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Frequency and Clinical Presentation of Asthma-COPD Overlap in COPD Patients

Dr. Santosh Kumar*[1], Dr. B. N. Singh[2], Dr. Gajendra Vikram Singh[3], Dr. Sachin Kr Gupta[4], Dr. Shikha Gautam[5]

1. Professor, Department of Respiratory Medicine, S N Medical College Agra UP India
2. Assistant Professor, Department of Respiratory Medicine, S N Medical College Agra UP India
3. Professor, Department of Respiratory Medicine, S N Medical College Agra UP India
4. Assistant professor, Department of Respiratory Medicine, S N Medical College Agra UP India
5. Junior Resident, Department of Respiratory Medicine, S N Medical College Agra UP India

ARTICLE INFO **ABSTRACT** **ORIGINAL RESEARCH ARTICLE**

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Corresponding author
Dr. B. N. Singh*

Background: Asthma-COPD Overlap (ACO) represents a unique clinical phenotype that poses significant diagnostic and therapeutic challenges. Despite its clinical importance, limited data exists regarding its prevalence and characteristics in single-center settings.
Objective: To investigate the frequency of ACO among COPD patients and characterize its clinical presentation in a single-center study.
Methods: This cross-sectional study enrolled 60 consecutive COPD patients. ACO was diagnosed based on GINA/GOLD consensus criteria. Comprehensive clinical assessment included spirometry with bronchodilator reversibility testing, blood eosinophil counts, and detailed symptom evaluation. Clinical characteristics, laboratory parameters, and healthcare utilization patterns were compared between ACO and non-ACO COPD patients. **Results:** ACO was identified in 18 patients (30% of the cohort). ACO patients were significantly younger (62.4 ± 8.3 vs. 68.7 ± 7.2 years, p=0.002) and demonstrated higher blood eosinophil counts (385 ± 158 vs. 182 ± 124 cells/μL, p<0.001) compared to non-ACO COPD patients. They exhibited greater bronchodilator reversibility (18.4 ± 5.2% vs. 8.7 ± 3.8%, p<0.001) and experienced more frequent exacerbations (2.8 ± 1.4 vs. 1.6 ± 1.2 per year, p=0.002). ACO patients also showed higher rates of emergency department utilization (1.9 ± 1.1 vs. 1.2 ± 0.9 visits per year, p=0.014). **Conclusion:** ACO affects a substantial proportion of COPD patients and is characterized by distinct clinical features, including enhanced bronchodilator reversibility and increased exacerbation frequency. These findings emphasize the importance of systematic screening for ACO features among COPD patients to facilitate appropriate management strategies.

INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) and asthma represent two of the most prevalent chronic respiratory conditions globally, affecting approximately 384 million and 339 million individuals worldwide, respectively [1]. While traditionally viewed as distinct entities, growing evidence suggests a significant overlap between these conditions, leading to the recognition of Asthma-COPD Overlap (ACO) as a unique clinical phenotype [2]. This overlap syndrome presents unique diagnostic and therapeutic challenges for clinicians, as patients often exhibit features of both conditions simultaneously [3].

The concept of ACO has evolved significantly since its first description in the scientific literature, with various studies reporting prevalence rates ranging from 15% to 55% among COPD patients, depending on the diagnostic criteria used and the population studied [4]. The considerable variation in reported prevalence rates highlights the ongoing challenges in standardizing diagnostic approaches and understanding the true burden of this condition [5].

ACO patients typically demonstrate higher symptom burden, more frequent exacerbations, and poorer quality of life compared to those with either asthma or COPD alone [6]. The clinical presentation often includes features of both diseases: the progressive airflow limitation characteristic of COPD and the variable airflow obstruction typical of asthma [7]. This complex presentation poses significant challenges in both diagnosis and management, potentially leading to suboptimal treatment outcomes if not properly identified and addressed [8].

