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Prevalence and predictors of suboptimal peak inspiratory flow rates in the management of chronic obstructive pulmonary disease

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Abstract

This cross-sectional study aimed to investigate the role of peak inspiratory flow rate (PIFR) in the management of inhalation therapy for patients with chronic obstructive pulmonary disease (COPD). Conducted in the Department of Pulmonary Medicine at a tertiary care institute from July 2021 to January 2022, this study included a total of 351 patients who were clinically diagnosed with stable COPD and currently receiving inhaler therapy.

Participants underwent comprehensive assessments that included demographic data collection, the use of the ABCD assessment tool to evaluate disease severity, the COPD Assessment Test (CAT) for quality of life measurement, and assessments for adherence to inhaler therapy and inhaler technique proficiency. The primary focus was on determining the prevalence of suboptimal PIFR and identifying associated demographic and clinical factors.

The results indicated that 45% of the patients exhibited suboptimal PIFR, which is critical for effective medication delivery in COPD management. Analysis revealed several significant predictors of suboptimal PIFR: female gender, lower CAT scores, the type of inhaler device used, and a Modified Medical Research Council grade of ≥2, which indicates increased levels of breathlessness.

These findings underscore the importance of assessing PIFR in COPD patients to ensure effective drug delivery. The study suggests that personalized inhaler device prescriptions tailored to individual PIFR can enhance treatment efficacy and improve overall management outcomes for COPD patients. By addressing factors contributing to suboptimal PIFR, healthcare providers can optimize inhalation therapy and ultimately improve patient quality of life.

Key words: COPD, dry powder inhaler, inhaler devices, inspiratory capacity.

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Introduction

Chronic obstructive pulmonary disease (COPD) is considered the third leading cause of death, with mortality of about 3 million annually and expected to rise to 5.4 million deaths annually by 2060 [1]. The global prevalence of COPD stands at 10.3% [95% confidence interval (CI) 8.2%,12.8%] [2]. The number of COPD cases in India increased from 28.1 million (27.0-29.2) in 1990 to 55.3 million (53.1-57.6) in 2016, with an increase in prevalence from 3.3% (3.1-3.4) to 4.2% (4.0-4.4) [3].

Treatment of COPD involves the use of β-2-agonists, muscarinic antagonists, and inhaled corticosteroids, which are delivered through specialized devices such as metered-dose inhalers (MDIs), dry powder inhalers (DPIs), and soft mist inhalers. The use of these inhaler devices requires coordination techniques. MDIs require a more complex coordination technique for drug delivery than DPIs. However, effective delivery of medication also requires the patient's inspiratory effort to overcome the internal resistance present in each device. This internal resistance offered by the flow channel of the device is set by the manufacturer to provide the energy required to disaggregate the drug formulation and allow effective delivery to the lungs. All inhaler devices do not have the same internal resistance. The internal resistance of the device, along with the inspiratory flow of the patient, allows the powder to disaggregate [4].

Peak inspiratory flow rate (PIFR) measures the patient's inspiratory effort and is used to assess a patient's ability to generate an adequate inspiratory flow rate to overcome internal resistance. As per the literature, a PIFR<60 L/min in COPD is considered ineffective for inhaled medications [5,6]. Spirometers can also measure the inspiratory flow rate using surrogates like maximal inspiratory pressure and correlate well with the PIFR. But spirometry-based measurements in a busy outpatient setup can be cumbersome. The internal resistance of each inhaler device varies, with MDIs having the least internal resistance and DPIs having the maximum internal resistance. Since COPD patients have hyperinflation and less respiratory muscle effort, it is important to evaluate the inspiratory capacity of COPD patients before prescribing inhaler devices. PIFR is also affected by factors like age, gender, race, ethnicity, and body mass index (BMI). Hence, we conducted this study with the intent

to determine the prevalence and factors predicting suboptimal PIFR value in a tertiary care hospital.

