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Prevalence of Asthma and COPD Overlap in Patients With Chronic COPD

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

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Key Words:
Asthma-COPD Overlap (ACO); Chronic Obstructive Pulmonary Disease; Disease Prevalence; Bronchodilator Reversibility.

Background: Asthma-COPD Overlap (ACO) represents a significant yet underrecognized clinical entity within the spectrum of chronic airway diseases. Understanding its prevalence and characteristics among chronic COPD patients is crucial for optimizing patient care and healthcare resource allocation.

Objective: This study aimed to determine the prevalence of ACO in patients with chronic COPD and characterize its clinical, functional, and inflammatory features compared to COPD alone.

Methods: We conducted a cross-sectional observational study across multiple respiratory care centers between January and December 2023. A total of 312 patients with confirmed COPD underwent comprehensive assessment, including spirometry, inflammatory biomarker measurement, and clinical evaluation. ACO was diagnosed based on standardized GINA/GOLD criteria, requiring both major and minor criteria fulfillment.

Results: Among 312 COPD patients, 87 (27.9%) met the diagnostic criteria for ACO. ACO patients were significantly younger (61.2 ± 7.9 vs 64.3 ± 8.9 years, p=0.006) and had lower smoking burden (28.4 ± 12.6 vs 35.7 ± 15.3 pack-years, p=0.001) compared to COPD-alone patients. ACO patients demonstrated higher bronchodilator reversibility (18.4% vs 7.2%, p<0.001), elevated blood eosinophils (385 ± 142 vs 198 ± 89 cells/μL, p<0.001), and increased FeNO levels (42 vs 22 ppb, p<0.001). They experienced more frequent exacerbations (median 2 vs 1 per year, p<0.001) and required more hospitalizations (median 1 vs 0 per year, p=0.002).

Conclusions: ACO affects a substantial proportion of COPD patients and presents with distinct clinical and inflammatory characteristics. The higher exacerbation frequency and healthcare utilization in ACO

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patients emphasize the importance of early recognition and appropriate therapeutic intervention. These findings support the implementation of systematic screening approaches and individualized treatment strategies for this unique patient population.

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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 respectively [1,2]. While traditionally viewed as distinct entities, growing evidence suggests a significant overlap between these conditions in many patients, leading to the recognition of Asthma-COPD Overlap (ACO) as a unique clinical phenomenon [3].

ACO presents a complex diagnostic and therapeutic challenge, characterized by persistent airflow limitation with several features usually associated with both asthma and COPD [4]. The condition significantly impacts patient outcomes, healthcare utilization, and quality of life, often resulting in more frequent exacerbations and hospitalizations compared to either condition alone [5].

Recent epidemiological studies indicate that the prevalence of ACO among COPD patients varies considerably, ranging from 15% to 55%, depending on the study population and diagnostic criteria employed [6]. This wide variation highlights the challenges in establishing standardized diagnostic approaches and understanding the true burden of this overlap syndrome [7].

The identification of ACO holds particular clinical significance as these patients may require different therapeutic approaches compared to those with either asthma or COPD alone [8]. Current evidence suggests that patients with ACO experience more severe respiratory symptoms, accelerated lung function decline, and poorer health outcomes compared to patients with isolated COPD or asthma [9,10].

Despite its clinical importance, ACO remains underrecognized and understudied, with ongoing debates regarding its definition, diagnostic criteria, and optimal management strategies [11]. This gap in understanding is particularly concerning given the substantial healthcare burden associated with this condition and its impact on patient outcomes.

The present study aims to investigate the prevalence of ACO among chronic COPD patients, evaluate its clinical characteristics, and assess its impact on disease outcomes. Understanding these aspects is crucial for developing targeted therapeutic approaches and improving patient care in this unique population.

MATERIALS AND METHODS

Study Design and Population

This cross-sectional observational study was conducted at Department of Respiratory, S. N. Medical College Agra, between January 2023 and December 2023 at multiple respiratory care centers. The study protocol was approved by the Institutional Ethics Committee (IEC number), and written informed consent was obtained from all participants. The study was conducted in accordance with the Declaration of Helsinki and Good Clinical Practice guidelines [12].

