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Pulmonary Function Testing in the Diagnosis and Monitoring of Interstitial Lung Diseases

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ABSTRACT
Diffuse parenchymal lung disease primarily affects the lung's interstitial tissue. The utilization of pulmonary function tests (PFTs) is common in diagnosing, assessing severity and monitoring treatment response. Among the various PFTs, spirometry and the measurement of diffusing capacity of carbon monoxide (DLco) are routinely employed. The objective of this study was to examine the demographic and radiological characteristics of interstitial lung diseases (ILDs) and to evaluate the severity and progression of these conditions. We conducted a prospective and observational study involving individuals aged over 12 years at a tertiary care center. Patients with clinical suspicion of ILDs were recommended to undergo high-resolution computed tomography (HRCT). Among those diagnosed with ILDs, spirometry was performed at their initial visit and then again at the 6-month follow-up. Treatment was administered according to established guidelines. 115 participants (67 males and 48 females) were enrolled in the study. The mean age was 42.5 years and the mean body mass index (BMI) was 25.1 kg m^{-2}. The participants included 32.17% smokers, 10.43% ex-smokers and 57.39% non-smokers. The most common symptoms encountered were exertional dyspnea and dry cough. Spirometry parameters, including forced expiratory volume at 1 sec (FEV1), forced vital capacity (FVC), FEV1/FVC ratio, DLCO, as well as the gender, age and physiology (GAP) index, had mean values of 48.75, 53.30, 94.20, 43.80 and 3.60, respectively. A significant decline in lung function was observed after 6 months ($p<0.05$). The most frequently observed radiological patterns were septal thickening and traction bronchiectasis. The spirometry data of ILD patients predominantly displayed a restrictive pattern of moderate severity, with a high incidence of idiopathic pulmonary fibrosis (IPF). Most ILDs were observed to be progressive, with a decline in lung function over time, regardless of smoking status.

INTRODUCTION

Diffuse parenchymal lung diseases (DPLDs) encompass a group of conditions that involve the space between the epithelial and endothelial basement membranes within the lungs. These diseases often exhibit similar clinical, physiological and radiographic manifestations. The literature categorizes DPLDs into four main classes: DPLDs with known causes, granulomatous DPLDs, rare DPLDs with well-defined clinical and pathological features and idiopathic interstitial pneumonias (IIPs). IIPs are further subdivided into various types, including usual interstitial pneumonia (UIP), desquamative interstitial pneumonia (DIP), respiratory bronchiolitis interstitial lung disease (RB-ILD), acute interstitial pneumonia (AIP), cryptogenic organizing pneumonia, non-specific interstitial pneumonia (NSIP) and lymphocytic interstitial pneumonia (LIP)[1].

Pulmonary function testing (PFT) plays a crucial role in the management of patients with DPLD[2]. Its clinical applications encompass aiding in diagnosis, assessing disease severity, determining prognosis and monitoring treatment response and disease progression[3].

Spirometry is employed to distinguish between obstructive and restrictive lung diseases. In DPLD, the diffusing capacity of carbon monoxide (DLCO) is typically more diminished compared to the lung volume at which it is measured[4]. Moreover, DLCO tends to be significantly reduced in idiopathic pulmonary fibrosis (IPF) compared to other DPLDs[5,6].

Interstitial lung diseases (ILDs) exhibit variability in pulmonary function. The progression and severity of ILDs are contingent on pathology, radiological findings and lung function. This study aims to explore the relationship between pulmonary function testing, radiological findings and the severity of various ILDs.

MATERIAL AND METHODS

The prospective and observational study was conducted at a tertiary care hospital in India. The study enrolled 128 adult patients aged over 12 years of both genders who visited the outpatient department and expressed their willingness to participate. 13 patients were lost to follow-up and were therefore excluded from the analysis. Additionally, participants who were non-compliant with spirometry and HRCT were also excluded. Patients with ILDs due to infections such as miliary tuberculosis or Pneumocystis jirovecii pneumonia, as well as ILDs associated with malignancies like lymphangitis carcinomatosis or miliary carcinomatosis, were not included in the study.

All patients underwent a comprehensive evaluation to diagnose restrictive lung diseases. Spirometry was performed at baseline (at the time of diagnosis) and again after 6 months.

