

# Understanding Non-Smoker COPD: Comparative Insights with Smoker COPD

**Meghaa Vashishht**

Swami Rama Himalayan University

**Rakhee Khanduri**

[rakhee.sodhi@gmail.com](mailto:rakhee.sodhi@gmail.com)

Swami Rama Himalayan University

**Manoj Kumar**

Swami Rama Himalayan University

**Varuna Jethani**

Swami Rama Himalayan University

**Sushant Khanduri**

Swami Rama Himalayan University

**Rahul Gupta**

Swami Rama Himalayan University

---

## Research Article

**Keywords:** Non-smoker COPD, smoker COPD, biomass exposure, post-tubercular COPD, emphysema, spirometry

**Posted Date:** September 8th, 2026

**DOI:** <https://doi.org/10.21203/rs.3.rs-10716823/v1>

**License:** © ⓘ This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

**Additional Declarations:** No competing interests reported.

---

# Abstract

## Background

Chronic Obstructive Pulmonary Disease (COPD) has long been inextricably linked with smoking, yet a burgeoning cohort of non-smoker patients challenges this paradigm as they remain a relatively underexplored entity due to limited research attention and understanding of its distinct characteristics. This study endeavors to elucidate the clinical and radiological disparities between the two groups, thereby illuminating the nuanced pathophysiology underlying this dichotomy with an attempt to enhance our understanding of COPD's heterogeneous nature. Understanding these differences is crucial for tailored diagnosis as well as appropriate treatment.

## Purpose

To compare the clinical, etiological, and radiological characteristics of non-smoker COPD with smoker COPD in a tertiary care setting.

## Methods

The study was prospective observational which was conducted over 12 months at the Department of Respiratory Medicine, Himalayan Institute of Medical Sciences, Dehradun. A total of 210 COPD patients (105 smokers and 105 non-smokers) were evaluated. Clinical data, comorbidity profiles, symptom severity (via CAT score), spirometry, diffusing capacity (DLCO), chest X-ray findings, and echocardiographic assessment for pulmonary hypertension were analyzed and compared between the two groups.

## Results

Smokers exhibited a higher prevalence of airflow obstruction and emphysematous radiological changes, along with significantly lower DLCO values ( $0.608 \pm 0.158$  vs.  $0.803 \pm 0.152$  in non-smokers;  $p < 0.0001$ ). Non-smokers had greater associations with risk factors such as biomass exposure, prior pulmonary tuberculosis, and occupational exposure. Radiologically, fibrotic and post-tubercular changes were more frequent in non-smokers, while hyperinflation and bullous changes predominated in smokers. The frequency of exacerbations, CAT scores, and pulmonary hypertension did not differ significantly between groups.

## Conclusion

Non-smoker COPD represents a clinically and radiologically distinct phenotype with unique etiological factors. These differences highlight the importance of recognizing non-smoking-related COPD as a separate clinical entity for appropriate diagnosis and individualized treatment strategies.

## Introduction

COPD is a progressive, inflammatory airway condition characterized by persistent respiratory symptoms and airflow limitation that is not fully reversible. While smoking remains the most well-recognized etiological factor globally, it is increasingly evident that a significant subset of patients develop COPD without any history of tobacco use, particularly in low- and middle-income countries such as India. This evolving clinical pattern highlights the multifactorial nature of the disease and calls attention to alternate risk factors including biomass smoke exposure, occupational dust and fumes, air pollution, and a history of pulmonary infections such as tuberculosis.[1]

Globally, over 300 million people are affected by COPD, with the disease contributing to a significant number of disability-adjusted life years. While cigarette smoking remains a dominant risk factor, recent estimates suggest that nearly one-third of individuals diagnosed with COPD are lifelong non-smokers. In low- and middle-income countries, especially in South Asia, alternative risk factors—such as biomass smoke from cooking stoves, occupational dust exposure, air pollution, and a history of pulmonary infections like tuberculosis—play a substantial role in COPD development. [2, 3]

In India, the prevalence of COPD is estimated at around 7.4%, with higher rates observed in males, urban populations, and northern regions. Notably, a growing number of patients diagnosed with COPD report no history of active smoking. This shift in the epidemiological profile challenges the conventional understanding of the disease and underscores the need to explore non-tobacco-related causes of chronic airflow limitation. [3, 4]

