Section: Pathology

Original Research Article

PATHOLOGICAL OBSERVATIONS OF INFLAMMATORY MARKERS IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE

P. Rammohan[1], Richards Kakumanu[2], Anil Kumar Kunchy[3]

[1]Associate Professor, Department of Pathology, Government Medical College and General Hospital, Rajanna Sircilla, Telangana, India
[2]Associate Professor, Department of Pathology, Government Medical College and General Hospital, Rajanna Sircilla, Telangana, India
[3]Assistant Professor, Department of Pathology, Government Medical College and General Hospital, Mahbubabad, Telangana, India

Received : 27/01/2025
Received in revised form : 25/03/2025
Accepted : 12/04/2025

Keywords:
COPD, Inflammatory markers, CRP, IL-6, TNF-α, Smoking, Histopathology, GOLD staging.

Corresponding Author:
Dr. P. Rammohan,
Email: drpeddiram@gmail.com

DOI: 10.47009/jamp.2025.7.2.215

Source of Support: Nil,
Conflict of Interest: None declared

Int J Acad Med Pharm
2025; 7 (2); 1066-1070

Abstract

Background: Chronic Obstructive Pulmonary Disease (COPD) is characterized by persistent airflow limitation and systemic inflammation. Inflammatory markers play a pivotal role in disease progression, severity, and exacerbation frequency. This study aims to assess the pathological profiles of key inflammatory markers and their correlation with disease severity and smoking status in COPD patients. **Materials and Methods:** A cross-sectional observational study was conducted on 100 patients diagnosed with COPD. Demographic data, smoking history, and GOLD staging were recorded. Blood samples were analyzed for C-Reactive Protein (CRP), Interleukin-6 (IL-6), Tumor Necrosis Factor-α (TNF-α), fibrinogen, and Erythrocyte Sedimentation Rate (ESR). Correlations between marker levels and COPD severity were assessed. Bronchial biopsies were performed in 30 selected patients to observe histopathological changes. **Result:** The mean age of participants was 64.3 ± 8.5 years, with a male predominance (62%). Elevated inflammatory markers were prevalent: CRP (82%), IL-6 (76%), TNF-α (70%), ESR (75%), and fibrinogen (69%). A strong positive correlation was found between COPD severity and CRP ($r = 0.68$, $p < 0.001$), IL-6 ($r = 0.64$, $p < 0.01$), and TNF-α ($r = 0.59$, $p < 0.01$). Smokers exhibited significantly higher levels of CRP and IL-6 compared to non-smokers ($p < 0.05$). Biopsy findings showed goblet cell hyperplasia (80%), mucosal inflammation (70%), and submucosal fibrosis (60%). **Conclusion:** Inflammatory markers such as CRP, IL-6, and TNF-α are significantly associated with COPD severity and smoking status. Histopathological findings further confirm chronic airway inflammation. These markers may serve as valuable indicators for disease monitoring and personalized interventions.

INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) is a progressive and debilitating respiratory condition characterized by persistent airflow limitation that is not fully reversible. It represents a major global health challenge and is projected to become the third leading cause of death worldwide in the coming years.[1-3] The pathophysiology of COPD involves chronic inflammation affecting the airways, alveolar structures, and pulmonary vasculature, resulting in irreversible structural remodeling and progressive decline in lung function.[4]

Recent research has increasingly recognized COPD as a systemic inflammatory disorder rather than one confined to the lungs. Systemic inflammation plays a significant role in disease progression, comorbidities, and exacerbation risk.[3,5] Key biomarkers such as C-reactive protein (CRP), Interleukin-6 (IL-6), and Tumor Necrosis Factor-alpha (TNF-α) have been identified as reliable indicators of disease activity, correlating with worsening respiratory symptoms, reduced lung function, and increased mortality risk.[1,6]

Multiple studies have demonstrated elevated levels of these inflammatory markers during both stable phases and acute exacerbations of COPD, underscoring their clinical utility in monitoring disease trajectory and guiding therapeutic decisions.[1,5,6] A recent meta-analysis also confirmed a strong association between elevated inflammatory biomarkers and increased risk of COPD, further supporting their diagnostic and prognostic value.[7]

