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Correlation of Pathogen and Biomarker Levels with COPD Severity and Exacerbation Frequency

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ABSTRACT

Background: Chronic obstructive pulmonary disease (COPD) severity is influenced by airway pathogens, systemic biomarkers, and clinical indices. Their combined evaluation may improve risk stratification.

Material and Methods: A cross-sectional study was conducted on COPD patients stratified by GOLD grade. Data included COPD Assessment Test (CAT), modified Medical Research Council (mMRC) scale, FEV_1% predicted, and exacerbation frequency in the previous 12 months. Sputum cultures identified pathogens, and serum biomarkers (CRP, IL-6, fibrinogen) were quantified. Correlations were analyzed between biomarkers/pathogens and COPD severity indices.

Results: Pathogen colonization was higher in GOLD III–IV patients. CRP and IL-6 levels strongly correlated with CAT scores and exacerbation frequency. FEV_1% predicted showed inverse correlation with both biomarkers and bacterial load. Patients with ≥2 exacerbations exhibited significantly higher biomarker levels and pathogen prevalence.

Conclusion: Specific pathogens and systemic biomarkers correlate with COPD severity and exacerbation frequency, supporting their role in risk stratification.

KEYWORDS: COPD, biomarkers, pathogens, GOLD grade, CAT score, exacerbations

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INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a leading cause of morbidity and mortality worldwide, characterized by persistent airflow limitation and progressive decline in lung function (1). Beyond spirometry, clinical assessment tools such as the COPD Assessment Test (CAT) and modified Medical Research Council (mMRC) dyspnea scale are widely used to evaluate disease impact (2). Frequent exacerbations, defined as acute worsening of respiratory symptoms requiring treatment, further accelerate disease progression and increase healthcare burden (3).

In recent years, research has focused on the role of airway pathogens and systemic biomarkers in influencing COPD severity and outcomes (4). Pathogens such as *Haemophilus influenzae* and *Pseudomonas aeruginosa* are commonly associated with colonization and recurrent exacerbations, especially in severe disease (5). Concurrently, systemic inflammation reflected by biomarkers like C-reactive protein (CRP), interleukin-6 (IL-6), and fibrinogen is increasingly recognized as an indicator of disease activity (6). Elevated levels of these biomarkers have been linked to symptom burden, lung function decline, and future exacerbation risk (7).

The Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines recommend integrating clinical, functional, and biological data to improve risk assessment (8). However, limited studies have simultaneously analyzed correlations between pathogen load, systemic biomarkers, COPD severity indices (CAT, mMRC, FEV_1%), and exacerbation history (9). Understanding these relationships may help identify patients at high risk of progression or frequent exacerbations, thereby informing individualized therapy (10).

This study was designed to evaluate associations between airway pathogens, systemic biomarkers, COPD severity (GOLD grade, CAT score, mMRC, FEV_1% predicted), and exacerbation frequency in the prior year. By integrating microbiological, biomarker, and clinical data, we aimed to provide a comprehensive approach to COPD characterization (11,12).

AIM AND OBJECTIVES

Aim

To assess correlations between pathogens, biomarker levels, and COPD severity indices with exacerbation frequency.

Objectives

1. To evaluate associations between systemic biomarkers and COPD severity indices.
2. To determine correlations between pathogen colonization, biomarkers, and exacerbation frequency.

MATERIAL AND METHODS

This cross-sectional study was conducted in a tertiary care hospital. **Inclusion criteria:** clinically diagnosed COPD patients aged ≥40 years, confirmed by post-bronchodilator $FEV_1/FVC < 0.70$. **Exclusion criteria:** patients with asthma-COPD overlap, active tuberculosis, lung cancer, or recent acute infection.

Patients were stratified into GOLD I–IV grades. CAT score and mMRC dyspnea scale were recorded. Spirometry was performed to measure FEV_1% predicted. Exacerbation frequency in the prior 12 months was documented from medical records.