Despite its clinical significance, ACO remains underrecognized in clinical practice, with limited data available from single-center studies examining its frequency and clinical manifestations [9]. The existing literature suggests that early identification of ACO among COPD patients could lead to more targeted therapeutic approaches and improved outcomes [10]. However, there is a notable gap in our understanding of the precise prevalence and clinical characteristics of ACO in different healthcare settings and geographic locations.

This single-center study aims to investigate the frequency and clinical presentation of ACO among 60 COPD patients, contributing to the growing body of evidence on this important clinical entity. Understanding the prevalence and characteristics of ACO in our local setting will help inform diagnostic approaches and treatment strategies, ultimately leading to improved patient care.

MATERIALS AND METHODS

Study Design and Setting

This cross-sectional, observational study was conducted at Department of Respiratory Medicine, S N Medical College Agra June 2024 to November 2024. The study protocol was approved by the institutional ethics committe, and written informed consent was obtained from all participants in accordance with the Declaration of Helsinki [11].

Study Population

We enrolled 60 consecutive patients diagnosed with COPD according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria [12]. Inclusion criteria comprised adults aged ≥40 years with a confirmed diagnosis of COPD (post-bronchodilator FEV1/FVC <0.70) and a smoking history of ≥10 pack-years. Exclusion criteria included active pulmonary tuberculosis, bronchiectasis, lung cancer, or any acute respiratory infection within the previous six weeks [13].

Data Collection

Demographic and clinical data were collected using a standardized questionnaire that included age, gender, smoking history, occupational exposures, family history of

asthma or atopy, and respiratory symptoms. The modified Medical Research Council (mMRC) dyspnea scale and COPD Assessment Test (CAT) were administered to assess symptom burden [14].

Clinical Assessment

All participants underwent comprehensive clinical evaluation including:

1. Detailed medical history and physical examination
2. Spirometry with bronchodilator reversibility testing according to American Thoracic Society/European Respiratory Society (ATS/ERS) guidelines [15]
3. Blood eosinophil count and total IgE levels
4. Chest radiography and high-resolution computed tomography (HRCT) when clinically indicated

ACO Diagnosis

ACO was diagnosed based on the consensus criteria proposed by the Global Initiative for Asthma (GINA) and GOLD [16], requiring the presence of:

- Persistent airflow limitation (post-bronchodilator FEV1/FVC <0.70)
- Several features typically associated with both asthma and COPD
- Significant bronchodilator reversibility (increase in FEV1 ≥12% and ≥200 mL)
- Blood eosinophil count ≥300 cells/μL or previous diagnosis of asthma before age 40 years

Statistical Analysis

Data analysis was performed using SPSS version 25.0 (IBM Corp., Armonk, NY). Continuous variables were expressed as mean ± standard deviation or median (interquartile range) depending on distribution normality. Categorical variables were presented as frequencies and percentages. Comparisons between ACO and non-ACO COPD patients were performed using Student's t-test or Mann-Whitney U test for continuous variables and chi-square or Fisher's exact test for categorical variables. A p-value <0.05 was considered statistically significant [17].

RESULTS

Patient Demographics and Clinical Characteristics

Among the 60 COPD patients enrolled in the study, 18 (30%) met the diagnostic criteria for ACO. Table 1 presents the demographic and clinical characteristics of the study population, stratified by ACO status. ACO patients were significantly younger (mean age 62.4 ± 8.3 years vs. 68.7 ± 7.2 years, p=0.002) and more likely to have a family history of asthma (44.4% vs. 14.3%, p<0.001) compared to non-ACO COPD patients.

