



## EARLY SMALL AIRWAY DYSFUNCTION IN SMOKERS AND NON-SMOKERS: A SPIROMETRIC ANALYSIS IN NORTH INDIAN POPULATION

### Respiratory Medicine

<b>Shruti Garg</b>	Junior Resident-3, Department of Anatomy, S.N.Medical College, Agra.
<b>Anjali Gupta</b>	Associate Professor & Head, Department of Anatomy, S.N.Medical College, Agra.
<b>Sachin Kumar Gupta*</b>	Associate Professor, Department of Respiratory Medicine, S.N.Medical College, Agra. *Corresponding Author

### ABSTRACT

**Background:** Small airway dysfunction represents an early pathological manifestation of smoking-related lung disease and often precedes the development of chronic obstructive pulmonary disease (COPD). Conventional spirometry may fail to detect these early changes, leading to underdiagnosis. Data on small airway involvement in the North Indian population remain limited. **Objective:** To evaluate and compare small airway function among smokers and non-smokers, with and without established COPD, using spirometric parameters. **Methods:** This observational cross-sectional study included individuals aged  $\geq 40$  years. Participants were categorized into non-smokers, healthy smokers, patients with small airway disease (SAD), and patients with COPD. COPD was diagnosed using post-bronchodilator  $FEV_1/FVC < 0.70$  according to GOLD-2025 guidelines. Small airway disease was defined by reduction of more than two out of three mid-expiratory flow parameters ( $FEF_{25-75\%}$ ,  $FEF_{50\%}$ ,  $FEF_{75\%}$ ) below 65% predicted. Spirometry was performed according to ATS/ERS guidelines. **Results:** While  $FEV_1$  and  $FEV_1/FVC$  were significantly reduced in COPD patients, marked impairment of small airway parameters was observed even among healthy smokers.  $FEF_{25-75\%}$  emerged as the most sensitive indicator of early airway dysfunction. Patients with SAD demonstrated spirometric patterns intermediate between healthy smokers and COPD patients. **Conclusion:** Small airway dysfunction is prevalent among smokers in North India and often precedes overt COPD. Incorporating small airway indices into routine spirometric assessment may facilitate early diagnosis and timely intervention.

### KEYWORDS

Small airway disease, COPD,  $FEF_{25-75\%}$

#### INTRODUCTION

Small airway dysfunction has gained increasing attention as a critical early event in the pathogenesis of chronic respiratory diseases, particularly chronic obstructive pulmonary disease (COPD). COPD now recognized as a 3<sup>rd</sup> most common cause of death worldwide after Ischemic Heart disease (IHD) and Cerebro vascular accident (CVA), with ~600 million projected cases by 2050.

The small airways (bronchioles with 2 mm or less in diameter without cartilage) contribute minimally to total airway resistance under normal conditions but are highly susceptible to inflammation, remodeling, and obliteration due to exposure to tobacco smoke<sup>1</sup>. These pathological changes frequently occur long before the development of clinically apparent airflow obstruction.

Smoking remains the most significant modifiable risk factor for COPD worldwide<sup>2</sup>. However, reliance on conventional spirometric indices such as forced expiratory volume in one second ( $FEV_1$ ) and the  $FEV_1$ /forced vital capacity (FVC) ratio may fail to identify early airway disease<sup>3</sup>. Mid-expiratory flow parameters, particularly forced expiratory flow between 25% and 75% of FVC ( $FEF_{25-75\%}$ ), reflect airflow in the distal airways and have been shown to be sensitive indicators of early small airway involvement<sup>4</sup>. Other Parameter of SAD in spirometry are lower  $FEF_3/FEF_6$  ratio and Large gap between SVC (slow vital capacity) and FVC.

India bears a substantial share of the global burden of tobacco-related respiratory disease, with regional variations influenced by genetic susceptibility, environmental pollution, and delayed access to healthcare<sup>5</sup>. Despite this, studies focusing on early small airway changes-especially in smokers without established COPD-are limited in the Indian context. Understanding these early changes is crucial for developing preventive strategies and reducing long-term morbidity.

This study was undertaken to assess small airway function in smokers and non-smokers in a North Indian population and to compare spirometric patterns across different stages of smoking-related airway disease.

#### MATERIALS AND METHODS

##### Study Design And Setting

This observational, cross-sectional study was conducted at a tertiary care center in North India over a defined study period. Ethical clearance was obtained from the institutional ethics committee, and informed consent was secured from all participants.

#### Study Population

Individuals aged **40 years and above** attending the outpatient department were screened for inclusion.

#### Inclusion Criteria

- Age  $\geq 40$  years
- Smoking history of  $\geq 10$  pack-years
- Diagnosis of COPD based on post-bronchodilator  $FEV_1/FVC < 0.70$ , in accordance with GOLD-2025 guidelines<sup>6</sup>

#### Participant Grouping

Participants were stratified into four groups:

1. Non-smokers
2. Healthy smokers
3. Small airway disease (SAD)
4. COPD

This stratification allowed assessment across the full spectrum of smoking exposure and airway involvement<sup>7</sup>.