Sputum samples were processed for bacterial culture to identify common pathogens. Blood samples were collected for CRP, IL-6, and fibrinogen estimation. Statistical analyses included Pearson correlation and regression models to assess associations between biomarkers, pathogens, severity indices, and exacerbations.

RESULTS

Table 1: Distribution of COPD Patients by GOLD Grade and Clinical Indices

GOLD Grade	n	Mean CAT Score	mMRC ≥2 (%)	FEV_1% Predicted (mean ± SD)	≥2 Exacerbations (%)
I	20	10 ± 3	15%	78 ± 5	10%
II	40	16 ± 4	40%	62 ± 6	25%
III	30	22 ± 5	65%	45 ± 7	50%
IV	10	28 ± 6	90%	28 ± 5	70%

Higher GOLD grades showed worse CAT, mMRC, lower FEV_1%, and more exacerbations.

Table 2: Biomarker Levels Across GOLD Grades

GOLD Grade	CRP (mg/L)	IL-6 (pg/mL)	Fibrinogen (mg/dL)
I	2.5 ± 0.6	4.2 ± 1.0	310 ± 40
II	4.8 ± 1.2	6.5 ± 1.5	350 ± 45
III	7.6 ± 1.8	10.2 ± 2.0	420 ± 50
IV	10.5 ± 2.2	14.8 ± 2.5	480 ± 60

Biomarkers rose significantly with increasing GOLD grade.

Table 3: Correlation of Biomarkers and Pathogen Presence with Exacerbation Frequency

Variable	Correlation with Exacerbations (r)	p-value
CRP	0.68	<0.001
IL-6	0.72	<0.001
Fibrinogen	0.60	<0.01

Pathogen colonization	0.65	<0.01
FEV_1% predicted	-0.58	<0.01

Higher biomarkers and pathogen colonization correlated with frequent exacerbations; FEV_1% inversely correlated.

DISCUSSION

This study demonstrates significant correlations between systemic biomarkers, pathogen colonization, COPD severity indices, and exacerbation frequency. As expected, higher GOLD grades were associated with elevated CAT scores, higher mMRC, reduced FEV_1%, and more frequent exacerbations, consistent with established evidence (1,2).

Biomarker analysis showed that CRP, IL-6, and fibrinogen levels increased with COPD severity. These findings support previous studies linking systemic inflammation with worse symptoms and exacerbation risk (3,4). Elevated IL-6 and CRP were particularly strong predictors of exacerbation frequency, suggesting their potential role as accessible clinical biomarkers (5).

Pathogen colonization was more prevalent in GOLD III–IV patients and correlated with higher biomarker levels and frequent exacerbations. Similar results have been reported in studies implicating *Haemophilus influenzae* and *Pseudomonas aeruginosa* in persistent airway infection and exacerbation risk (6,7). These pathogens contribute to airway inflammation, which may explain elevated systemic biomarkers in colonized patients (8).

The inverse correlation between FEV_1% predicted and both biomarkers and exacerbations reinforces spirometry as a key marker of severity but highlights its limitations in predicting systemic inflammation and exacerbation risk alone (9,10). Integration of biomarker and microbiological data with clinical indices may thus provide a more complete risk profile.

Our results align with GOLD recommendations emphasizing multidimensional assessment of COPD (11). They also support ongoing exploration of biomarkers for guiding therapy and predicting outcomes (12). While the study is limited by cross-sectional design and modest sample size, the findings underscore the value of combining clinical, functional, biomarker, and microbiological data for comprehensive COPD evaluation.

CONCLUSION

This study highlights that systemic biomarkers (CRP, IL-6, fibrinogen) and pathogen colonization significantly correlate with COPD severity and exacerbation frequency. Higher GOLD grades were associated with worse clinical indices, increased biomarker levels, and greater exacerbation burden. CRP and IL-6 demonstrated strong predictive value for frequent exacerbations, while pathogen presence amplified disease severity. Integrating biomarkers and microbiological findings with clinical assessment provides a more robust framework for COPD risk stratification and management. Routine incorporation of such multidimensional evaluation may enhance individualized treatment and improve outcomes in COPD patients.

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