To define a restrictive pattern in line with the Global Initiative for Chronic Obstructive Lung Disease, the study employed spirometry criteria, including an FVC <80% of the predicted value and a fixed ratio of FEV1 to FVC (in absolute values) $\geq$70%[7-10]. This definition allowed for comparison with various epidemiological studies. Predicted spirometric variables were calculated using reference values for the Asian population[11]. Spirometry was conducted using a hand-held computerised spirometer. All spirometry procedures followed the guidelines of the American Thoracic Society/European Respiratory Society (ATS/ERS)[12-15]. Acceptability standards were established, including an extrapolated volume of <0.5% of FVC or 150 mL, the absence of a 1 sec plateau in the volume-time curve, no coughing during the first second of the maneuver, no early termination of expiration and no glottis closure. Multiple maneuvers were repeated until three acceptable tests were achieved. Tests were considered repeatable if the largest and second largest values for FVC and FEV1 were within 150 ml of each other. If the initial maneuvers were unsatisfactory, additional attempts were made until the reproducibility criteria were met, or a maximum of eight maneuvers was reached. The spirometry tests were conducted by a trained technician.

Patients presenting with clinical signs and symptoms of ILDs and advised for HRCT were evaluated for PFT if their HRCT findings were consistent with ILDs. Patients were then advised to have close follow-up every month with routine medications based on standard guidelines. At the 6-month follow-up, each patient underwent PFT and the collected data were analyzed.

Data were entered into an Excel file and analysis was performed using SPSS 21.0 software. Descriptive statistics were presented as Mean±Standard Deviations (SD) for continuous variables and as frequencies (percentage) for categorical variables. The differences in proportions of categorical variables were assessed using t-tests, chi-square tests and analysis of variance (ANOVA). A significance level of $p<0.05$ was considered for all analyses.

RESULTS

We employed the gender, age and physiology (GAP) model to evaluate the disease's level of seriousness in the context of ILDs in our research[16]. Table 1 provides a depiction of participant demographics, revealing that the average age of the individuals in the study was 42.5 years, with a higher representation of male patients (male to female ratio -1.40:1). The mean Body Mass Index (BMI) was recorded as 25.1 kg m^{-2}. Among the participants, 37 were identified as current smokers, 12 as ex-smokers and 66 as non-smokers. Regarding occupation, the majority of participants were housewives, followed by individuals engaged in farming.

Table 1: Sociodemographic details of study population

Variables		Mean±SD
Age in years		42.5±12.00
Weight in kg		67.2±10.85
Height in cm		165.8±07.20
BMI in kg m^{-2}		25.1±03.95
Gender	No.	Percentage
Male	67	58.26
Female	48	41.74
History of smoking		
Smokers	37	32.17
Ex-smokers	12	10.43
Non-smokers	66	57.39
Occupation		
Home maker	46	40.00
Agriculture	18	15.65
Manual labour	12	10.43
Office work	9	7.83
Mill work	7	6.09
Unemployed	7	6.09
Rickshaw driver	3	2.61
Others	13	11.30

Table 2: Clinical presentation of symptoms in study population

Symptoms	Frequency	Percentage
Dyspnea on exertion	107	93.04
Cough with expectoration	33	28.70
Dry cough	52	45.22
Gastro esophageal Reflux	24	20.87
Fever	28	24.35
Chest pain	10	8.70
Pedal edema	21	18.26
Pneumothorax	2	1.74
Hemoptysis	2	1.74
Skin lesions	5	4.35
Joint Pain	7	6.09

Table 3: Comparison of spirometry parameters in study population

	First visit	6 months f.up	
Parameters	----------Mean±SD ----------		p-value
FEV1 (%)	48.75±12.80	47.20±14.30	<0.05
FVC (%)	53.30±14.10	50.85±15.40	<0.05
FEV1/FVC	94.20±17.75	96.10±18.50	<0.05
DLCO (%)	43.80±10.60	37.50±15.80	<0.05
GAP index	3.60±1.65	3.40±1.70	<0.05

