Choong Won Lee, Won-Il Choi, Sun Hyo Park and Jae Seok Park. Risk factors for interstitial lung disease: a 9-year Nationwide population-based study. BMC Pulmonary Medicine 2018;18:96.
8. Glazer CS, Newman LS. Occupational interstitial lung disease. Clin Chest Med 2004;25:467–78.
9. Baumgartner KB, Samet JM, Coultas DB. Occupational and environmental risk factors for Idiopathic Pulmonary Fibrosis: A Multicenter Case-Control Study. Am J Epidemiol 2000;152(4):307-15.
10. Woldeyohannes M, Bergevin Y, Mgeni AY, Theriault G. Respiratory problems among cotton textile millworkers in Ethiopia. British Journal of Industrial Medicine 1991;48:110-5.
11. Schwaiblmair M, Behr W, Haeckel T, Märkl B, Foerg W, Berghaus T. Drug Induced Interstitial Lung Disease. The Open Respiratory Medicine Journal 2012;6:63-74.
12. MonaemRabea AE, Zidan A, Daabis R, et al. Prevalence of chronic hepatitis C virus (HCV) infection in patients with idiopathic pulmonary fibrosis. Egyptian Journal of Chest Diseases and Tuberculosis 2015;64:907–13.
13. RYU J, Olson EJmidthun DE, Swensen SJ. Diagnostic Approach to the Patient With Diffuse Lung Disease. Mayo Clin Proc 2002;77:1221-7.
14. Lederer DJ, Martinez FJ. Idiopathic Pulmonary Fibrosis. N Engl J Med 2018;378:1811-23.
15. Demedts M, Wells AU, Anto AM, et al. Interstitial lung diseases: an epidemiological overview. EurRespir J 2001;18:2s-16s.
16. Duchemann B, Annesi-Maesano I, de Naurois CJ, et al. Prevalence and incidence of interstitial lung diseases in a multi-ethnic county of Greater Paris. Eur Respir J 2017;50:1-13.
17. Dhooria S, Agarwal R, SehgalI S, et al. Spectrum of interstitial lung diseases at a tertiary center in a developing country: A study of 803 subjects. PLoS ONE 2018;13:2-14.
18. Karakatsani A, Papakosta D, Rapti A, et al. Epidemiology of interstitial lung diseases in Greece. Respiratory Medicine 2009;103:1122–9.
19. Xaubet A, Ancochea J, Morelletal F. Report on the incidence of interstitial lung diseases in Spain. World Association Of Sarcoidosis and Other Granulomatous Disorders 2004; 21: 64–70.
20. Musellim B, Okumus G, Uzaslan E, et al. Epidemiology and distribution of interstitial lung diseases in Turkey. The Clinical Respiratory Journal 2014;8:55–62.
21. Yamin HS, Alastal AY, Bakri I. Epidemiology of interstitial lung disease in Palestine: first national data. Chest Disease Reports 2017;5.
22. Rivera-Ortega P, Maria Molina-Molina. Interstitial Lung Diseases in Developing Countries. Annals of Global Health 2019;85(4):1–14.
23. Antoniou KM, Margaritopoulos GA, Tomassetti S, et al. Interstitial lung disease. Eur Respir Rev. 2014; 23: 40–54.
24. Coultas DB, Zumwalt RE, Black WC, et al. The epidemiology of interstitial lung diseases. Am J Respir Crit Care Med. 1994;150:967-72.
25. opez-Campos JLL, ıguez-Becerra ER. Incidence of interstitial lung diseases in the south of Spain 1998–2000: the RENIA Study. European Journal of Epidemiology 2004;19:155–61.

26. Travis WD, Costabel U, Hansell DM, 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.