#### Definition Of Small Airway Disease

Small airway disease was diagnosed when **more than two of the following parameters** were reduced to **<65% of predicted values**:

- $FEF_{25-75\%}$
- $FEF_{50\%}$
- $FEF_{75\%}$

This definition enabled differentiation of isolated small airway involvement from established COPD<sup>8</sup>.

#### Exclusion Criteria

- Patients who did not want to participate in study
- Pulmonary Tuberculosis (active cases and Previously treated both)
- History of bronchial asthma and Asthma -COPD Overlap (ACO)
- Other chronic respiratory diseases (e.g., interstitial lung disease, bronchiectasis)
- Acute respiratory infection within the preceding six weeks

These exclusions minimized confounding influences on spirometric measurements<sup>9</sup>.

#### Spirometry

Pulmonary function testing was performed using a calibrated spirometer following American Thoracic Society/European

Respiratory Society (ATS/ERS) standards. Post-bronchodilator values were recorded. Parameters analyzed included FEV<sub>1</sub>, FVC, FEV<sub>1</sub>/FVC ratio, FEF25–75%, FEF50%, and FEF75%.

## RESULTS

Spirometric evaluation revealed distinct patterns of airway involvement across the four study groups.

### Baseline Characteristics

Participants across groups were comparable in age. Smoking exposure increased progressively from healthy smokers to COPD patients.

**Table 1: Baseline Demographic And Smoking Characteristics**

Parameter	Non-smokers	Healthy Smokers	SAD	COPD
Mean age (years)	Comparable	Comparable	Comparable	Comparable
Smoking exposure (pack-years)	0	≥10	≥10	≥10
Duration of smoking	-	Moderate	Longer	Longest

**Table 2: Conventional Spirometric Parameters (% Predicted)**

Parameter	Non-smoker	Healthy Smokers	SAD	COPD
FEV <sub>1</sub>	Normal	Near-normal	Mildly reduced	Markedly reduced
FVC	Normal	Normal	Mildly reduced	Reduced
FEV <sub>1</sub> /FVC	Normal	Normal	Preserved	<0.70

FEV<sub>1</sub> and FEV<sub>1</sub>/FVC ratio were significantly reduced only in COPD patients, while healthy smokers and SAD patients largely retained normal ratios.

**Table 3: Small Airway Parameters (% Predicted)**

Parameter	Non-smokers	Healthy Smokers	SAD	COPD
FEF25–75%	Normal	Reduced	Markedly reduced	Severely reduced
FEF50%	Normal	Reduced	Markedly reduced	Severely reduced
FEF75%	Normal	Mildly reduced	Significantly reduced	Severely reduced

FEF25–75% showed the earliest and most consistent decline among smokers, even when FEV<sub>1</sub> remained within normal limits.

## DISCUSSION

The present study demonstrates that small airway dysfunction is common among smokers in a North Indian population and frequently precedes the development of spirometrically defined COPD. The findings highlight the limitations of conventional spirometry in detecting early airway disease and emphasize the value of mid-expiratory flow parameters.

Our observations are consistent with studies by Qin et al. and Kim et al., who reported significant reductions in FEF25–75% among smokers with preserved FEV<sub>1</sub>, suggesting early distal airway obstruction<sup>12,13</sup>. Park et al. similarly demonstrated that small airway indices effectively differentiate isolated SAD from established COPD<sup>8</sup>.

Compared with Western cohorts, the degree of small airway impairment observed in this study appears pronounced, possibly reflecting higher exposure to biomass fuel, ambient air pollution, and delayed smoking cessation in the Indian context<sup>5</sup>. Studies utilizing impulse oscillometry have shown that small airway dysfunction is frequently underestimated when spirometry alone is used<sup>14</sup>.

Recent advancements integrating artificial intelligence and machine learning with pulmonary function testing have further improved early detection of obstructive patterns and prediction of disease progression<sup>15</sup>. Such approaches may be particularly beneficial in resource-limited settings.

Clinically, early identification of small airway dysfunction offers an opportunity for smoking cessation and targeted interventions,

potentially preventing progression to irreversible airflow limitation. Routine reporting of small airway indices should therefore be encouraged in high-risk populations.

## CONCLUSION

Small airway dysfunction is prevalent among smokers in the North Indian population and often occurs before the onset of overt COPD. Mid-expiratory flow parameters, particularly FEF25–75%, are sensitive indicators of early airway involvement and should be incorporated into routine spirometric assessment.

Early diagnosis, combined with preventive strategies and smoking cessation, may significantly reduce the clinical and economic burden of chronic respiratory disease. Future longitudinal studies using advanced diagnostic modalities and artificial intelligence-based models are warranted to refine early detection and personalize management strategies.

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