Table 4: Comparison of spirometry parameters according to smoking

	Smokers	Ex-smokers	Non-smokers	
Parameters	----------Mean±SD----------			p-value
First visit				
FEV1 (%)	47.20±12.60	39.8±15.20	55.60±12.40	0.06
FVC (%)	56.30±13.40	49.4±21.30	54.20±12.80	0.74
FEV1/FVC	85.60±19.80	85.8±27.10	102.10±12.50	0.06
DLCO (%)	47.80±11.90	35.2±11.20	40.60±11.00	0.1
GAP index	3.70±1.85	4.3±1.70	3.60±1.40	0.09
6 months f. up				
FEV1 (%)	46.80±13.40	38.9±15.80	54.10±12.90	0.48
FVC (%)	55.50±14.70	46.2±22.80	53.40±12.50	0.052
FEV1/FVC	86.40±23.60	88.2±29.80	101.20±12.60	0.06
DLCO (%)	46.40±15.20	23.9±20.50	36.10±13.20	0.27
GAP index	3.90±1.90	4.5±1.90	3.80±1.50	0.31

Table 2 illustrates the clinical symptoms observed in all study participants. The most prevalent symptom reported by the participants was exertional dyspnea, with a prevalence rate of 93.04%.

As demonstrated in Table 3, we conducted a comparative analysis of spirometry data for participants during their initial visit and at the 6-month follow-up. Notably, the follow-up assessments revealed a significant decline in the values for FVC, FEV1 and DLCO. Concurrently, the FEV1/FVC ratio and GAP value exhibited an increase during the follow-up period and these changes were statistically significant with a $p<0.05$.

We also conducted a similar analysis within the smoker, ex-smoker and non-smoker groups. As presented in Table 4, all variables, including the GAP index, displayed an even distribution among these groups, with no statistically significant differences observed.

DISCUSSIONS

A study conducted by Hieba *et al*.[17] focused on various variables related to patients with interstitial lung diseases (ILDs). In terms of age, the mean age of participants in both studies was quite similar, with no statistically significant difference observed. However, there was a substantial difference in the gender distribution, with the present study comprising a higher percentage of male participants (58%) compared to the previous study (25.8%). Etiology factors such as smoking, CT-ILDs and hypersensitive pneumonitis showed statistically significant differences between the two studies, with higher prevalence rates in the present study. Moreover, occupational diseases were more prevalent in the current study. Spirometry results revealed significant differences in various parameters, including FVC, FEV1 and FEV1/FVC ratio, indicating potential variations in lung function between the two study populations. Nevertheless, no significant difference was observed in DLCO values. These findings highlight key disparities in demographic and clinical characteristics between the two studies, emphasizing the importance of considering these factors in the evaluation of ILD patients.

We compared the radiological appearances and corresponding diagnoses across different studies, including Wani *et al*.[18], the present study, the Indian registry of ILD[19,20]. Septal thickening was a common radiological feature, with Wani *et al*.[18] reporting the highest prevalence at 90.7%, while the present study found it in 71% of cases. Idiopathic pulmonary fibrosis (IPF) was the most frequent diagnosis associated with septal thickening in the present study (38.8%), whereas the Indian registry of ILD reported it in 13.7% of cases. Traction bronchiectasis was another notable feature, with Wani *et al*.[18] observing it in 49.3% of cases and the present study finding it in 43% of cases. High-resolution computed tomography-interstitial lung disease (CT-ILD) was the most common diagnosis linked to traction bronchiectasis in the present study (22%). Honeycombing was observed in 42% of cases in the present study and it was often associated with non-specific interstitial pneumonia (NSIP). Ground glass opacity, nodules and other radiological findings also exhibited variations in prevalence and associated diagnoses across the different studies, highlighting the heterogeneity of ILD manifestations and the importance of accurate radiological interpretation for diagnosis.

In our study, we examined the progression of interstitial lung disease (ILD) over a span of six months, utilizing spirometry and DLco estimation in conjunction with an assessment of clinical symptoms, radiological patterns and their correlation with smoking habits. It is important to note that participants who experienced mortality during the study period were excluded from the analysis. Furthermore, our study did not investigate the treatment response to various drugs for different types of ILDs. The diagnosis of ILD was primarily based on High-Resolution Computed Tomography (HRCT) and no surgical lung biopsies, which are sometimes necessary for conclusive diagnosis of ILD, were performed as part of this study.

CONCLUSION

In patients with ILD, spirometry data predominantly reveal a restrictive pattern and there is a high incidence of idiopathic pulmonary fibrosis (IPF). Most patients initially present with a dry cough and display a moderate disease severity during their first visit. Radiologically, the leading pattern detected is septal thickening. The majority of ILDs exhibit a progressive nature, resulting in a decline in lung function over time. Interestingly, this decline is observed consistently across different smoking statuses.

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