Emerging evidence suggests that non-smoker COPD may represent a distinct clinical phenotype with unique underlying mechanisms, radiological features, and disease outcomes. While smokers with COPD tend to exhibit emphysematous changes and extensive alveolar destruction, non-smokers often present with airway-predominant disease or fibrotic changes, possibly linked to biomass exposure, prior infections, or environmental factors. [5, 6]

Despite this evolving understanding, few studies have directly compared the clinical and radiological profiles of smoker and non-smoker COPD. Furthermore, non-smoking-related COPD remains underrepresented in both research and clinical practice, resulting in a lack of awareness and potentially suboptimal management. This knowledge gap is particularly relevant in the Indian context, where environmental exposures and tuberculosis burden are high.

The present study was undertaken to compare the demographic characteristics, risk factor profiles, clinical presentations, pulmonary function parameters, and radiographic features of non-smoker versus smoker COPD patients. The goal was to better characterize the differences between these two

phenotypes and improve our understanding of COPD in non-smoking populations, which could have significant implications for diagnostic and treatment strategies.

## Methods

This observational prospective study was conducted over a 12-month period in the Department of Respiratory Medicine after obtaining clearance from Institutional Research Committee and ethical committee (SRHU/ Reg./Int/2024-82(60) )

A total of 210 patients diagnosed with COPD were enrolled during the study period. Of these, 105 were lifelong non-smokers, and 105 were current or former smokers with a minimum smoking history of 10 pack-years. Participants were selected from both outpatient and inpatient departments after obtaining written informed consent.

For including patients in our study, we considered following criteria.

- **Smoker COPD group:** Patients aged > 18 years with spirometry-confirmed COPD and a smoking history of at least 10 pack-years.
- **Non-smoker COPD group:** Patients with spirometry-confirmed COPD and no history of tobacco smoking, but with alternative risk exposures such as biomass smoke, occupational dust, previous pulmonary tuberculosis, chronic asthma, childhood lower respiratory tract infections, or passive smoke exposure.

Patients with active pulmonary infections, including current tuberculosis, Coexisting pulmonary conditions such as interstitial lung disease, bronchiectasis, asthma, lung malignancy, pneumonia, or pulmonary embolism, Cardiac conditions such as heart failure or dilated cardiomyopathy, obstructive sleep apnea and those who declined to provide informed consent were excluded from the study.

Each participant underwent a comprehensive clinical evaluation, including history of presenting symptoms, risk factor assessment (biomass, occupational, or infectious exposure), and comorbidity profiling. Details regarding frequency of exacerbations in the past year and symptom severity (via the COPD Assessment Test [CAT] score) were recorded. Smoking history, if applicable, was documented in pack-years. All patients underwent posteroanterior chest radiographs, which were interpreted for findings such as hyperinflation, fibrotic changes, bullae, and bronchiectasis. Pulmonary function tests were performed using standard spirometry to assess the severity of airflow obstruction according to GOLD guidelines. Diffusion capacity of the lung for carbon monoxide (DLCO) was measured when feasible to assess gas-exchange abnormalities. Two-dimensional echocardiography (2D-Echo) was performed to assess the presence and severity of pulmonary hypertension. Data were analyzed using appropriate statistical tools. Continuous variables were presented as means and standard deviations, and categorical variables as frequencies and percentages.

