Gender Differences in Clinical Presentation of Idiopathic Pulmonary Fibrosis at Lahore, Pakistan

Rasul S.,[1] Khalid M.C.,[2] Imran N.,[3] Khan S.U.,[4] Younus M.[5]
Address for Correspondence: *Institute of Chest Medicine, King Edward Medical University, Lahore*

Objective: To study gender differences in the clinical profile of idiopathic pulmonary fibrosis.

Study Setting: Institute of Chest Medicine, Mayo Hospital – A Tertiary Care Hospital affiliated to King Edward Medical University, Lahore.

Study Design: Prospective observational, evidence based study.

Material and Methods: Thirty two consecutive patients visiting Institute of Chest Medicine, who were diagnosed as idiopathic pulmonary fibrosis on the basis of history, physical signs, restrictive pulmonary functions and HRCT scan chest, were analyzed to study the clinical profile according to the gender.

Results: Amongst thirty two patients, 22 were females and 10 males with a mean age of 42.2 years and 49.6 years respectively. Breathlessness and dry cough were the most common symptoms. Arthralgia was present in 4.6% of females. Two of the males and one of the female were smoker. Results were analyzed according to symptoms, their duration and physical signs. There was no difference in clinical profile but there was an early presentation in 4th decade and preponderance of females. The females dominated the males in age group 31 to 50 years with the ratio of 7.5 : 1.

Conclusion: No gender difference in clinical presentation of idiopathic pulmonary fibrosis but predominance in females. There is an early presentation in both genders, compared to the Western world.

Key Words: Gender differences, Age, cryptogenic Fibrosing Alveolitis, idiopathic pulmonary fibrosis, Restrictive pulmonary functions, High Resolution Computed Tomography (HRCT) chest.

Introduction

The diffuse parenchymal lung diseases are a heterogeneous group of inflammatory processes affecting the alveolar wall and often associated with exudates or transudates in the alveolar air spaces. They represent 15% of all cases seen in respiratory practice. In about 30% patients, no definite etiological agent can be identified. This subgroup had been conventionally designated as idiopathic pulmonary fibrosis (IPF). However it is well recognized that IPF constitutes a subgroup of diffuse parenchymal lung diseases[1] with distinct clinical and histopathological features. Fibrosing alveolitis is a well known clinical syndrome; seven different patterns have been recognized in this clinical syndrome, now termed as "The Interstitial Pneumonias". Usual interstitial pneumonia (UIP) and nonspecific interstitial pneumonia are the most common. Histopathologically UIP is characterized by areas of fibrosis with fibroblastic foci alternating with areas of patchy, predominantly peripheral and basal reticular and honey comb changes with irregular septal thickening and traction bronchiectasis. The term idiopathic pulmonary fibrosis and cryptogenic fibrosing alveolitis are now reserved for cases with the histological and HRCT scan appearance of UIP.[2]

Overall prevelence of interstitial pneumonias in New Mexico is 80.9 per 100,000 in males and 67.2 per 100,000 in females, corresponding with annual incidence rate of 31.5 per 100,000/yr in males and 26.1 per 100,000/yr in females. The interstitial pneumonias are rare in children but increase with advancing age.[3] The mean age at presentation is about 67 years. Familial disease is rare (< 2%). Idiopathic pulmonary fibrosis is more common in males.[4] Onset of symptoms is usually gradual. The dyspnea is the most prominent and disabling symptom.[5] A non-productive cough is usual and may be paroxysmal.[6] Digital clubbing develops in 25 – 50% of patients. Velcro type fine expiratory crackles, initially confined to the basal area are audible on chest auscultation. These progress to involve the entire lung. Features of right heart failure and peripheral edema develop only in late stage. Constitutional symptoms are unusual. Most patients' exhibits restrictive pattern of ventillatory defect with a decrease in DLCO and low resting Pao2 which falls on exercise. Pulmonary function tests and chest radiographs may be normal in the early phase of IPF.[7]

In smokers and ex-smokers with IPF, coexisting COPD may result in relatively higher lung volumes compared with non smoking patients with IPF.[8]

Symptoms had been present for more than six months in most patients. The clinical course is invariably one of gradual detoriation. Median survival from the time of diagnosis varies between 2.5 – 3.5 years.[9] Occasionally periods of rapid decline are recognized.[10] Improvement in lung physiology and radiological abnormalities is rare.[11]

Objectives

To study the gender differences in clinical presentation of idiopathic pulmonary fibrosis.