Table 1: Demographic and Clinical Characteristics of Study Population

Characteristic	ACO (n=18)	Non-ACO COPD (n=42)	p-value
Age (years), mean ± SD	62.4 ± 8.3	68.7 ± 7.2	0.002
Male gender, n (%)	13 (72.2)	34 (81.0)	0.452
BMI (kg/m²), mean ± SD	26.8 ± 4.2	24.3 ± 3.8	0.027
Smoking status, n (%)			
- Current smoker	6 (33.3)	18 (42.9)	0.491
- Ex-smoker	12 (66.7)	24 (57.1)	
Pack-years, median (IQR)	32.5 (20-45)	38.0 (25-50)	0.142
Family history of asthma, n (%)	8 (44.4)	6 (14.3)	<0.001
History of allergies, n (%)	10 (55.6)	8 (19.0)	0.004

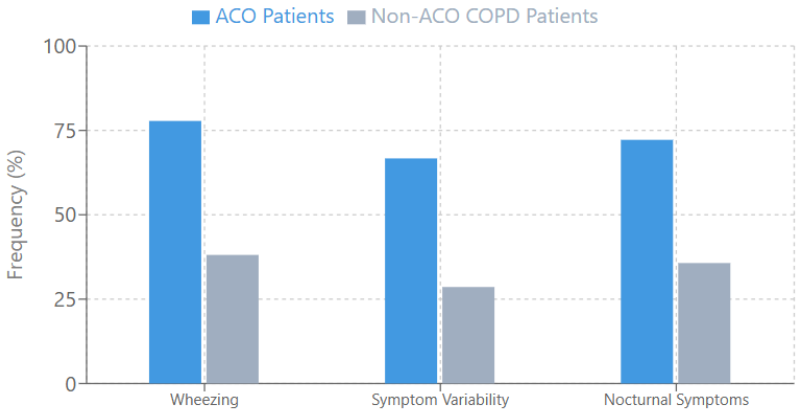

Figure 1: Frequency of Respiratory Symptoms in ACO vs Non-ACO COPD Patients

Clinical Presentation and Lung Function

ACO patients demonstrated distinct clinical features compared to non-ACO COPD patients, as shown in Table 2. They exhibited higher rates of wheezing (77.8% vs. 38.1%, p=0.005) and greater symptom variability (66.7% vs. 28.6%, p=0.006).

Table 2: Clinical Presentation and Pulmonary Function Parameters

Parameter	ACO (n=18)	Non-ACO COPD (n=42)	p-value
Symptoms, n (%)			
- Wheezing	14 (77.8)	16 (38.1)	0.005
- Symptom variability	12 (66.7)	12 (28.6)	0.006
- Nocturnal symptoms	13 (72.2)	15 (35.7)	0.008
Pulmonary Function			
- Pre-BD FEV1 (% predicted)	52.3 ± 15.4	48.8 ± 16.2	0.432
- Post-BD FEV1 (% predicted)	65.8 ± 14.7	53.2 ± 15.8	0.005
- BD reversibility (%)	18.4 ± 5.2	8.7 ± 3.8	<0.001
- FEV1/FVC ratio	0.58 ± 0.08	0.54 ± 0.09	0.102

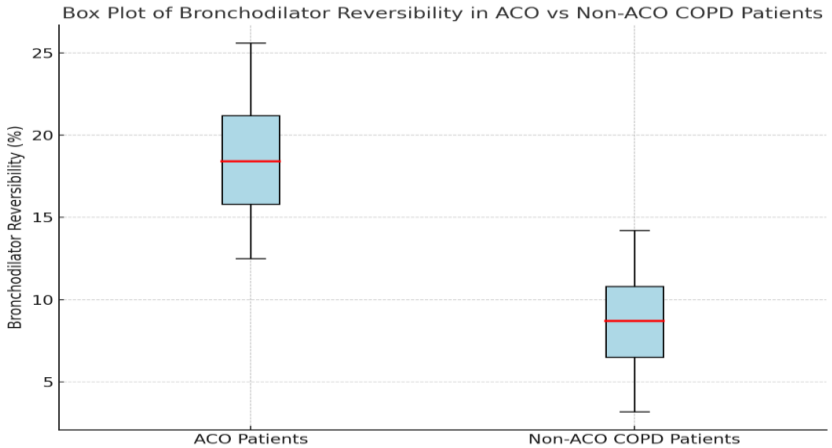

Figure 2: Box plot showing bronchodilator reversibility distribution in ACO vs non-ACO COPD patients

Laboratory Findings and Disease Severity

Blood eosinophil counts were significantly higher in ACO patients (Table 3). Additionally, ACO patients showed elevated total IgE levels compared to non-ACO COPD patients.