## Results

A total of 210 patients diagnosed with COPD were included, 105 non-smokers and 105 smokers. The overall mean age was  $63.10 \pm 12.13$  years, with no statistically significant difference between the two groups. A clear male predominance was seen, more pronounced among smokers (83.81%) than non-smokers (57.14%). Body mass index was significantly lower in smokers ( $20.41 \pm 2.71$  kg/m<sup>2</sup>) compared to non-smokers ( $21.86 \pm 2.98$  kg/m<sup>2</sup>;  $p = 0.0115$ ). Among non-smokers, a significant association was found with prior pulmonary tuberculosis (61.90% vs. 31.43%;  $p < 0.0001$ ) and biomass exposure (40.00% vs. 26.67%;  $p = 0.0570$ ). Clinically, both groups presented similarly with dyspnea and cough being the most common symptoms, and there were no significant differences in the number of exacerbations per year (1.15 vs. 1.20), duration of symptoms (5.41 vs. 5.05 years), or CAT scores (26.15 vs. 25.91). Among comorbidities, hypertension and diabetes were common in both groups, but hypothyroidism was significantly more frequent in non-smokers (13.33% vs. 1.90%;  $p = 0.0042$ ). Chest radiography revealed stark differences; fibrotic bands, cicatricial changes, and tractional bronchiectasis were more prevalent in non-smokers, while hyperinflation, bullous lung changes, and emphysematous features were dominant among smokers ( $p < 0.0001$ ). (Table 1)

Table 1  
Comparative Demographic, Clinical, Radiological, and Functional Profile of Non-Smoker and Smoker COPD Patients (N = 210)

| Parameter                                     | Non-smoker (n = 105) | Smoker (n = 105)  | p-value  |
|-----------------------------------------------|----------------------|-------------------|----------|
| <b>Age (years)</b> – Mean $\pm$ SD            | 62.20 $\pm$ 13.13    | 64.26 $\pm$ 10.82 | 0.3917   |
| <b>Male (%)</b>                               | 57.14% (n = 60)      | 83.81% (n = 88)   | < 0.0001 |
| <b>BMI (kg/m<sup>2</sup>)</b> – Mean $\pm$ SD | 21.86 $\pm$ 2.98     | 20.41 $\pm$ 2.71  | 0.0115   |
| <b>IPD Admissions (%)</b>                     | 61.90% (n = 65)      | 65.71% (n = 69)   | 0.6667   |
| <b>Exacerbations/year</b> – Mean $\pm$ SD     | 1.15 $\pm$ 1.13      | 1.20 $\pm$ 1.02   | 0.7317   |
| <b>Duration of Symptoms (years)</b>           | 5.41 $\pm$ 2.76      | 5.05 $\pm$ 2.78   | 0.3009   |
| <b>CAT Score</b> – Mean $\pm$ SD              | 26.15 $\pm$ 4.89     | 25.91 $\pm$ 4.34  | 0.3973   |
| <b>DLCO</b> – Mean $\pm$ SD                   | 0.803 $\pm$ 0.152    | 0.608 $\pm$ 0.158 | < 0.0001 |
| <b>Fibrotic Bands/Cicatricial Changes (%)</b> | 34.29% (n = 36)      | 11.43% (n = 12)   | —        |
| <b>Tractional Bronchiectasis (%)</b>          | 1.90% (n = 2)        | 0.00% (n = 0)     | —        |

Etiologically, the smoker group predominantly exhibited smoking-related COPD (COPD-C) in 70.48% of cases, whereas non-smokers more frequently had post-tubercular (COPD-I; 52.38%) and pollution-related (COPD-P; 28.57%) forms, with a highly significant difference in etio-distribution ( $p < 0.0001$ ). (Fig. 1)

On pulmonary function testing, smokers had more severe obstruction, and significantly lower DLCO values ( $0.608 \pm 0.158$  vs.  $0.803 \pm 0.152$ ;  $p < 0.0001$ ), indicating worse gas exchange. Small airway

involvement was notably higher in smokers (11.54% vs. 1.89%;  $p = 0.0115$ ). Although reversibility with bronchodilators was more frequently seen in non-smokers. (41.90% vs. 28.57%;  $p = 0.0604$ ). (Fig. 2)

Echocardiographic evaluation revealed that while the prevalence of pulmonary arterial hypertension (PAH) was slightly higher among smokers. Mild PAH was more frequent in smokers, whereas moderate PAH was observed more commonly in non-smokers. (Fig. 3) Similarly, the occurrence of dilated cardiomyopathy was not significantly different (41.90% in non-smokers vs. 51.43% in smokers).

## Discussion

While chronic obstructive pulmonary disease (COPD) has historically been considered nearly synonymous with tobacco use, emerging epidemiological evidence underscores a significant and complex burden of the disease among non-smokers. In our cohort of 210 patients, the demographic and etiological profiles diverged sharply based on smoking status. The smoker group was overwhelmingly male (83.81%) with a significantly lower body mass index ( $P = 0.0115$ ), classically aligning with the systemic cachexia often observed in tobacco-induced emphysema. Conversely, non-smokers presented with a notably higher female predominance (42.86%) and distinct etiologic drivers.