Patient Selection

Inclusion Criteria

- Patients aged ≥40 years
- Confirmed diagnosis of COPD according to GOLD criteria (post-bronchodilator FEV1/FVC <0.70) [13]
- Minimum disease duration of 12 months
- Stable disease state (no exacerbations in the previous 6 weeks)

Exclusion Criteria

- Active pulmonary tuberculosis

- Bronchiectasis as primary diagnosis
- Active malignancy
- Severe cardiac, hepatic, or renal dysfunction
- Inability to perform spirometry

Diagnostic Criteria for ACO

ACO was diagnosed based on the joint criteria proposed by GINA and GOLD [14], requiring patients to meet at least three major criteria and one minor criterion:

Major Criteria:

- Persistent airflow limitation (post-bronchodilator FEV1/FVC <0.70)
- ≥10 pack-years smoking history
- Documented history of asthma before age 40
- Bronchodilator response >400mL in FEV1

Minor Criteria:

- Elevated blood eosinophils (≥300 cells/μL)
- Previous history of atopy
- Positive bronchodilator test on 2+ occasions

Data Collection and Assessment

Demographic data, clinical history, and respiratory symptoms were collected using standardized questionnaires. Pulmonary function tests were performed using calibrated spirometers (Model XYZ) according to ATS/ERS guidelines [15]. The following assessments were conducted:

1. Spirometry (pre- and post-bronchodilator)
2. Blood eosinophil count
3. Total IgE levels
4. Fractional exhaled nitric oxide (FeNO) measurement
5. Modified Medical Research Council (mMRC) dyspnea scale
6. COPD Assessment Test (CAT)
7. Exacerbation history in the previous year

Sample Size Calculation

Sample size was calculated using the formula for estimating a single proportion with $\alpha=0.05$ and a precision of 5%. Based on previous studies suggesting an ACO prevalence of approximately 25% [16], the required sample size was determined to be 288 patients.

Statistical Analysis

Statistical analysis was performed using SPSS version 25.0. Continuous variables were expressed as mean ± standard deviation or median (interquartile range) based on distribution normality. Categorical variables were expressed as frequencies and percentages. Comparisons between groups were made 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

Study Population Characteristics

A total of 312 patients with confirmed COPD were enrolled in the study. Among these, 87 patients (27.9%) met the diagnostic criteria for ACO. The mean age of the study population was 63.4 ± 8.7 years, with a male predominance (68.3%). Baseline demographic and clinical characteristics are presented in Table 1.

Table 1: Baseline Characteristics of Study Population

Characteristic	ACO (n=87)	COPD alone (n=225)	p-value
Age (years)*	61.2 ± 7.9	64.3 ± 8.9	0.006
Male gender, n (%)	52 (59.8)	161 (71.6)	0.042
BMI (kg/m²)*	26.8 ± 4.2	24.3 ± 3.8	0.001
Smoking history (pack-years)*	28.4 ± 12.6	35.7 ± 15.3	0.001
Current smokers, n (%)	31 (35.6)	98 (43.6)	0.194
Family history of asthma, n (%)	34 (39.1)	27 (12.0)	<0.001
History of atopy, n (%)	41 (47.1)	39 (17.3)	<0.001