Materials and Methods

This cross-sectional study was conducted in the Department of Pulmonary Medicine of a tertiary care institute from July 2021 to January 2022. The study protocol was approved by the Institute Scientific Committee, Institute Ethics Committee (JIP/IEC/2021/063), and written informed consent was obtained from all participants before enrollment in the study. Patients aged more than 40 years who were clinically diagnosed with stable COPD and on inhaler therapy attending the outpatient clinic were included in the study. Stable COPD patients who were on inhaled medications but not on systemic steroids during the last 3 months and without exacerbation, were recruited. Patients who had active tuberculosis, had undergone thoracic surgery, had bronchial asthma and interstitial lung disease, were pregnant women, and were using nebulizers for inhaled medications were excluded from the study. The demographic data of patients were noted down in a prerequisite proforma. The Modified Medical Research Council (MMRC) dyspnea score and COPD assessment score (CAT score) were noted down. Spirometry was done by a Jager Masterscreen PFT machine (Care Fusion Ltd., Basingstoke, UK) to assess the severity of airflow obstruction. Post-bronchodilator forced expiratory value for 1 second (FEV1) was recorded after administering 400 mcg of salbutamol by MDI. Based on post FEV1 value, patient airflow limitation was graded as per the Global Initiative for Chronic Obstructive Lung Disease (GOLD) stages 1, 2, 3, and 4. The history of previous exacerbation of COPD in terms of hospitalization or use of oral corticosteroid in the last year was also evaluated at the same time. Patients were then categorized into groups A, B, C, and D based on MMRC grade, CAT score, and number of exacerbations using the refined ABCD assessment tool. Information regarding inhaler medication adherence was collected using the Test of Adherence to Inhaler Questionnaire. An erratic and deliberate poor adherent behavioral pattern was defined by the presence of scores <45 and good adherence with a score of 50. A technical error in using the inhaler device was observed, and using the inhaler technique checklist of the NHS Liverpool Clinical Commissioning Group, present in the public domain, they were scored 0-3 if patients had poor inhaler technique, 4-5 moderate inhaler technique, and 6-7 for good inhaler technique. The patient's adequate drug delivery capacity was determined by measuring the PIFR. PIFR was done by asking patients to inhale as quickly as possible with the InCheck DIAL device, which is a handheld inspiratory flow measurement device, after a complete exhalation. The highest PIFR value for each patient was considered after three attempts of deep inspiration. Since DPI discus has the highest resistance amongst devices, a PIFR of <60 L/min was considered low, and >60 L/min is considered normal as per the literature. The PIFR value of each patient was then matched with the type of inhaler device used by the patient to see whether the correct drug delivery device had been prescribed.

Statistical analysis

Data entry was done using REDcap Software (Vanderbilt University Medical Center, Nashville, Tennessee, USA), and the statistical analysis was done using Statistical Package for the Social Sciences (SPSS), version 19 (IBM Corporation, Armonk, NY, USA). The normality of continuous data was assessed by the Kolmogorov-Smirnov test. Depending on the distribution of the data, the variables were described as mean with standard deviation or median and interquartile range. Categorical data were described using frequencies and percentages. The prevalence was estimated with a 95% CI. The outcome variable was compared with the independent variables using the Chi-square test for significance. The outcome measures were reported with 95% CI, and statistical analysis was considered to be significant at 5% level of significance ($p<0.05$). Multiple regression analysis was done to evaluate the effect of multiple factors on low PIFR.

Assuming the prevalence of low PIFR to be around 32% as per a study done by Sharma *et al*., with absolute precision of 5%, CI of 95% and attrition of 10%, the sample size calculated was 368 [7].

Results

A total of 368 patients were screened for the study, and 351 patients were recruited following the inclusion criteria, while 6 patients were excluded as they were on nebulizers, and 11 patients had bronchial asthma. The mean age of our study population was 61.28±9.05 years, with the majority of them belonging to the age range of 50-69 years. Males were the predominant gender in our study subjects. The majority of our patients were nonsmokers and had a history of biomass fuel exposure. The BMI of our study participants was in the range of 18.5-22.9, and most of them had at least a primary education (Table 1). Prevalence of suboptimal PIFR was found in 159 COPD patients (45%) (Figure 1).

The distribution of different clinical scores in COPD patients was also analyzed. The majority of the study participants were found to have a CAT score of <10 with a good inhaler technique score of >3. However, the test for adherence to inhaler score was found to be similar, with most of the COPD patients having good adherence to treatment. Most of the COPD patients belonged to the A group of the refined ABCD assessment test (Table 2).