Etiological distribution differed significantly between the two groups. While smoking-related COPD (COPD-C) predominated in smokers, infection-related (COPD-I) and pollution-related (COPD-P) forms were more prevalent among non-smokers. This distinction underscores the heterogeneous nature of COPD in India, especially among non-smokers. Rather than cigarette smoke (COPD-C), the non-smoking cohort was primarily driven by post-infectious sequelae, particularly a history of pulmonary tuberculosis (COPD-I, 52.38%,  $P < 0.0001$ ), and biomass fuel or occupational exposure (COPD-P, 28.57%). Similar findings were included in a study by Shah DM et al. [6] and Salvi SS et al. [7], which emphasize biomass exposure and prior tuberculosis as paramount structural precursors to non-smoking COPD in developing nations.

Despite these fundamentally different pathophysiological origins, the clinical symptom burden between the two groups was remarkably convergent. Both cohorts exhibited nearly identical frequencies of dyspnea, cough, and annual exacerbation rates, resulting in statistically indistinguishable COPD Assessment Test (CAT) scores. However, a deeper clinical evaluation revealed phenotypic differences. Smokers demonstrated a significantly higher prevalence of decreased air entry ( $P = 0.0351$ ) and small airway involvement ( $P = 0.0115$ ) on physical examination. Various studies such as done by Takiguchi H et al. [8] and Sexton P et al. [9], also noted that while symptomatic presentation may be similar, tobacco exposure drives more pronounced peripheral airway destruction and functional limitation, whereas non-smokers often exhibit distinct, sometimes less severe, structural airway changes.

The divergence in structural damage becomes strikingly apparent when analyzing pulmonary function and gas exchange mechanics. Our spirometric analysis demonstrated that smokers trended toward more advanced disease, exhibiting a higher frequency of moderate to severe obstruction ( $P = 0.0220$ ). This functional decline was mirrored by a profound impairment in the diffusing capacity of the lungs for

carbon monoxide (DLCO). Non-smokers maintained a significantly higher mean DLCO compared to smokers ( $P < 0.0001$ ). As highlighted by Zhang J et al. [10], chronic tobacco exposure causes direct destruction of the alveolar-capillary interface and induces elevated carboxyhemoglobin levels, drastically impairing gas exchange efficiency—a pathological hurdle less prominent in biomass or post-tubercular COPD. Additionally, while bronchodilator reversibility did not reach strict statistical significance ( $P = 0.0604$ ), it trended higher in non-smokers, suggesting an element of differing airway hyperresponsiveness or baseline remodeling that warrants further longitudinal investigation.

Radiological and echocardiographic assessments further delineated the distinct phenotypes of these two cohorts. Chest radiography confirmed that smokers were significantly more likely to develop hyperinflation and emphysematous bullae, whereas non-smokers frequently exhibited post-infectious cicatricial changes, fibrotic bands, or entirely normal radiographs ( $P < 0.0001$ ), a pattern supported by Rani R et al. [11]. Interestingly, despite these morphological differences, the downstream cardiovascular complications—specifically pulmonary artery hypertension (PAH) and dilated cardiomyopathy (DCMP)—did not show statistically significant prevalence differences between the groups. While pulmonary artery hypertension (PAH) was more common among smokers, the differences were not statistically significant. The mechanisms may vary, with hypoxia playing a central role in smokers and structural lung changes contributing to PAH in non-smokers. Although echocardiographic findings did not differ significantly, vigilance for right heart dysfunction remains essential in both cohorts. As noted in the broader literature [12, 13], the pathogenesis likely differs: smokers typically develop PAH secondary to chronic hypoxia and vascular remodeling, whereas non-smokers may develop right heart strain secondary to extensive parenchymal and interstitial fibrosis.