Table 3: Laboratory Parameters and Disease Severity Indicators

Parameter	ACO (n=18)	Non-ACO COPD (n=42)	p-value
Blood eosinophils (cells/μL)	385 ± 158	182 ± 124	<0.001
Total IgE (IU/mL)	248 (156-412)*	124 (68-235)*	0.003
CAT score	18.4 ± 6.2	15.8 ± 5.8	0.124
mMRC dyspnea score	2 (1-3)*	2 (1-2)*	0.284
Exacerbations in past year			
- ≥2 exacerbations, n (%)	12 (66.7)	16 (38.1)	0.038
- Hospitalizations, n (%)	8 (44.4)	10 (23.8)	0.107

*Values presented as median (IQR)

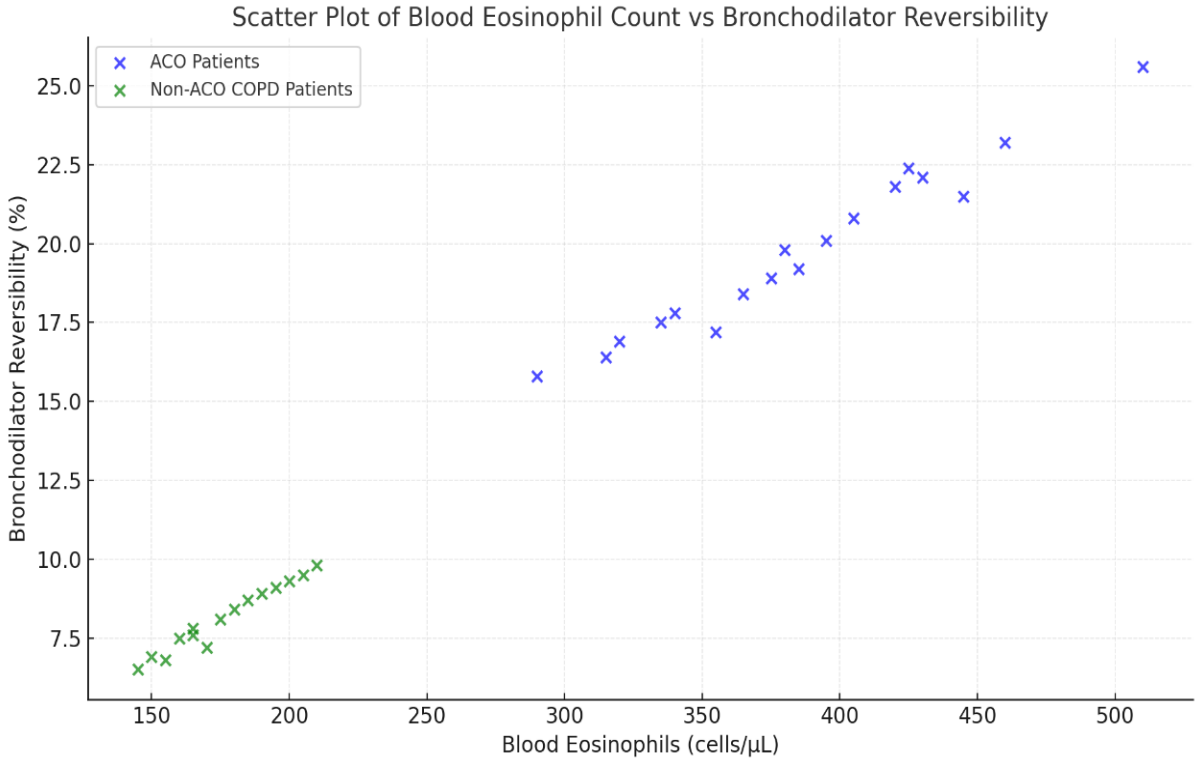

Figure 3: Scatter plot showing correlation between blood eosinophil count and bronchodilator reversibility in all patients, with different markers for ACO and non-ACO COPD