ISSN (O): 2687-5365; ISSN (P): 2753-6556

Tobacco smoking remains the principal etiological factor, exacerbating oxidative stress and systemic inflammation, thereby accelerating pulmonary injury and functional decline.[3,4] Histopathological evidence, including goblet cell hyperplasia, submucosal fibrosis, and inflammatory cell infiltration, reflects the ongoing epithelial damage and airway remodeling that contribute to airflow obstruction.[1,4]

Despite growing evidence, the relationship between systemic inflammatory markers, COPD severity, smoking status, and histopathological alterations remains inadequately characterized in many clinical settings. This study aims to evaluate the levels of key inflammatory markers in COPD patients and explore their association with disease severity and smoking, along with supportive histopathological findings from bronchial biopsies.

MATERIALS AND METHODS

Study Design and Setting: This was a cross-sectional observational study conducted in the Department of General Medicine at Government Medical College, Rajanna Sircilla, Telangana, India, over a period of six months from September 2024 to February 2025.

Study Population: A total of 100 patients clinically diagnosed with Chronic Obstructive Pulmonary Disease (COPD) based on GOLD (Global Initiative for Chronic Obstructive Lung Disease) criteria were enrolled in the study. All participants were either outpatients or inpatients attending the General Medicine department during the study period.

Inclusion Criteria

- Patients aged ≥ 40 years
- Diagnosed with COPD based on spirometry (FEV1/FVC < 0.7)
- Stable patients (not experiencing acute exacerbation at the time of recruitment)
- Patients willing to give informed consent

Exclusion Criteria

- Patients with concurrent asthma, tuberculosis, pneumonia, or other acute/chronic respiratory illnesses
- Patients with autoimmune disorders, malignancies, or on long-term immunosuppressive therapy
- Patients with acute infections at the time of sampling

Data Collection Procedure: Detailed clinical history, including age, sex, smoking status, and comorbidities, was recorded. Pulmonary function was assessed using spirometry, and patients were categorized into GOLD stages I–IV based on FEV1 values.

Inflammatory Marker Assessment: Venous blood samples were collected under aseptic precautions to assess the following markers:

C-Reactive Protein (CRP): Measured using high-sensitivity immunoturbidimetry

Interleukin-6 (IL-6) and TNF-α: Quantified using ELISA kits (Enzyme-Linked Immunosorbent Assay)

Fibrinogen: Determined using Clauss method

Erythrocyte Sedimentation Rate (ESR): Assessed via Westergren method

Histopathological Analysis: Bronchial biopsies were performed in a subset of 30 consenting patients using bronchoscopy. The tissue samples were fixed in formalin, stained with Hematoxylin and Eosin (H&E), and examined microscopically for:

Goblet cell hyperplasia

Neutrophilic and macrophage infiltration

Submucosal fibrosis and epithelial metaplasia

Statistical Analysis: Data were entered in Microsoft Excel and analyzed using SPSS software version 25.0. Descriptive statistics were used for demographic and clinical variables. Correlation between COPD severity and inflammatory markers was analyzed using Pearson's correlation coefficient (r). A p-value < 0.05 was considered statistically significant.

Ethical Considerations: Ethical clearance was obtained from the Institutional Ethics Committee of Government Medical College, Rajanna Sircilla. Written informed consent was obtained from all study participants prior to enrollment.

RESULTS

Demographic and Clinical Characteristics: A total of 100 patients diagnosed with Chronic Obstructive Pulmonary Disease (COPD) were included in the study. The mean age of the cohort was 64.3 ± 8.5 years. Among them, 62% were male and 38% were female. A majority of the participants (70%) reported a history of smoking, while 30% were either non-smokers or former smokers [Table 1].

COPD Severity Classification: Patients were classified according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) staging criteria. The distribution showed that 14% of patients were in Stage I (mild), 38% in Stage II (moderate), 34% in Stage III (severe), and 14% in Stage IV (very severe) [Table 2].

Inflammatory Marker Profiles: Analysis of systemic inflammatory markers revealed elevated levels across most patients. The mean levels of C-Reactive Protein (CRP), Interleukin-6 (IL-6), and Tumor Necrosis Factor-alpha (TNF-α) were 11.4 ± 6.8 mg/L, 15.2 ± 9.3 pg/mL, and 13.6 ± 7.1 pg/mL respectively. In addition, fibrinogen and erythrocyte sedimentation rate (ESR) were elevated beyond normal physiological ranges in a substantial proportion of participants. Notably, 82% of patients had elevated CRP, 76% had elevated IL-6, and 70% had elevated TNF-α [Table 3].