## Significance of study

Our data reinforces the necessity of phenotyping COPD beyond the traditional smoker-centric model. Non-smoker COPD, heavily driven by post-tubercular structural damage and biomass exposure, presents with an equal symptomatic burden but structurally distinct pulmonary mechanics—characterized by preserved gas exchange, differing radiologic patterns, and unique etiologies. Recognizing these distinct profiles is critical for modern respiratory practice, as it demands tailored approaches to diagnosis, physiological monitoring, and potentially divergent therapeutic strategies to address the specific pathophysiological mechanisms driving each etiology.

### Limitations

The study should have more number of subjects for having better results

## Conclusion

This comparative study highlights key differences between smoker and non-smoker COPD patients. While clinical symptoms and exacerbation rates were similar, smokers showed more severe airflow

obstruction, significantly lower DLCO, and typical radiographic findings like hyperinflation and bullous changes. In contrast, non-smokers were more often linked to prior tuberculosis, biomass exposure, and showed fibrotic changes on imaging.

## Declarations

**Conflict of interest:** The authors declare they have no competing interests, and all authors confirm accuracy.

**Funding:** None

**Ethics Approval:** The study protocol was reviewed and approved by the Institutional Ethics Committee, Himalayan institute of medical sciences, Swami Rama Himalayan University, Dehradun vide no SRHU/Reg/Int/2024-82(60)

**Consent:** Written informed consent for the use of data was obtained from the index cases during the study.

**Use of AI-** none

**Contributions:** MK, RK, VJ, SK, and RKG helped treat patients, retrieve data, and conceptualize the manuscript. MV and RK drafted the manuscript. All authors read and revised it critically for important intellectual concepts. RK, MK, VJ, RKG, and SK approved the final version of the manuscript.

## References

1. Agustí A, Celli BR, Criner GJ, Halpin D, Anzueto A, Barnes P, Bourbeau J et al (2023) Global Initiative for Chronic Obstructive Lung Disease 2023 Report: GOLD Executive Summary. *Am J Respir Crit Care Med* 207(7):819–837 PMID: 36856433; PMCID: PMC10111
2. Ruvuna L, Sood A (2020) Epidemiology of Chronic Obstructive Pulmonary Disease. *Clin Chest Med*. ;41(3):315–327. 10.1016/j.ccm.2020.05.002. PMID: 32800187
3. Daniel RA, Aggarwal P, Kalaivani M, Gupta SK (2021 Nov-Dec) Prevalence of chronic obstructive pulmonary disease in India: A systematic review and meta-analysis. *Lung India* 38(6):506–513. 10.4103/lungindia.lungindia\_159\_21. PMID: 34747730; PMCID: PMC8614617
4. Gnatiuc L, Caramori G (2014) COPD in nonsmokers: the biomass hypothesis—to be or not to be? *Eur Respir J*. ;44(1):8–10. 10.1183/09031936.00029114. PMID: 24982047
5. Zhao D, Zhou Y, Jiang C, Zhao Z, He F, Ran P (2018) Small airway disease: A different phenotype of early stage COPD associated with biomass smoke exposure. *Respirology* 23(2):198–205. 10.1111/resp.13176. Epub 2017 Sep 14. PMID: 28906034
6. Shah DM, Kshatriya RM, Paliwal R (2021) Comparison of demographic, clinical, spirometry, and radiological parameters between smoking and non-smoking COPD patients in rural Gujarat, India. *J*