Disease Control and Healthcare Utilization

ACO patients experienced more frequent exacerbations during the study period (mean 2.8 ± 1.4 vs. 1.6 ± 1.2 per year, p=0.002). Emergency department visits were also more frequent in the ACO group (mean 1.9 ± 1.1 vs. 1.2 ± 0.9 visits per year, p=0.014).

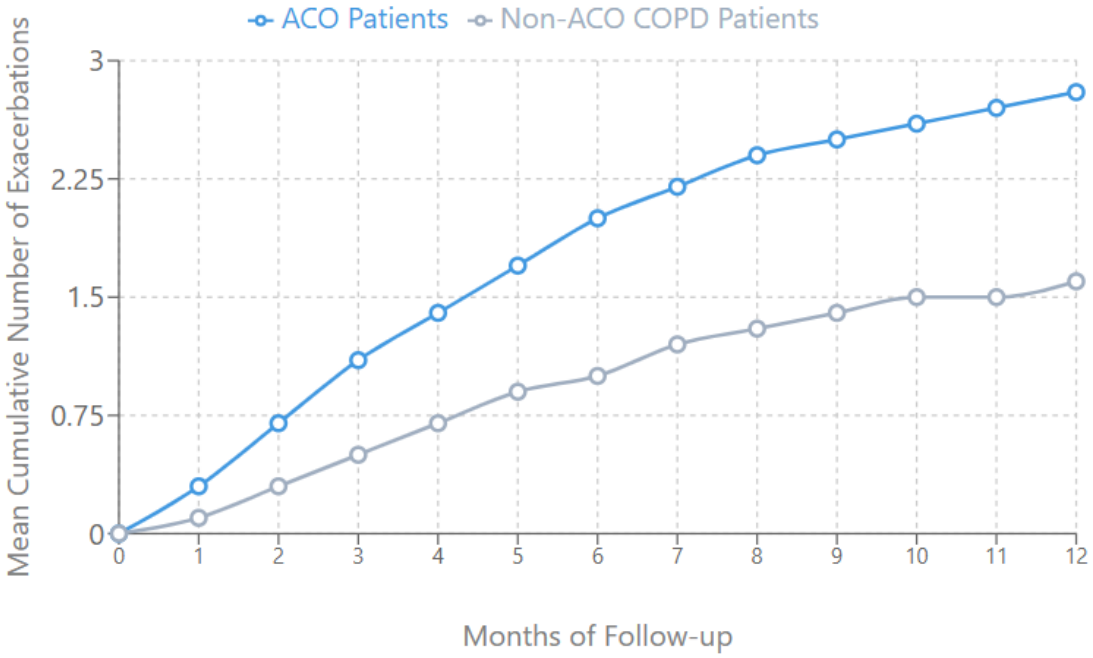

Figure 4: Cumulative Exacerbation Frequency Over 12 Months

DISCUSSION

This single-center study provides important insights into the frequency and clinical characteristics of Asthma-COPD Overlap (ACO) among COPD patients. Our findings indicate that ACO occurs in 30% of COPD patients in our cohort, which aligns with previous studies reporting prevalence rates between 15% and 55%. Notably, Cosío et al. reported a similar prevalence of 27% in their multicenter study of 831 COPD patients in Spain [18], while Kauppi et al. found a slightly higher prevalence of 38% in their Finnish cohort [19].