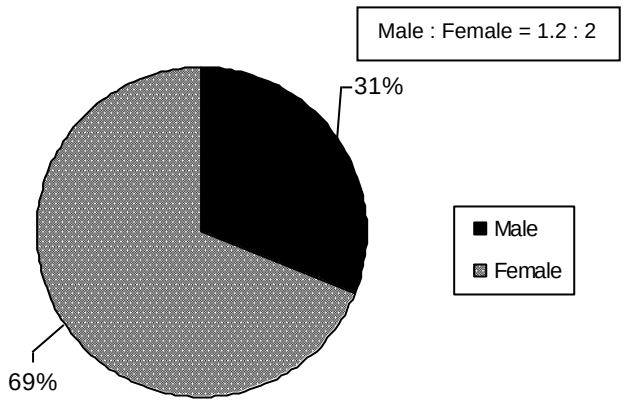
Study Setting
Institute of Chest Medicine, Mayo Hospital – A Tertiary Care Hospital affiliated to King Edward Medical University, Lahore.

Study Design
Prospective analysis of clinical presentation of idiopathic pulmonary fibrosis as regards gender.

Material and Methods
This study includes thirty two consecutive patients visiting Institute of Chest Medicine, KEMU Lahore, diagnosed as cases of idiopathic pulmonary fibrosis.

A detailed history was taken and physical examination performed in all patients at the time of initial presentation. Laboratory workup included complete blood count, urine examination, renal and liver function tests, electrocardiography, chest radiography and spirometry. The diagnosis of IPF was based on HRCT scan chest findings consistent with IPF. Lung biopsy was not performed in the study.

Results
A total thirty two patients who were diagnosed as cases of idiopathic pulmonary fibrosis on the basis of history, clinical examination, spirometry and HRCT chest were studied for their clinical presentation. Amongst thirty two patients, ten were males and twenty two were females (Graph 1). Men were of age between 26 – 79 years with mean age of 49.6 years and women were between 22 – 72 years with mean age of 42.2 years (Table 1).



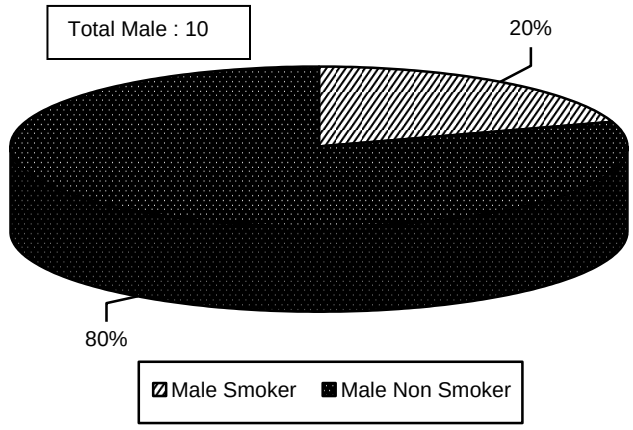
Graph 1: *Gender Distribution.*

Amongst males, two (20%) were smokers (Graph 2) and amongst females one (4.5%) was smoker (Graph 3). Patients were analyzed as regards gender proportion and demographic characteristics (Graph 1 and Table 1), smoking habits (Graph 2 and 3), their symptoms, duration of symptoms (Table 2), and physical signs (Table 3).