7. Salvi SS, Brashier BB, Londhe J, Pyasi K, Vincent V, Kajale SS, Tambe S, Mandani K, Nair A, Mak SM, Madas S, Juvekar S, Donnelly LE, Barnes PJ (2020) Phenotypic comparison between smoking and non-smoking chronic obstructive pulmonary disease. *Respir Res* 21(1):50. 10.1186/s12931-020-1310-9. PMID: 32050955; PMCID: PMC7017521
8. Takiguchi H, Takeuchi T, Niimi K, Tomomatsu H, Tomomatsu K, Hayama N, Oguma T, Aoki T, Urano T, Asai S, Miyachi H, Asano K (2018) Proportion and clinical characteristics of non-asthmatic non-smokers among adults with airflow obstruction. *PLoS ONE* 13(5):e0196132. 10.1371/journal.pone.0196132. PMID: 29742176; PMCID: PMC5942827
9. Sexton P, Black P, Wu L, Sommerville F, Hamed M, Milne D, Metcalf P, Kolbe J (2014) Chronic obstructive pulmonary disease in non-smokers: a case-comparison study. *COPD*. ;11(1):2–9. doi: 10.3109/15412555.2013.800853. Epub 2013 Jul 11. PMID: 23844977
10. Zhang J, Lin XF, Bai CX (2014) Comparison of clinical features between non-smokers with COPD and smokers with COPD: a retrospective observational study. *Int J Chron Obstruct Pulmon Dis* 9:57–63. 10.2147/COPD.S52416. Epub 2014 Jan 8. PMID: 24426780; PMCID: PMC3890400
11. Rani R, Singh PK, Govindagoudar MB, Gupta T, Parul, Chaudhry D (2023) Nonsmoker COPD represents a clinically Distinct Phenotype: A Prospective Observational Study. *J Assoc Physicians India*. ;71(8):11–12. 10.59556/japi.71.0285. PMID: 37651243
12. Frost AE, Zhao C, Farber HW, Benza R, Yen J, Selej M, Elliott CG (2023) Smoking history and pulmonary arterial hypertension: demographics, onset, and outcomes. *J Heart Lung Transplantation* 42(3):377–389
13. Halvani A, Haddad H (2019) Comparison of the Factors Influencing Pulmonary Arterial Pressure in Smoker and Non-smoker COPD Patients with Pulmonary Hypertension. *Tanaffos* 18(1):41–46 PMID: 31423139; PMCID: PMC6690321

