STUDENTS' CORNER
SHORT REPORT

Challenges in the management of idiopathic pulmonary fibrosis from a low- and middle-income country

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Abstract

Idiopathic pulmonary fibrosis (IPF) is the most common progressive form of interstitial lung disease (ILD) that leads to gradual deterioration of lung function and ultimately death. Data from low- and middle-income countries (LMIC) on IPF is scarce. In this communication, we report the challenges encountered in managing IPF from Pakistan's largest tertiary care centre. A total of 108 patients with IPF were evaluated at the Aga Khan University Hospital in Karachi, Pakistan from January 2017 to March 2020. A significant concern was that most patients with IPF presented late during their disease. A bigger challenge encountered in clinical practice was the cost and non-availability of antifibrotic therapy in the country until mid-2020. Successfully addressing these limitations, it is anticipated that better care will be available for the patients suffering from IPF in this part of the world.

Keywords: Interstitial Lung Disease, Pulmonary Fibrosis; Idiopathic Pulmonary Fibrosis, LMIC.

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Introduction

Idiopathic pulmonary fibrosis (IPF) is the most common progressive form of interstitial lung disease (ILD) that leads to gradual deterioration of lung function and ultimately death.[1] The median survival rate of IPF is 2.5-3.5 years,[2] with a five-year survival rate of only 20%-40%, which is similar to non-small cell lung cancer and lower than several other cancers.[3] Data from low- and middle-income countries (LMIC) on IPF is scarce, making it difficult to accurately assess the morbidity and burden of interstitial lung disease. In this communication, we report the challenges encountered in the management of IPF at Pakistan's largest tertiary care centre.

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Methods and Results

This study was approved by the Ethics Review Committee (ERC) of Aga Khan University Hospital, Karachi. All subjects underwent careful evaluation by a multidisciplinary ILD team. The diagnosis of IPF was made according to the official guidelines of the American Thoracic Society, the European Respiratory Society, the Japanese Respiratory Society, and the Latin American Thoracic Association. (ATS/ERS/JRS/ALAT).[1] A total of 108 patients with IPF were evaluated at the Aga Khan University Hospital in Karachi, Pakistan from January 2017 to March 2020. All included participants provided written informed consent prior to their inclusion into the study. Among them, 9 (8.3%) had other interstitial lung diseases and were excluded. Another 21 (19.4%) patients were not eligible due to insufficient clinical, radiological, or physiological data, and inadequate follow-up. This left a total of 78 patients enrolled for the study analysis. Baseline characteristics of these patients are recorded in Table.

Majority of the patients were males 49(62.8%), and the average age was 69.1±9.7 years, which is similar to other regional and international data.[1,4,5] A total of 51 (65.4%) patients were non-smokers, 25 (32.1%) were ex-smokers, and only 2 (2.6%) were current smokers. These observations were incongruent with most literature, which report that a majority of patients with IPF have a history of cigarette smoking.[1]

Pulmonary function tests (PFTs) were done at intervals throughout the course of the disease. Baseline forced vital capacity (FVC %), categorised by ATS criteria, showed that 33 (42.3%) patients had mild disease, 30 (38.5%) had moderate disease, and 15 (19.2%) had severe disease. A similar ratio was seen in the disease severity of patients who returned for follow-up tests. Of the 78 patients who were diagnosed with IPF, 35 did not undergo repeat pulmonary function test.

At the end of the study, 39 (50%) patients were alive, 14 (17.9%) were lost to follow-up, and 25 (32.1%) had expired at the time of telephonic interview. The two most common causes of death in these patients were respiratory failure in 17(68%) cases and ischaemic heart disease in 5(20% cases.

Complications were seen in 29 (37.2%) patients. The most common complication was respiratory failure in 29(37.2%), followed by pulmonary hypertension in 6(7.7%). Hypertension was encountered in 41(52.6%) cases and Diabetes in 32(41%) being the most frequent comorbid conditions in patients of this study. Additionally, ischaemic heart disease and gastroesophageal reflux disease were each seen in roughly 20% of the patients (n=17 and n=18, respectively). Six (7.7%) patients with IPF had concomitant chronic obstructive pulmonary disease (COPD), an entity known as Combined Pulmonary Fibrosis and Emphysema (CPFE).