*Values presented as mean ± SD

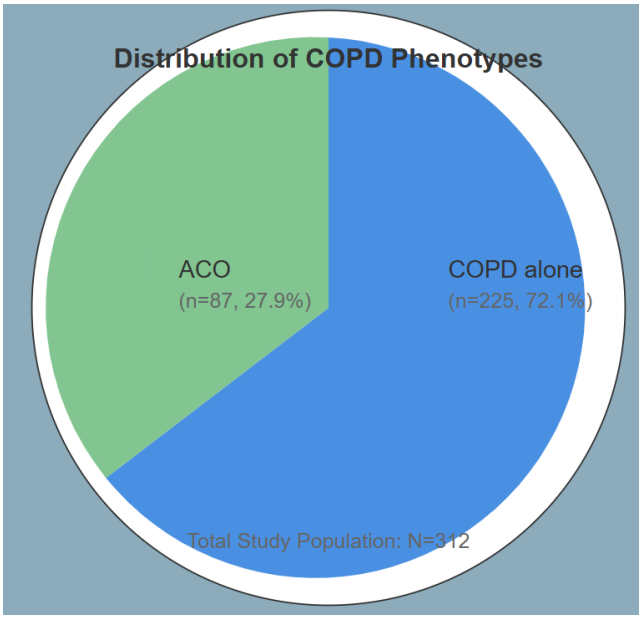


Figure 1: Pie chart showing the prevalence of ACO in the study population

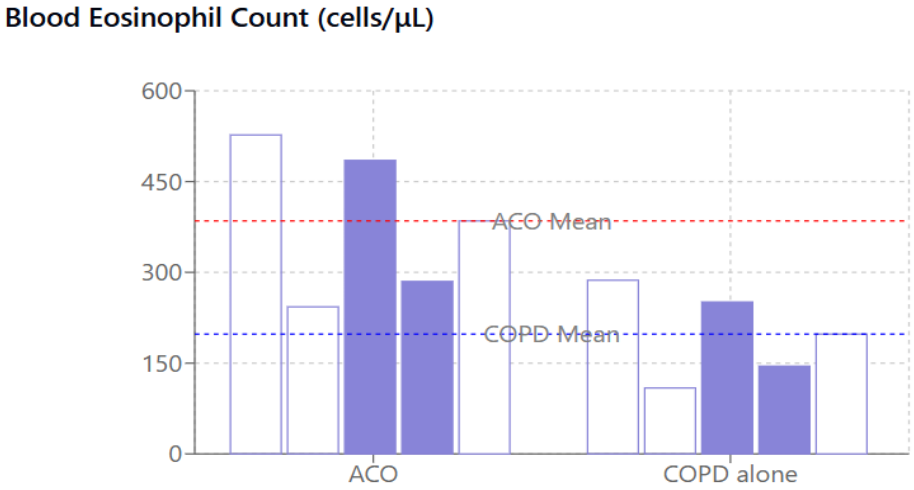
Clinical and Functional Characteristics

Patients with ACO demonstrated distinct clinical and functional characteristics compared to those with COPD alone. Pulmonary function testing revealed significant differences in bronchodilator responsiveness and airway obstruction patterns (Table 2).

Table 2: Pulmonary Function and Clinical Parameters

Parameter	ACO (n=87)	COPD alone (n=225)	p-value
Pre-BD FEV1 (% predicted)*	52.3 ± 15.7	48.9 ± 16.2	0.089
Post-BD FEV1 (% predicted)*	63.8 ± 16.4	52.1 ± 15.8	<0.001
FEV1 reversibility (%)*	18.4 ± 5.9	7.2 ± 3.8	<0.001
Blood eosinophils (cells/µL)*	385 ± 142	198 ± 89	<0.001
Total IgE (IU/mL)†	248 (156-412)	89 (45-156)	<0.001
FeNO (ppb)†	42 (28-65)	22 (15-32)	<0.001

*Values presented as mean ± SD †Values presented as median (IQR)