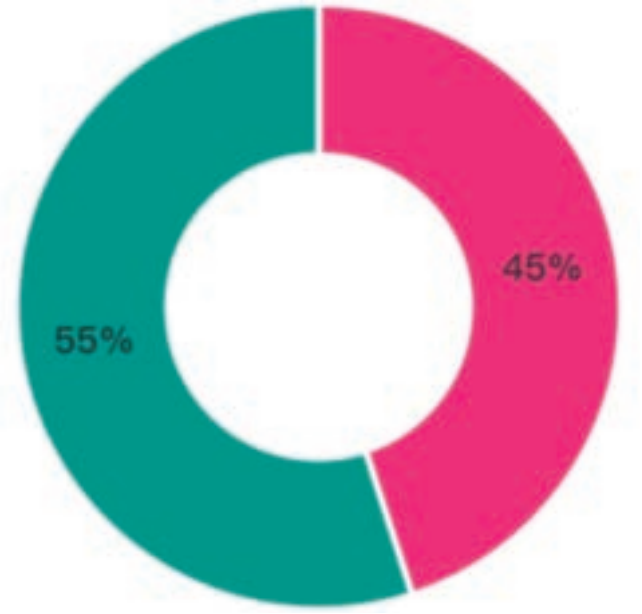

Figure 1. Prevalence of suboptimal peak inspiratory flow rate (PIFR) (<60 L/min) among chronic obstructive pulmonary disease patients included in the study (n=351).

Table 1. Sociodemographic characteristics of chronic obstructive pulmonary disease patients included in the study (n=351).

Characteristic	Categories	n	%
Age group in years	40-49	23	7
	50-59	123	35
	60-69	126	36
	≥70	79	23
Gender	Male	257	73
	Female	94	27
Education	No formal education	103	29
	Class 1-5	125	36
	Class 6-10	113	32
	Class 11 and above	10	3
Body mass index (in kg/m²)	<18.5	109	31
	18.5-22.9	174	50
	23.0-24.9	37	11
	≥25.0	31	9
Smoking status	Nonsmoker	192	55
	Smoker	141	39
	Ex-smoker	18	5
Biomass exposure	No	149	42
	Yes	202	58
Type of inhaler use	MDI	25	7
	DPI	326	93
FEV1/FVC [mean (SD)]	-	56.51 (9.88)	
FVC [mean (SD)]	-	55.33 (12.68)	
FEV1 [mean (SD)]	-	44.28 (15.57)	

MDI, metered-dose inhalers; DPI, dry powder inhalers; FEV1, forced expiratory value for 1 second; FVC, forced vital capacity; SD, standard deviation.

Table 2. Distribution of chronic obstructive pulmonary disease patients included in the study by different clinical scores (n=351).

Characteristic	Categories	n	%
CAT score	Score <10)	293	83
	Score>10)	58	17
Test for adherence to inhaler score	<45 (poor adherence)	169	48
	>50 (good adherence)	182	52
Inhaler technique score	<3 (poor inhaler technique)	200	57
	>3 (good inhaler technique)	151	43
COPD ABCD assessment	A	286	81.5
	B	47	13.4
	C	17	4.8
	D	1	0.3

COPD, chronic obstructive pulmonary disease; CAT, COPD assessment test.

The predictors for suboptimal PIFR in COPD patients were also analyzed. Female gender was found to be an important predictor for suboptimal PIFR and was found to be statistically significant compared to male gender (p=0.001). Patients with a BMI range of 18.5-22.9 were found to have suboptimal PIFR in COPD patients as compared to patients with lower BMI. Patients who had lower CAT scores performed better as their PIFR were in the optimal range compared to those with higher CAT scores. Most of the patients in our study were using DPI compared to MDI. However, since MDI has low internal resistance, suboptimal PIFR was seen in only 15.4% and in patients using DPI, suboptimal PIFR was seen in 47.7%, which was statistically significant. In MMRC grading, most of the patients had MMRC grade≥2 (55.7%) in the suboptimal PIFR group, and it was found to be statistically significant compared to that of patients with MMRC grade 0-1 (p=0.05) (Table 3).

Table 3. Predictors of suboptimal peak inspiratory flow rate among chronic obstructive pulmonary disease patients included in the study (n=351).

