

Role of The Lung Microbiome in The Progression and Severity of Chronic Obstructive Pulmonary Disease (COPD)

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Abstract

Background: The lung microbiome, once considered negligible, is now recognized as a key regulator of pulmonary immunity and inflammation. Emerging evidence suggests that alterations in microbial composition (dysbiosis) contribute significantly to the progression and severity of Chronic Obstructive Pulmonary Disease (COPD). The aim is to evaluate the association of lung microbiome diversity and composition with disease severity and exacerbation frequency in COPD patients. **Material and Methods:** A prospective observational study was conducted on 120 COPD patients. Sputum samples were analyzed using 16S rRNA sequencing to assess microbial diversity. Patients were categorized based on GOLD staging and exacerbation frequency. **Results:** Reduced microbial diversity and increased abundance of Proteobacteria (especially Haemophilus) were significantly associated with severe COPD and frequent exacerbations. Dysbiosis correlated with declining lung function (FEV1%). **Conclusion:** Alterations in lung microbiome composition play a critical role in COPD progression and may serve as potential biomarkers and therapeutic targets.

Keywords: COPD, Lung Microbiome, Dysbiosis, Exacerbation, 16S rRNA, Proteobacteria.

Received: 01 March 2026

Revised: 28 April 2026

Accepted: 04 May 2026

Published: 09 May 2026

INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) is a progressive inflammatory lung disorder characterized by airflow limitation and recurrent exacerbations. Traditionally, COPD pathogenesis has been linked to smoking and environmental exposures; however, recent advances have highlighted the role of the lung microbiome in disease progression.^[1] The lung, previously thought to be sterile, harbors a dynamic microbial community consisting of bacteria, fungi, and viruses that influence immune homeostasis.^[2] In healthy individuals, this microbiome maintains a balance between microbial immigration and clearance mechanisms. However, in COPD, this balance is disrupted, leading to dysbiosis characterized by reduced diversity and dominance of pathogenic taxa.^[3] Studies have demonstrated that patients with COPD exhibit increased abundance of Proteobacteria, particularly Haemophilus species, which are associated with airway inflammation and exacerbations.^[4] Furthermore, microbial dysbiosis has been linked to accelerated decline in lung function and disease severity.^[5] The interaction between the lung microbiome and host immunity, including the gut–lung axis, has also emerged as an important contributor to COPD pathophysiology.^[6] Despite growing evidence, the precise relationship between microbiome alterations and clinical outcomes remains incompletely understood.

Therefore, this study aims to evaluate the role of lung microbiome composition in determining the progression and severity of COPD.

MATERIALS AND METHODS

This prospective observational study was carried out over 12 months in a tertiary care center, enrolling 120 patients diagnosed with Chronic Obstructive Pulmonary Disease (COPD) according to GOLD criteria.

Inclusion Criteria

- Age \geq 40 years
- Diagnosed COPD (spirometry confirmed: FEV1/FVC $<$ 0.7)
- Clinically stable or exacerbation cases
- Willing to provide informed consent

Exclusion Criteria

- Active pulmonary tuberculosis
- Lung malignancy
- Recent antibiotic use (within 4 weeks)
- Immunocompromised patients
- Bronchiectasis

Data Collection: Data collection included recording demographic and clinical details of all enrolled participants. Pulmonary function was assessed using spirometry, and forced

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DOI:
10.21276/amit.2026.v13.i2.641

How to cite this article: Anusha P, Kumar BA, Tamrakar S. Role of The Lung Microbiome in The Progression and Severity of Chronic Obstructive Pulmonary Disease (COPD). Acta Med Int. 2026;13(2):43-45.

expiratory volume in one second (FEV1%) was documented. A detailed history of exacerbations was obtained for each patient. Sputum samples were collected under aseptic conditions for further microbiological analysis.

Microbiome Analysis: Microbiome analysis was performed by extracting DNA from sputum samples, followed by 16S rRNA gene sequencing to characterize the microbial composition. Bioinformatics analysis was conducted to evaluate microbial diversity using the Shannon diversity index. Additionally, dominant bacterial taxa present in the samples were identified and analyzed.

Statistical Analysis: Data were analyzed using IBM SPSS Statistics version 25. Continuous variables were expressed as

mean \pm SD and categorical variables as percentages. Group comparisons were performed using ANOVA and Chi-square test as appropriate. Pearson's correlation was used to assess the relationship between microbial diversity and lung function. A p-value <0.05 was considered statistically significant.

RESULTS

A total of 120 COPD patients fulfilling the inclusion criteria were enrolled and analyzed. Baseline demographic and clinical characteristics were recorded, and microbiome profiles were evaluated. The study population was stratified according to GOLD stages and exacerbation frequency. The results are summarized in [Table 1–4 and Figure 1–2].