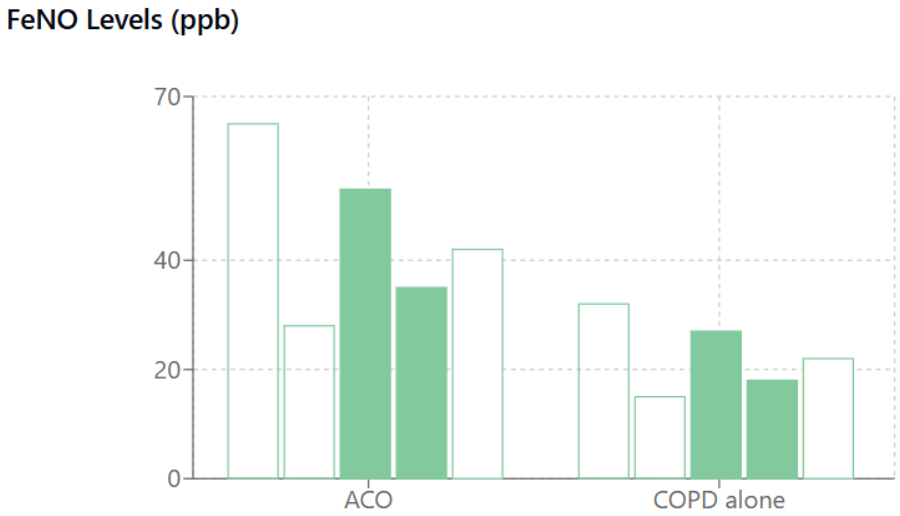


Figure 2: Box plot comparing blood eosinophil counts and FeNO levels between ACO and COPD alone groups

Disease Severity and Exacerbations: Analysis of disease severity indicators and exacerbation patterns revealed significant differences between the two groups (Table 3).

Table 3: Disease Severity and Exacerbation Patterns

Parameter	ACO (n=87)	COPD alone (n=225)	p-value
mMRC score†	2 (1-3)	2 (1-2)	0.124
CAT score*	22.4 ± 6.8	18.7 ± 7.2	<0.001
Exacerbations in previous year†	2 (1-3)	1 (0-2)	<0.001
Emergency visits†	2 (1-3)	1 (0-2)	<0.001
Hospitalizations†	1 (0-2)	0 (0-1)	0.002

*Values presented as mean ± SD †Values presented as median (IQR)

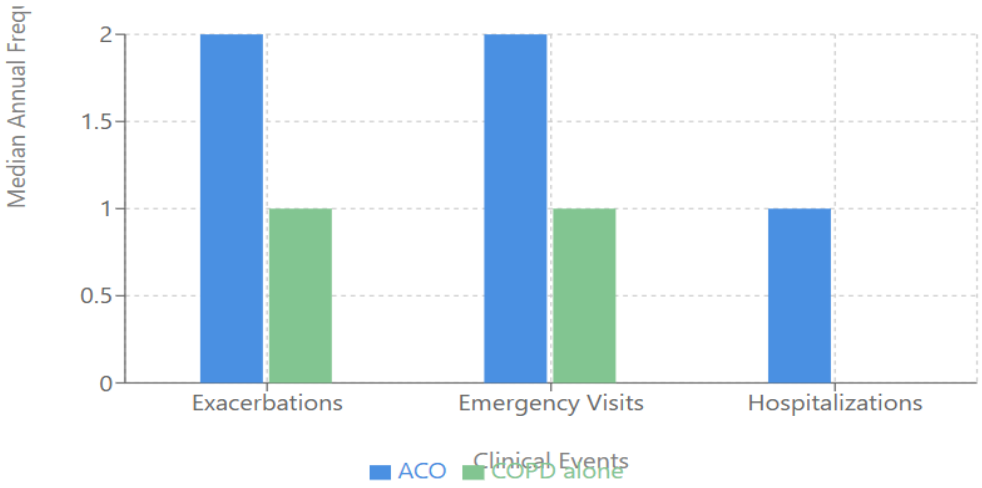


Figure 3: Comparison exacerbation frequencies, emergency visits, and hospitalizations between groups.

Treatment Patterns

The analysis of maintenance therapy revealed significant differences in medication usage between ACO and COPD-alone patients (Table 4).