## Figures

# Etiotype

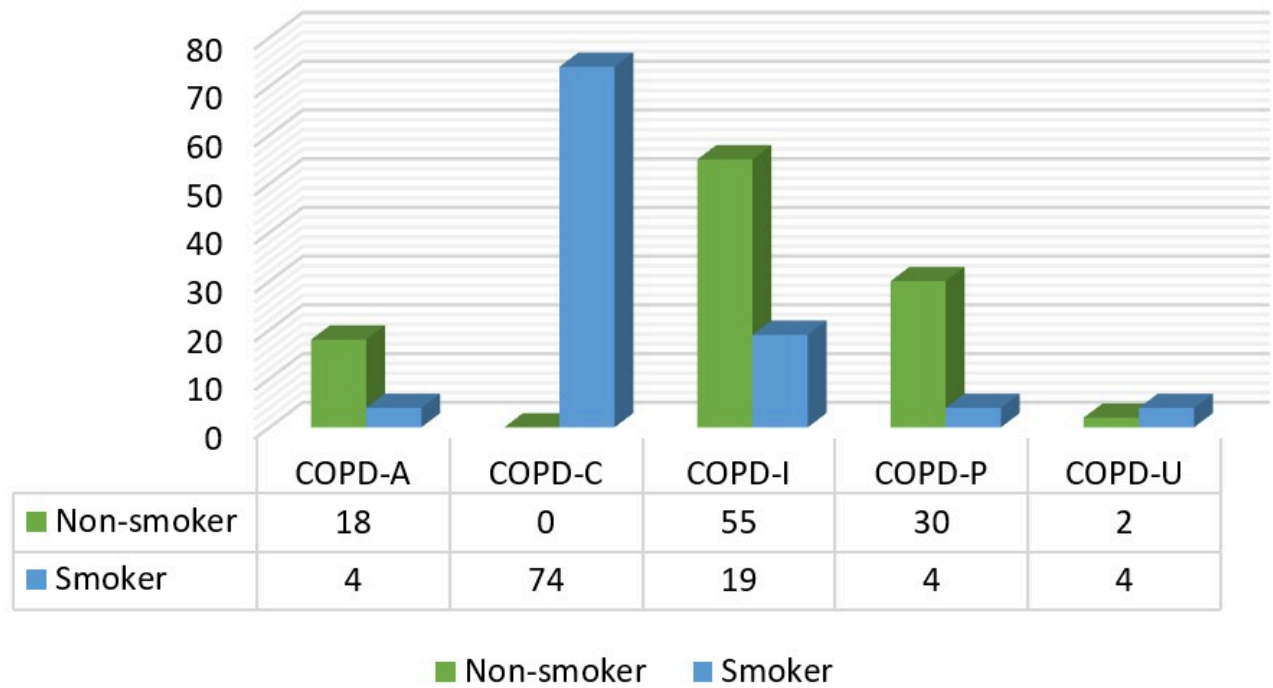


**Figure 1**

COPD Etiotype Findings

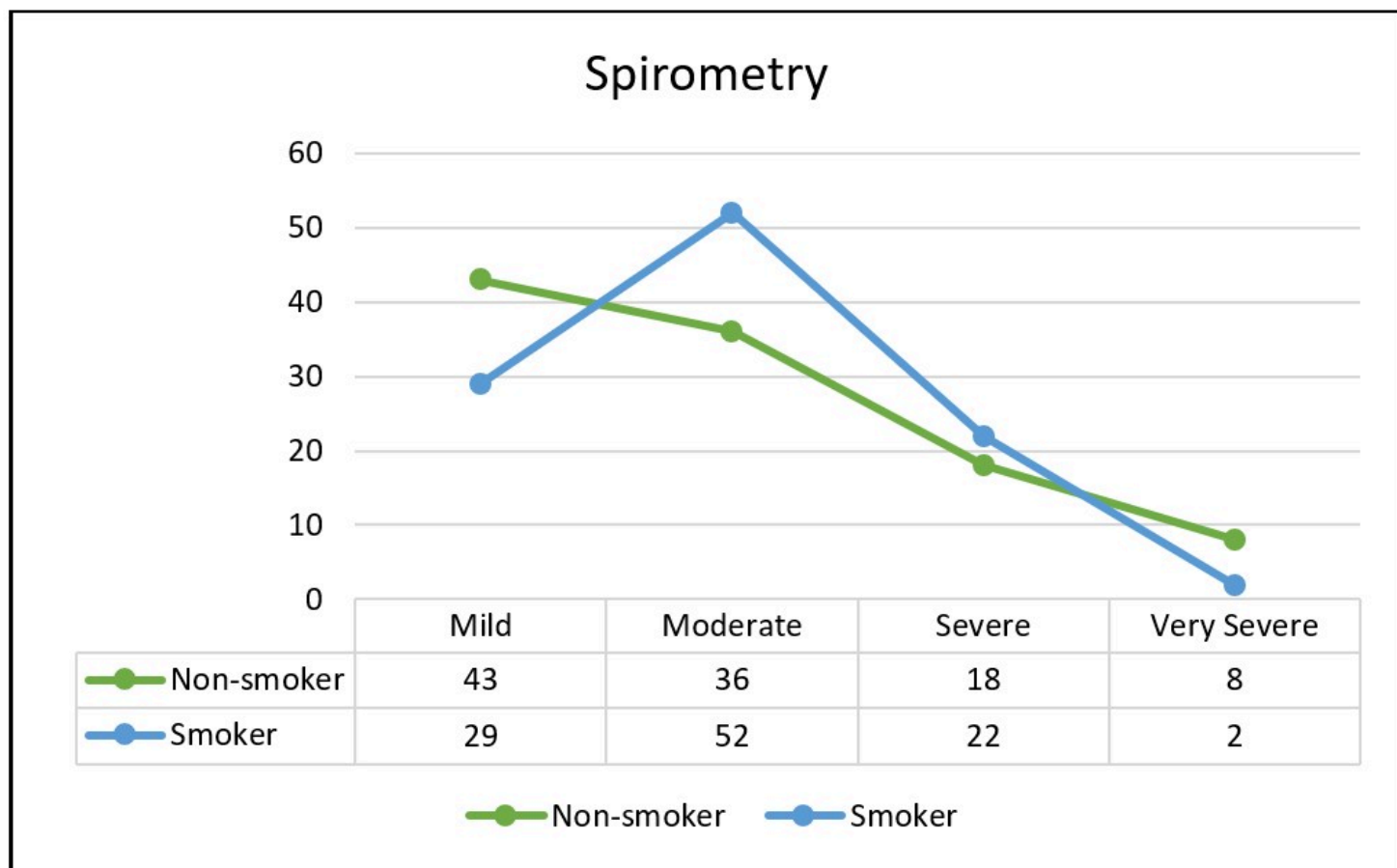