Table: Baseline Characteristics of Patient Population.

	n (%)
Mean Age (years)	69.1±9.7
Gender	
Male	49 (62.8)
Female	29 (37.2)
Smoking habits	
Smoker	2 (2.6)
Ex-smoker	25 (32.1)
Non-smoker	51 (65.4)
FVC% at baseline; (n=78)	
Mild	33 (42.3)
Moderate	30 (38.5)
Severe	15 (19.2)
FVC% at follow-up; (n=43)	
Mild	19 (24.4)
Moderate	15 (19.2)
Severe	9 (11.5)
Average treatment time duration (months)	29.3 ± 21.9
Median duration; (IQR)	22.5 (11.7-39.2)
Dosage; median (IQR)	1200 (800-1800)
Dosage of Pirfenidone; (n=77)	
<600 mg	9 (11.7)
600 mg	8 (10.3)
1200 mg	25 (32.1)
1800 mg	18 (23.1)
2400 mg	5 (6.4)
Discontinuation of Pirfenidone therapy	
No	49 (62.8)
Yes	29 (37.2)
Reason for stopping Pirfenidone;	
GI problems	12 (41.4)
Rash	4 (113.8
Weight loss	4 (13.8)
Drug unavailable	1 (3.4)
Started homeopathic medicine	1 (3.4)
Not known	7 (24.1)
Did the patient develop any complications?	
No	49 (62.8)
Yes	29 (37.2)
Complications	
Respiratory Failure	29 (37.2)
Superimposed infection	7 (9.0)
Pulmonary hypertension	6 (7.7)
Cardiomyopathy	1 (1.3)
Patient status	
Alive	39 (50)
Expired	25 (32.1)
Lost to follow-up	14 (17.9)
Cause of death; (n=25)	
Respiratory Failure	17 (68)
Ischaemic Heart Disease	5 (20)
Invasive fungal infection	1 (4.0)
COVID-19	1 (4.0)
Unknown	1 (4.0)

FVC- Forced

Antifibrotic treatment with Pirfenidone was given to all patients diagnosed with IPF, of which 49 (62.8%) patients were continued on their original dose, while 29 (37.2%) patients required a decrease in the dosage or discontinuation of treatment. The recommended dose of 2400mg/day was tolerated by only 5 (6.4%) patients, while most patients received a dose of 1200mg/day. The average treatment duration was 29.3±21.9 months. Utilisation of optimum dosage of Pirfenidone was limited by side effects, such as gastrointestinal symptoms in 12(44.2%), photosensitivity in 4(13.8%), and weight loss in 4(13.8%). A study by Agrawal et al demonstrated that the dose of 1200mg/day was given in their population due to similar side effects.[6] Another study conducted in a Japanese population showed an optimum tolerable dosage of 1800mg/day.[7] Similar physical parametres, such as height and weight, observed between the two populations may be an attributing factor to this dose. In contrast, a study in India showed that out of 115 patients with IPF, 49 (42.6%) tolerated a full dosage of 2400mg/day.[8]

The biggest challenge encountered in our clinical practice was the cost and non-availability of antifibrotic therapy in the country until mid-2020. Although Pirfenidone is now available, it bears a hefty price, limiting its accessibility to the general population. The cost of 60 doses of Pirfenidone (801mg) amounts to Rs. 5,868 (US $20.5). An additional challenge faced was the unavailability of another FDA-approved antifibrotic, Nintedanib, in Pakistan. Furthermore, a significant number of patients assessed for this study were in the last stages of their disease, leaving lung transplant as the only intervention to increase survival and improve the quality of life. Lack of lung transplant facilities serves as a major limitation for Pakistan in the management of IPF.

Studies suggest that pulmonary rehabilitation (PR) is effective as a therapy in managing symptomatic patients with ILD in the early stages of the disease.[9] Lack of logistics for developing a multidisciplinary PR programme is another challenge faced by healthcare providers.

A major limitation of the current study was the number of patients who were lost to follow-up during treatment. About 17% of the patients were lost to follow-up either after their first visit or during treatment. Longitudinal follow-up of patients with IPF helps in identifying complications that may influence the dosage, commencement, or discontinuation of antifibrotic treatment.

Several of the aforementioned challenges exacerbated during the Covid-19 pandemic. Less face-to-face interactions consequently resulted in the inability to comprehensively evaluate patients with IPF, as well as difficulty in continuous monitoring of antifibrotic treatment.

A higher risk of developing severe Covid-19 has been seen in patients with pre-existing ILD, due to impaired lung function, and propensity for development of acute exacerbation of pulmonary fibrosis. Higher mortality was noted in patients with pre-existing fibrotic lung disease, including IPF.[10]

Conclusion

A significant concern in our setting was that most patients with IPF presented late in the course of their disease with symptoms justified as part of an aging process. Recently, an IPF registry has been established in Pakistan. Although the treatment landscape of IPF is improving in Pakistan, there are still many challenges and unmet needs for the successful management of patients. Further emphasis should be placed on the availability of antifibrotic treatment, development of lung transplant facilities, and multidisciplinary PR programmes in Pakistan. Successfully addressing these limitations would dramatically reduce the morbidity and mortality of this illness in LMICs.

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