Correlation Between Inflammation and Disease Severity: A statistically significant positive correlation was observed between the severity of COPD (as defined by GOLD stage) and the levels of inflammatory markers. CRP demonstrated the

ISSN (O): 2687-5365; ISSN (P): 2753-6556

strongest correlation ($r = 0.68$, $p < 0.001$), followed by IL-6 ($r = 0.64$, $p < 0.01$) and TNF-α ($r = 0.59$, $p < 0.01$), indicating that systemic inflammation increases with disease progression [Table 4].

Effect of Smoking on Inflammatory Response: Smokers had significantly higher levels of CRP and IL-6 compared to non-smokers and former smokers ($p < 0.05$). Additionally, elevated TNF-α levels were particularly noted among patients in GOLD Stage III and IV with a positive smoking history, suggesting a compounding effect of smoking on systemic inflammation.

Histopathological Observations: Bronchial biopsy samples were obtained from a subset of 30 patients for pathological assessment. Goblet cell hyperplasia was observed in 80% of samples, while 70% exhibited mucosal infiltration with neutrophils and macrophages. Submucosal fibrosis and epithelial metaplasia were identified in 60% of cases, indicating chronic airway remodeling and inflammation characteristic of advanced COPD [Table 5].

Table 1: Study Population Characteristics.

Parameter	Value
Mean Age (years)	64.3 ± 8.5
Male (%)	62%
Female (%)	38%
Smokers (%)	70%
Non-smokers/Former Smokers (%)	30%

Table 2: Distribution of COPD Severity (GOLD Classification)

GOLD Stage	No. of Patients	Percentage
Stage I (Mild)	14	14%
Stage II (Moderate)	38	38%
Stage III (Severe)	34	34%
Stage IV (Very Severe)	14	14%

Table 3: Inflammatory Markers in COPD Patients (n=100)

Marker	Normal Range	Mean ± SD	Elevated (%)
C-Reactive Protein (CRP, mg/L)	<5	11.4 ± 6.8	82%
Interleukin-6 (IL-6, pg/mL)	<7	15.2 ± 9.3	76%
Tumor Necrosis Factor-α (TNF-α, pg/mL)	<8	13.6 ± 7.1	70%
Fibrinogen (g/L)	2–4	5.1 ± 1.3	69%
Erythrocyte Sedimentation Rate (mm/hr)	<20	38.7 ± 12.6	75%

Table 4: Correlation Between COPD Severity and Inflammatory Markers

Marker	Correlation Coefficient (r)	p-value
CRP	0.68	< 0.001
IL-6	0.64	< 0.01
TNF-α	0.59	< 0.01

Table 5: Histopathological Findings in Bronchial Biopsies (n=30)

Finding	Prevalence (%)
Goblet cell hyperplasia	80%
Mucosal infiltration with neutrophils and macrophages	70%
Submucosal fibrosis and epithelial metaplasia	60%

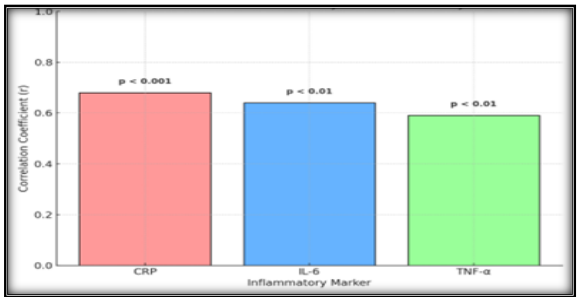

Figure 1: Correlation Between COPD Severity and Inflammatory Markers

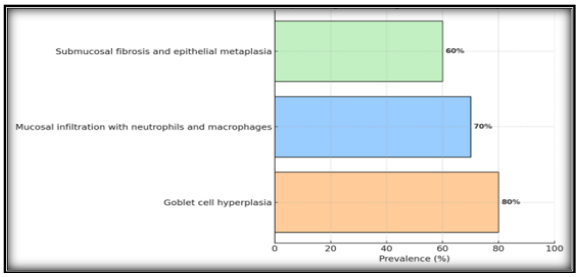

Figure 2: Histopathological Findings in Bronchial Biopsies

DISCUSSION

This study evaluated systemic inflammatory markers and histopathological patterns in patients with chronic obstructive pulmonary disease (COPD),