Characteristic	Categories	PIFR<60 L/min n	PIFR<60 L/min %	PIFR≥60 L/min n	PIFR≥60 L/min %	Unadjusted PR+	p	Adjusted PR+	95% CI
Age group in years	40-49	9	39.1	14	60.9	Ref			
	50-59	55	44.7	68	55.3	1.14	0.632		
	60-69	50	39.7	76	60.3	1.01	0.960		
	≥70	45	56.9	34	43.0	1.45	0.177		
Gender	Male	104	40.5	153	59.5	Ref			
	Female	55	58.5	39	41.5	1.45	0.001	1.31	1.05-1.66
Education	No formal education	49	47.6	54	52.4	Ref			
	Class 1-5	64	51.2	61	48.8	1.08	0.587		
	Class 6-10	42	36.3	71	62.0	0.78	0.117		
	Class 11 and above	4	40.0	6	60.0	0.84	0.665		
Smoking status	Non-smoker	92	47.9	100	52.1	Ref			
	Smoker	61	43.3	80	56.7	0.90	0.404		
	Ex-smoker	6	33.3	12	66.7	0.69	0.288		
Biomass exposure	No	70	47.0	79	53.1	Ref			
	Yes	89	44.1	113	55.9	0.94	0.592		
Inhaler type	DPI	155	47.7	170	52.3	Ref		Ref	
	MDI	4	15.4	22	84.6	0.32	0.015	0.10	0.14-0.73
CAT score	<10	126	43.0	167	57.0	Ref		Ref	
	>10	33	56.9	25	43.1	1.32	0.035	1.20	0.83-1.74
Adherence to inhaler score	<45	76	45.0	93	55.0	Ref			
	>50	83	45.6	99	54.4	1.01	0.905		
Inhaler technique score	<3	130	65.0	70	35.0	Ref		Ref	
	>3	29	19.2	122	80.8	0.29	<0.001	0.39	0.28-0.55
MMRC grading	0-1	125	43.1	165	56.9	Ref			
	≥2	34	55.7	27	44.3	1.29	0.05		
COPD ABCD assessment	A	122	42.7	164	57.3	Ref		Ref	
	B	26	55.3	21	44.7	1.30	0.079	1.38	0.89-2.10
	C	11	64.7	6	35.3	1.52	0.030	1.54	0.99-2.39
	D	0	0.0	1	100.0	-		-	
GOLD staging	Stage 1	5	71.4	2	28.6	Ref			
	Stage 2	51	44.3	64	55.7	0.62	0.067		
	Stage 3	74	44.8	91	55.2	0.62	0.067		
	Stage 4	29	45.3	35	54.7	0.63	0.098		
BMI (in kg/m^2)	Mean (SD)	20.5 (3.4)	19.8 (3.5)	0.97	0.067				
Post FEV1/FVC	Mean (SD)	56.1 (10.3)	55.7 (9.4)	0.99	0.783				
Post FVC	Mean (SD)	56.7 (11.7)	52.8 (12.9)	0.98	<0.001	0.98	0.97-0.99		
Post FEV1	Mean (SD)	45.3 (15.7)	44.4 (16.8)	0.99	0.619				

PIFR, peak inspiratory flow rate; PR+, prevalence ratio; CI, confidence interval; MDI, metered-dose inhalers; DPI, dry powder inhalers; COPD, chronic obstructive pulmonary disease; CAT, COPD assessment test; MMRC, Modified Medical Research Council; GOLD, Global Initiative for Chronic Obstructive Lung Disease; BMI, body mass index; FEV1, forced expiratory value for 1 second; FVC, forced vital capacity; SD, standard deviation.

Discussion

In our study, we found that around 45% of COPD patients had suboptimal PIFR. A similar prevalence was noted in studies done by other investigators [8-10]. The prevalence was found to be higher when the PIFR threshold was changed to <45 L/min for all ranges of resistance [10]. The suboptimal PIFR was found in 4 patients of COPD when a low resistance device like MDI was used, while 155 COPD patients had lower PIFR when DPI, which is a medium resistance device, was used by them. However, a suboptimal PIFR in one device cannot be used to predict the suboptimal PIFR value for other devices. This implies that a patient who does not receive an adequate dose of medication from one device may switch to another device. Therefore, the choice of inhaler device should be customized based on the patient's individual PIFR value for various resistance ranges. The majority of our patients using medium resistance devices had optimal PIFR (52.3%) and suboptimal PIFR (47.7%), while patients using low resistance devices had optimal PIFR (84.6%) and suboptimal PIFR (15.4%).