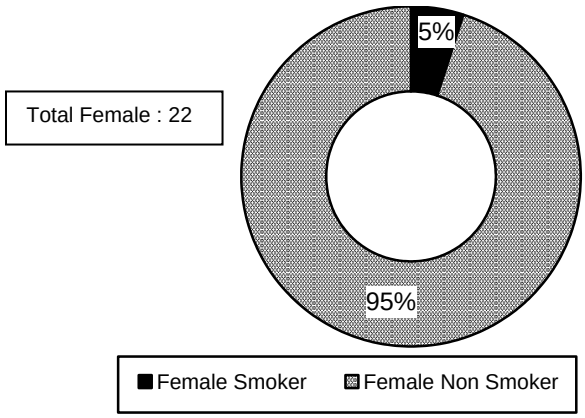
As regards age distribution, between the group of 31 to 40 years, female to male ratio was 7:1 and in the age group 41 – to 50 years this ratio was 8:1 and average ratio of 7.5:1 in the age group of 31 to 50 years.

Table 1: *Demographic Characteristics*

Age Group	Male	Female	Total
21 – 30	2	3	5
31 – 40	1	7	8
41 – 50	1	8	9
51 – 60	3	4	7
61 – 70	2	0	2
71 – and above	1	0	1
Total	10	22	32



Graph 2: *Gender Proportion according to Smoking History (Male).*



Graph 3: *Gender Proportion according to Smoking History (Female).*

Discussion
Idiopathic pulmonary fibrosis is a progressive fibrosing inflammatory disease of the lungs of unknown etiology. It

affects males more than females, which is approximately twice common in males[11]. The mean age in the largest survey reported being 67 years.[12] However it may occur in either sex at any age. In the present study incidence regarding gender is reverse (F > M) and the disease occurred at much earlier age i.e. 4th decade instead of 7th decade as in western world. These variations of findings could be due to geographical, racial distribution and increased median survival in the developed countries. Though in the present study both sexes presented earlier compared to the west, yet it is similar to the study published from India by Maheshwar IU et al.[14] This may be because of similar social constitutions, habits and environment. Further mega studies are needed to confirm this geographical, racial and age distribution differences.

Table 2: *Symptoms Analysis According to Duration and Gender.*

Sr. No.	Symptoms	Duration (Mean)		Gender Proportion	
		Males	Females	Males	Females
1.	Dyspnea	2 years	1.8 years	10 (100%)	22 (100%)
2.	Dry Cough	2 years	1.8 years	10 (100%)	22 (100%)
3.	Arthralgia		1.6 years		1 (4.5%)

Table 3: *Physical Signs and Gender.*

Sr. No.	Physical Signs	Gender Proportion	
		Male	Female
01	Clubbing	10 (100%)	19 (86.4%)
02	Bilateral Basal inspiratory crackles (unzipping Velcro type)	10 (100%)	22 (100%)

As regards the clinical presentation, IPF presents in 90% of patients with progressive dyspnea on exertion and non productive cough in 75% cases.[15]

Finger clubbing is present in about half of the cases[16]. Chest revealed gravity dependent unzipping Velcro type inspiratory crackles in all cases. Arthralgia is present in 19% of cases. Occasionally patients present after routine chest radiography and 5% are asymptomatic. Above mentioned findings were reported by British Thoracic Society study published in 1977. The mean time from the onset of symptoms to presentation is 15 months. Our study results represent average 2 years duration of symptoms in males and 1.8 years in females. Dyspnea was the commonest symptoms which was present in all male and female cases (100%). Arthralgia was present in female cases and there was no obvious sign of connective tissue disease. Clubbing was present in all male cases (100%) but it was present in 86.4% of female cases. Basal crackles were present in all male and female cases. Two of the males and one of the females were smokers but none of them had COPD. Analysis of clinical presentation revealed early presentation in females but as regards the symptomatology of dyspnea, dry cough and physical signs of clubbing and basal crackles, no significant difference was detected in male and female cases(P>.05). Clinical presentation is the same as mentioned in the literature. The introduction of HRCT as an imaging modality has decreased the need for lung biopsy in many patients. Characteristic findings on HRCT scan are often sufficient to diagnose IPF. Trained observer can make a confident diagnosis of IPF in 90% of patients in the presence of radiological findings.[17] For this reason we mainly relied on HRCT chest in addition to other supportive investigations like spirometry, and did not proceed for lung biopsy.