Table 1: Demographic Characteristics of Study Population

Parameter	Value
Mean Age (Years)	62.4 \pm 8.3
Male (%)	78%
Smokers (%)	72%
Mean FEV1 (%)	54.2 \pm 15.6

COPD was more prevalent among older male smokers with moderate airflow limitation. [Table 1]

Table 2: Microbial Diversity across GOLD Stages

GOLD Stage	Shannon Index
Mild	3.8 \pm 0.5
Moderate	3.1 \pm 0.6
Severe	2.4 \pm 0.4
Very Severe	1.9 \pm 0.3

Microbial diversity significantly decreased with increasing disease severity. [Table 2]

Table 3: Dominant Bacterial Phyla in COPD

Phylum	Percentage (%)
Proteobacteria	48%
Firmicutes	28%
Bacteroidetes	15%
Others	9%

Proteobacteria dominance indicates dysbiosis associated with inflammation. [Table 3]

Table 4: Microbiome vs Exacerbation Frequency

Exacerbations/year	Diversity Index
<2	3.5 \pm 0.4
≥ 2	2.2 \pm 0.5

Frequent exacerbations are associated with reduced microbial diversity. [Table 4]

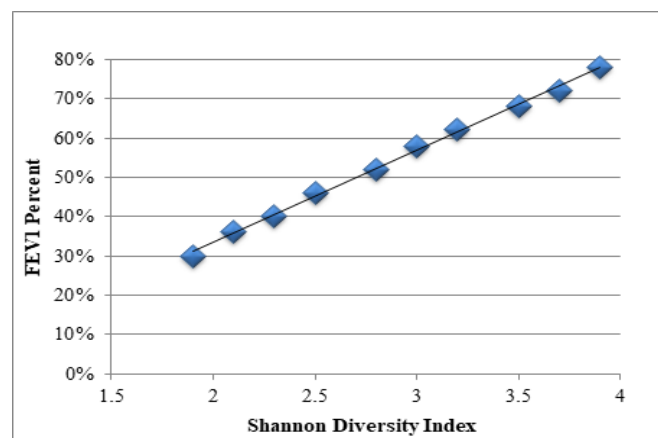


Figure 1: Correlation between Microbial Diversity and Lung Function

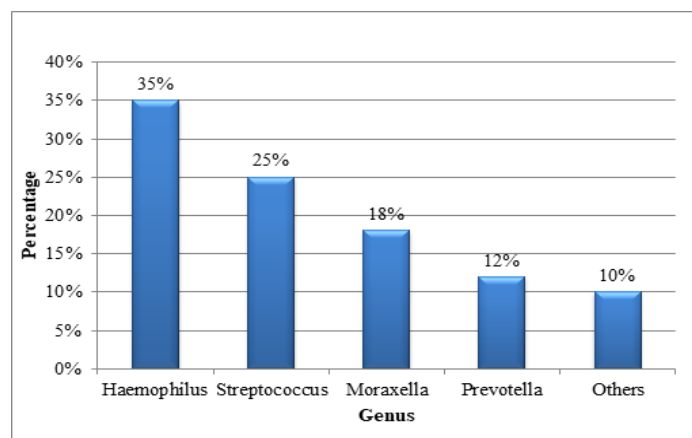


Figure 2: Distribution of Dominant Bacterial Genera in COPD Patients

A positive correlation was observed between microbial diversity and lung function, indicating that reduced diversity is associated with worsening airflow limitation. [Figure 1] Haemophilus species were the most predominant genus, supporting their role in COPD-associated airway inflammation. [Figure 2]

DISCUSSION

Recent evidence suggests that the lung microbiome plays a pivotal role in COPD pathogenesis and progression.^[7] Our study demonstrated a significant reduction in microbial diversity with increasing disease severity, supporting earlier findings that dysbiosis contributes to chronic inflammation and airway damage.^[8] These findings are consistent with the growing body of evidence supporting the role of microbiome dysbiosis in COPD progression. The predominance of Proteobacteria observed in the present study is consistent with previous research linking these organisms to exacerbations and disease severity.^[9] These bacteria are known to trigger pro-inflammatory responses, thereby accelerating lung function decline. Furthermore, reduced diversity in patients with frequent exacerbations indicates that microbial imbalance may predispose individuals to recurrent infections and worsening clinical outcomes.^[10] This aligns with longitudinal studies showing that microbiome instability predicts exacerbation risk. The concept of the gut–lung axis further strengthens the understanding of COPD as a systemic disease influenced by microbial interactions beyond the lungs.^[11] Alterations in microbiota may modulate immune responses, influencing disease severity.

Despite these insights, limitations include reliance on sputum samples and inability to establish causality. Larger longitudinal studies are needed to explore therapeutic interventions targeting the microbiome.

CONCLUSION

This study demonstrates that lung microbiome dysbiosis is closely associated with the progression and severity of COPD. Reduced microbial diversity and increased predominance of pathogenic bacteria were linked to worsening lung function and higher exacerbation frequency. These findings suggest that the lung microbiome may serve as a potential biomarker for disease assessment and a target for personalized therapeutic strategies. However, further large-scale and longitudinal studies are needed to better establish causal relationships and explore microbiome-based interventions in COPD management.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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