**Figure 2**

Spirometry findings comparing two groups

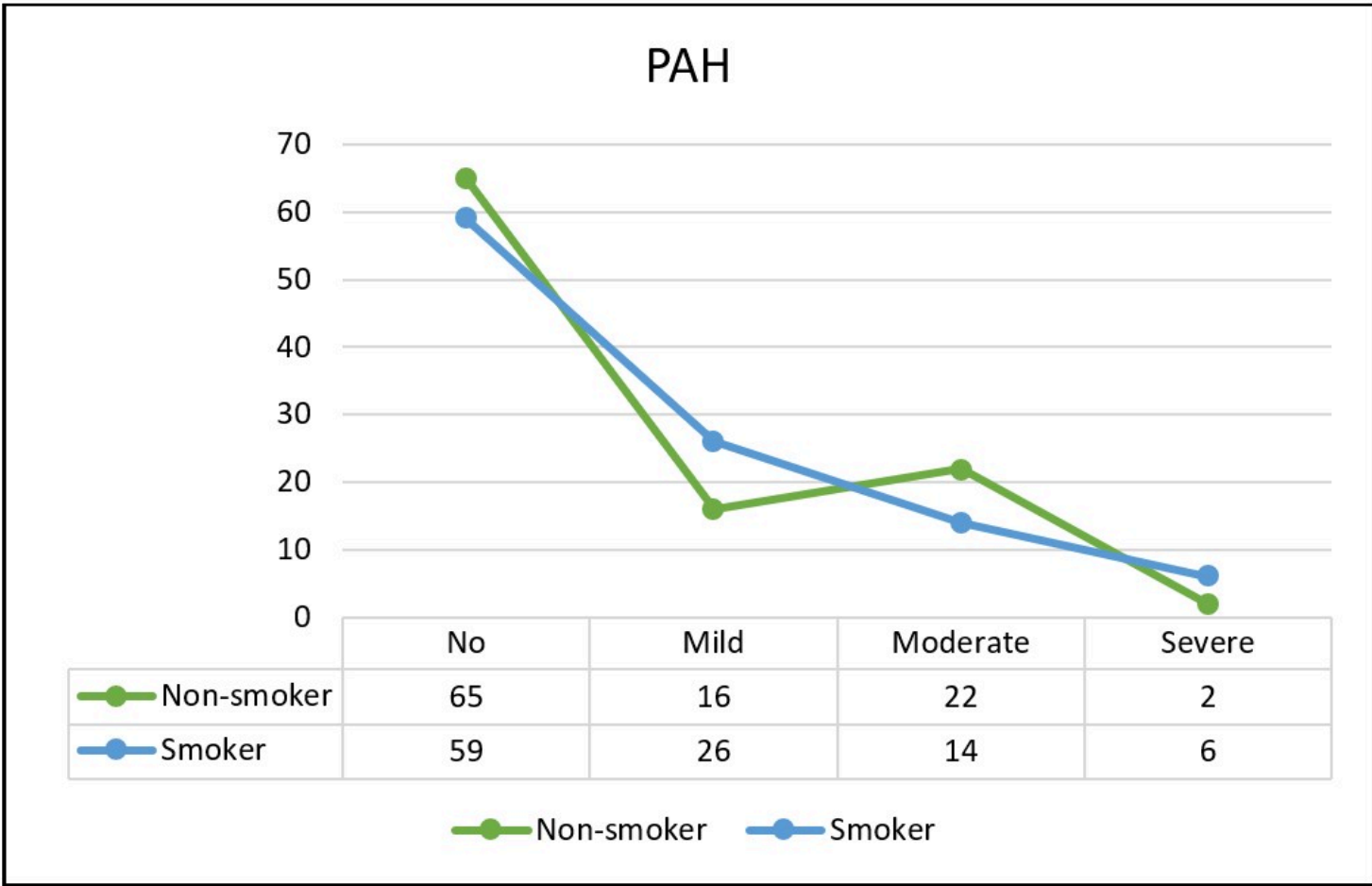


**Figure 3**

Pulmonary Artery Hypertension amongst two groups