ISSN (O): 2687-5365; ISSN (P): 2753-6556

emphasizing their association with disease severity and smoking status. The elevated levels of CRP (82%), IL-6 (76%), and TNF-α (70%) observed in this study reinforce the recognition of COPD as a systemic inflammatory disorder rather than a disease confined to the lungs, a notion increasingly supported in the literature.[8,11]

CRP showed the strongest positive correlation with GOLD staging ($r = 0.68$, $p < 0.001$), consistent with previous findings that highlighted its role as a reliable surrogate marker of disease activity and cardiovascular comorbidity in COPD patients.[8] IL-6 and TNF-α, known for their pro-inflammatory and catabolic roles, also demonstrated significant positive associations with COPD severity. These cytokines contribute to systemic manifestations such as skeletal muscle dysfunction, cachexia, and heightened exacerbation frequency.[9-12] In particular, Formiga et al. demonstrated that higher systemic levels of these markers were associated with inspiratory muscle dysfunction, underscoring their physiological impact beyond pulmonary involvement.[9]

Larsson,[11] and Meshram et al,[12] similarly reported that elevated inflammatory markers, especially in patients with higher BODE index scores, reflect an underlying systemic process contributing to overall morbidity. Moreover, the inflammatory burden was notably higher in smokers compared to non-smokers in our study. This observation is well-supported by studies indicating that ongoing exposure to tobacco smoke perpetuates the systemic inflammatory state and accelerates disease progression.[8,13]

Histopathological examination revealed structural changes typical of chronic inflammation, including goblet cell hyperplasia, neutrophilic and macrophage infiltration, epithelial metaplasia, and submucosal fibrosis. These findings mirror those reported by O'Donnell et al., who described a similar inflammatory cell profile in bronchial biopsies of COPD patients.[13] Furthermore, the relationship between inflammation and genetic predisposition was also emphasized by Serapinas et al., who showed that patients with different α1 antitrypsin genotypes manifested varying degrees of inflammatory marker expression, suggesting the influence of genetic factors on systemic inflammation in COPD.[14]

Overall, the integration of biochemical markers and histopathological evidence presents a compelling case for the routine use of inflammatory profiling in COPD. Such profiling could improve disease monitoring, risk stratification, and personalized therapeutic strategies.

Strengths and Limitations: The major strength of this study lies in its holistic approach, incorporating inflammatory biomarkers, clinical staging, and histopathological findings. This comprehensive methodology offers a clearer understanding of the pathophysiological underpinnings of COPD. Nevertheless, limitations include the single-center, cross-sectional design and relatively modest sample size, which may limit generalizability and prevent causal inferences. Longitudinal studies with serial biomarker measurements are needed to establish temporal patterns and predict exacerbation risk more accurately.

Clinical Implications: The results underline the utility of inflammatory markers—particularly CRP, IL-6, and TNF-α as potential biomarkers for COPD severity stratification. Their integration into routine evaluation may help identify patients at higher risk for rapid progression or frequent exacerbations, enabling tailored therapeutic strategies, including anti-inflammatory interventions.

CONCLUSION

This study highlights the significant role of systemic inflammation in the pathogenesis and progression of Chronic Obstructive Pulmonary Disease (COPD). Elevated levels of inflammatory markers such as CRP, IL-6, and TNF-α were strongly associated with increasing disease severity as per GOLD staging. Smoking was identified as a major contributor to heightened inflammatory responses. Histopathological findings further supported the presence of chronic airway remodeling in advanced cases. These results emphasize the potential utility of inflammatory biomarkers in clinical assessment, risk stratification, and therapeutic decision-making. Integrating biomarker profiling into routine COPD management may facilitate early intervention and improved disease monitoring, ultimately leading to better patient outcomes and reduced healthcare burden.