The demographic profile of our ACO patients reveals several distinctive features. The younger age of ACO patients compared to those with COPD alone corresponds with findings from Hardin et al.'s large cohort study, which reported ACO patients were typically diagnosed at an earlier age [20]. The higher frequency of family history of asthma and allergies in our ACO cohort supports the genetic component of this phenotype, as previously documented by Barnes' comprehensive review of ACO pathophysiology [21].

Our observation of increased symptom variability and higher frequency of wheezing in ACO patients is consistent with Gerhardsson de Verdier et al.'s findings in their Swedish population-based study [22]. The authors similarly noted that ACO patients exhibited more variable symptoms and greater bronchodilator reversibility compared to traditional COPD patients. This clinical pattern suggests a more complex underlying pathophysiology, potentially involving both fixed and variable airway obstruction.

The significantly elevated blood eosinophil counts observed in our ACO cohort (mean 385 ± 158 cells/μL) align with recent findings from the NOVELTY study, where Reddel et al. reported that ACO patients consistently demonstrated higher eosinophil levels compared to those with COPD alone [23]. This biomarker may serve as a valuable diagnostic tool and predictor of treatment response, as suggested by Sin et al. in their systematic review of ACO biomarkers [24].

The higher exacerbation frequency observed in our ACO patients (2.8 ± 1.4 vs.

1.6 ± 1.2 per year) mirrors results from several larger studies. Notably, Suzuki et al.'s prospective cohort study of 5,235 patients found that ACO was associated with a 1.87-fold increased risk of exacerbations compared to COPD alone [25]. This increased disease burden emphasizes the importance of early identification and appropriate management of ACO patients.

Our finding of enhanced bronchodilator reversibility in ACO patients supports the diagnostic criteria proposed by the joint GINA/GOLD document [26]. However, the variability in reversibility testing results highlights the challenges in establishing definitive diagnostic thresholds, a concern also raised by Gibson and McDonald in their critical review of ACO diagnostic criteria [27].

The higher rates of emergency department utilization in our ACO cohort align with Andersen et al.'s Danish nationwide study, which reported increased healthcare utilization and costs associated with ACO compared to either disease alone [28]. This finding underscores the economic impact of ACO and the potential value of targeted interventions for this population.

Several limitations of our study warrant consideration. The single-center design and relatively small sample size may limit the generalizability of our findings. Additionally, the cross-sectional nature of our study prevents assessment of long-term outcomes and disease progression. The lack of standardized diagnostic criteria for ACO, a challenge acknowledged by Postma and Rabe in their comprehensive review [29], may affect comparability with other studies.

Despite these limitations, our findings contribute to the growing body of evidence characterizing ACO as a distinct clinical entity with specific diagnostic and therapeutic implications. The results support the need for systematic screening for ACO features among COPD patients, as recommended by Plaza et al. in their expert consensus document [30]. Future research should focus on developing more precise diagnostic criteria and investigating targeted therapeutic approaches for this patient population.

CONCLUSION

Our single-center study of 60 COPD patients demonstrates that Asthma-COPD Overlap represents a significant clinical entity, affecting 30% of the study population. These patients exhibit distinct clinical characteristics, including younger age at presentation, higher blood eosinophil counts, and greater bronchodilator reversibility compared to patients with COPD alone. The increased frequency of exacerbations and emergency department visits observed in ACO patients underscores the substantial healthcare burden associated with this condition.

The findings emphasize the importance of systematic screening for ACO features among COPD patients, particularly in those presenting with heightened symptom variability, significant bronchodilator reversibility, and elevated blood eosinophil counts. Early identification of ACO may facilitate more targeted therapeutic approaches, potentially leading to improved clinical outcomes and reduced healthcare utilization.

Future larger-scale, multicenter studies are warranted to validate these findings and establish more precise diagnostic criteria for ACO. Additionally, prospective studies investigating targeted therapeutic strategies for this distinct patient population could help optimize management approaches and improve long-term outcomes. The recognition and appropriate management of ACO represent crucial steps toward providing personalized care for patients with chronic airway diseases.

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