Based on various clinical scores, the majority of our COPD patients (about 83%) had a CAT score of <10 and belonged to group A of the ABCD assessment test. This is because the majority of our subjects who were recruited for the study were stable patients. However, the majority of our COPD patients did not have good inhaler technique scores, with a score of less than 3 points despite having good adherence to medications.

Using multiple regression analysis, the various clinical factors that were responsible for low PIFR were evaluated. Female gender was found to be a significant clinical predictor of low PIFR in COPD patients, confirming the findings of prior studies [7,11,12]. The majority of our patients with suboptimal PIFR were of older age, although there was no statistical difference in age groups among patients with optimal PIFR. The weak strength of respiratory muscles and the presence or absence of intrinsic positive end-expiratory pressure could potentially contribute to suboptimal PIFR in older individuals. Nevertheless, no significant difference was observed in BMI between the two groups, which is consistent with the results of previous studies.

The CAT score was observed to be higher among the suboptimal PIFR group compared to the optimal group in our study, suggesting that higher symptom burden and poor health status could be responsible for impaired inspiratory capacity. This is in concordance with the study by Loh *et al*., where there was a higher CAT score in the suboptimal group compared to the optimal group [13,14]. However, a study done by Sharma *et al.* suggested that there was no difference in the CAT score between the two groups. This could be due to the distribution of study subjects and the two groups, and the level of severity of the enrolled participants [7].

The inhaler technique score of patients between both groups was compared, and there was a significant difference in the score between the suboptimal and optimal groups, with the majority of patients belonging to the suboptimal group having poor inhaler technique scores. Hua *et al*., in their study, demonstrated that training and orientation of COPD patients is required to improve inhaler technique, and poor inhaler technique was associated with low PIFR, which was in accordance with our study [15].

The majority of our patients with suboptimal PIFR belonged to the A category (122 patients) of the refined ABCD assessment tool for COPD. This tool is mainly based on the patient's symptoms and history of exacerbations. This was followed by the majority of patients belonging to the B category. In our study, the majority of patients with optimal PIFR also belonged to the A category, followed by the B category of the refined ABCD assessment tool. However, in our study, there was a significant difference between patients with optimal and suboptimal PIFR groups in the C category of the ABCD assessment tool, with more patients in the C category having low PIFR. This may be because these patients have more symptoms and exacerbations, leading to decreased inspiratory capacity and suboptimal PIFR. A study by Parekh *et al*. suggested that the inspiratory capacity of the A and B categories is lower than that of the C category, and this difference is statistically significant with $p<0.001$ [16]. The majority of our study participants had GOLD stage 3, followed by GOLD stage 2. This may be because the majority of our patients belonged to old age with decreased capacity to perform spirometry and poor health status.

In our study, MMRC grading of 0-1 is present in 82.6%, and 43.1% have suboptimal PIFR, whereas MMRC≥2 grading is present in 17.3% of patients, among which 55.7% have suboptimal PIFR. This indicates that PIFR values may vary according to the dyspnea scale (suboptimal PIFR is present in patients with MMRC grade ≥2), but results are found to be not statistically significant ($p=0.05$). Similar to our study, MMRC grading was not significant in other studies [7,15,17].

The spirometric parameters of FEV1% predicted and FEV1/forced vital capacity (FVC) ratio showed no difference between the cohorts. The absence of difference in FEV1% between the cohort was also found in the study conducted by Sharma *et al*. [6]. However, there was a significant difference in FVC% predicted between the suboptimal and optimal groups. This was found to be in agreement with the studies by Mahler *et al*. and Duarte *et al*. [12,18].

Limitations

Our study has a few limitations. It was a single-centered cross-sectional study. The PIFR value was measured against a single DPI device, while other high and medium internal resistance device was not checked to assess the performance of PIFR. In our study, we have taken PIFR of <60 L/min as a suboptimal value from previous studies, but recent studies have shown that even with PIFR >30 L/min, adequate clinical effects can be obtained.

Conclusions

Female gender, higher CAT score, high MMRC grade, and poor inhaler technique are important predictors of suboptimal PIFR. The majority of our study subjects with suboptimal PIFR. Hence, it is imperative to perform a simple routine measurement of PIFR value so that a personalized inhaler device can be prescribed so that the patient may benefit from adequate therapy.

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