REFERENCES

1. Ramya PA, Mohapatra MM, Saka VK, Kar R, Chakkalakkoombil SV, Vemuri MB. Haematological and Inflammatory Biomarkers Among Stable COPD and Acute Exacerbations of COPD Patients. Sultan Qaboos Univ Med J. 2023 May;23(2):239-244. doi: 10.18295/squmj.12.2022.062. Epub 2023 May 31. PMID: 37377829; PMCID: PMC10292595.
2. Dahl M, Nordestgaard BG. Markers of early disease and prognosis in COPD. Int J Chron Obstruct Pulmon Dis. 2009;4:157-67. doi: 10.2147/copd.s3106. Epub 2009 Apr 15. PMID: 19436688; PMCID: PMC2672792.
3. Wechsler ME, Wells JM. What every clinician should know about inflammation in COPD. ERJ Open Res. 2024 Sep 23;10(5):00177-2024. doi: 10.1183/23120541.00177-2024. PMID: 39319045; PMCID: PMC11417604.
4. Kim V, Rogers TJ, Criner GJ. New concepts in the pathobiology of chronic obstructive pulmonary disease. Proc Am Thorac Soc. 2008 May 1;5(4):478-85. doi: 10.1513/pats.200802-014ET. PMID: 18453359; PMCID: PMC2645323.
5. Stockley RA. Biomarkers in COPD: time for a deep breath. Thorax. 2007 Aug;62(8):657-60. doi: 10.1136/thx.2007.084228. PMID: 17687095; PMCID: PMC2117266.
6. Heidari B. The importance of C-reactive protein and other inflammatory markers in patients with chronic obstructive pulmonary disease. Caspian J Intern Med. 2012 Spring;3(2):428-35. PMID: 24358439; PMCID: PMC3861908.
7. Su B, Liu T, Fan H, Chen F, Ding H, Wu Z, et al. Inflammatory Markers and the Risk of Chronic Obstructive Pulmonary Disease: A Systematic Review and Meta-Analysis. PLoS One. 2016 Apr 22;11(4):e0150586. doi:

ISSN (O): 2687-5365; ISSN (P): 2753-6556

10.1371/journal.pone.0150586. PMID: 27104349; PMCID: PMC4841528.
8. Sevenoaks MJ, Stockley RA. Chronic Obstructive Pulmonary Disease, inflammation and co-morbidity--a common inflammatory phenotype? Respir Res. 2006 May 2;7(1):70. doi: 10.1186/1465-9921-7-70. PMID: 16669999; PMCID: PMC1479815.
9. Formiga MF, Vital I, Urdaneta G, Masters B, Herrera J, Campos MA, et al. Higher serum levels of systemic inflammatory markers are linked to greater inspiratory muscle dysfunction in COPD. Clin Respir J. 2019 Apr;13(4):247-255. doi: 10.1111/crj.13006. Epub 2019 Mar 10. PMID: 30773817.
10. Oishi K, Matsunaga K, Shirai T, Hirai K, Gon Y. Role of Type2 Inflammatory Biomarkers in Chronic Obstructive Pulmonary Disease. J Clin Med. 2020 Aug 18;9(8):2670. doi: 10.3390/jcm9082670. PMID: 32824775; PMCID: PMC7464674.
11. Larsson K. Inflammatory markers in COPD. Clin Respir J. 2008 Oct;2 Suppl 1:84-7. doi: 10.1111/j.1752-699X.2008.00089.x. PMID: 20298355.
12. Meshram PL, Shinde SN, Ramraje NN, Hegde RR. Study of inflammatory markers and BODE index in chronic obstructive pulmonary disease. Lung India. 2018 Jan-Feb;35(1):37-40. doi: 10.4103/lungindia.lungindia_46_17. PMID: 29319032; PMCID: PMC5760865.
13. O'Donnell R, Breen D, Wilson S, Djukanovic R. Inflammatory cells in the airways in COPD. Thorax. 2006 May;61(5):448-54. doi: 10.1136/thx.2004.024463. PMID: 16648353; PMCID: PMC2111192.
14. Serapinas D, Sitkauskiene B, Sakalauskas R. Inflammatory markers in chronic obstructive pulmonary disease patients with different α1 antitrypsin genotypes. Arch Med Sci. 2012 Dec 20;8(6):1053-8. doi: 10.5114/aoms.2012.32414. Epub 2012 Dec 19. PMID: 23319981; PMCID: PMC3542496.

ISSN (O): 2687-5365; ISSN (P): 2753-6556