Conclusions

1. There is no gender difference in clinical presentation of idiopathic pulmonary fibrosis compared to the rest of the world.
2. The disease predominates in females in our community.
3. There is an early presentation in both genders, almost a decade earlier compared to the West but it is similar to that observed in India.
4. It is safe to make a diagnosis of IPF on the basis of HRCT especially in third world countries like Pakistan, where there is lack of facilities.
5. The overall prevalence of respiratory symptoms and signs has almost been similar in our study as in the West.

References

1. Coults PB, Hughs MI, Accuracy of mortality rate for interstitial lung disease in New Mexico, USA. Thorax 1996; 51: 717-720.
2. Johnston IDA. Parenchymal lung disease, Med Int Respiratory Disorders, 2004: 114-120.
3. American Thoracic Society / European Respiratory Society International Multidisciplinary consensus classification of the idiopathic interstitial pneumonias. Am J respire crit care Med. 2002; Volume 165: 277-304.
4. Jhonston DA, diffuse parenchymal lung diseases. Med Int, 1999: 160-166.
5. Turner, Warklier M, Barrows B, Johnson A, Cryptogenic Fibrosing Alveolitus; Clinical Features and their influences on the survival, Thorax1980; 35: 171-180.
6. King TEJR, Constable 4, Conrdier JF, Dopico GA, Dubois RM, Lynch D et al. Idiopathic Pulmonary Fibrosis. Diagnosis and Treatment. Am J Respir Crit Care Med 2000; 161: 646-664.

7. Epler GR, Mcloud TC, Gaensler EA, Mikus JP,Akira M et al. Normal Chest roentgenography in chronic diffuse infiltrative lung diseases. N Engl J Med 1978; 298: 934-939.
8. Johkoh J, Muller NL, Taniguchi H, Koudoh Y, Akira M et al. Acute Interstitial pneumonias: Thin section CT findings in 36 patients, Radiology 1999, 16: 209 – 214.
9. Selman M, King TE, Pardo A, Idopathic Pulmonary Fibrosis; Prevailing and evolving hypothesis about the pathogenesis and implications for therapy, Ann Intern Med 2001; 134: 136 – 151.
10. Kondoh Y, Taniguchi H, Kaswabata Y, Yokoi T, Suzuki K et al, Acute exacerbation in idiopathic pulmonary fibrosis. Analysis of clinical and pathological finding in three cases. Chest 1993; 103: 1808 – 1812.
11. Schwartz DA, Van Fossa DS, Davis CS, Helmer RA, Dayton CS, et al. Determinants of progression in idiopathic pulmonary fibrosis. Am J Respir Crit Care Med 1994; 149: 444 – 449.
12. Johnston IDA, Procott RJ, Ehalmes JE, Rudd RM, British Thoracic Society study of Cryptogenic Fibrosing Alveolitus, Current presentation and initial management. Thorax 1997; 52: 38.
13. Johnston IDA, Blend JM, Anderson HR, Ethnic variations in respiratory morbidity and lung functions in childhood. Thorx 1987; 42: 452.
14. Maheshwari U, Gupta D, Aggar wal A.N, Jindal S.K, Spectrum and diagnosis of Idiopathic pulmonary fibrosis. Indian T.Chest dis Allied Sci 2004; 46: 23 – 26.
15. Balamamugesh T, Beherm D, Idiopathic pulmonary fibrosis. JAPI May 2007: Vol. 55.
16. Anthony Seation, pulmonary fibrosis, Crofton and Douglas`s Respiratory Disease 2, 5th Edi., 2004: 877 – 892.
17. Grevier P, valeyre D, Cluzel P.Brauner MW, Lenon S, Chastang C:Chronic diffuse interstitial lung disease: Diagnostic value of chest radiography and high resolution CT. Radiology 1991; 179: 123 – 132.