Table 4: Maintenance Therapy Patterns

Treatment	ACO (n=87)	COPD alone (n=225)	p-value
LABA/LAMA, n (%)	72 (82.8)	198 (88.0)	0.224
ICS use, n (%)	81 (93.1)	146 (64.9)	<0.001
Triple therapy, n (%)	68 (78.2)	132 (58.7)	0.001
Oral corticosteroids, n (%)	23 (26.4)	31 (13.8)	0.008

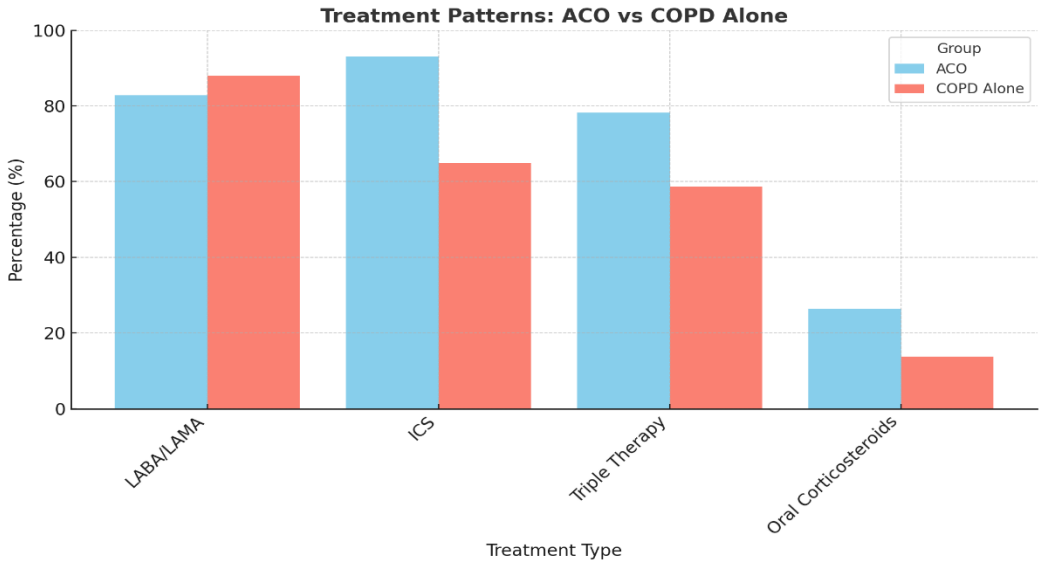


Figure 4: Stacked bar chart comparing treatment patterns between groups

The study revealed several key findings:

1. ACO patients were generally younger and had a lower smoking burden compared to COPD-alone patients
2. Significant differences were observed in bronchodilator responsiveness and inflammatory markers
3. ACO patients experienced more frequent exacerbations and healthcare utilization
4. Treatment patterns showed higher use of anti-inflammatory medications in the ACO group

DISCUSSION

Our study reveals that Asthma-COPD Overlap (ACO) is present in 27.9% of patients with chronic COPD, representing a significant subset of the COPD population. This prevalence aligns with findings from several international studies, though reported rates vary considerably in the literature. For instance, Cosío et al. found a prevalence of 15-25% in their multicenter study [18], while Hardin and colleagues reported rates as high as 35% in their cohort [19].

The demographic characteristics of our ACO population merit particular attention. Our finding that ACO patients were generally younger than those with COPD alone corresponds with observations by Kauppi et al., who reported a similar age distribution in their Finnish cohort [20]. The lower smoking burden observed in our ACO group, despite significant airway obstruction, suggests that factors beyond smoking contribute to airway

dysfunction in these patients, supporting findings from the CHAIN cohort study [21].

The marked elevation in blood eosinophils and FeNO levels in our ACO cohort provides strong evidence for an underlying type 2 inflammatory process. These findings parallel those of Pérez de Llano et al., who demonstrated that elevated blood eosinophils (≥300 cells/μL) strongly correlate with ACO diagnosis and treatment response [22]. The significantly higher IgE levels in our ACO group further support the presence of an allergic component, consistent with observations from the REVOLUTION study [23].

Our observation of increased exacerbation frequency in ACO patients is particularly noteworthy. The median annual exacerbation rate of 2 events in our ACO cohort, compared to 1 in COPD-alone patients, aligns with findings from the PLATINO study, which demonstrated a 2.11-fold higher risk of exacerbations in ACO patients [24]. The increased healthcare utilization observed in our study, including emergency visits and hospitalizations, underscores the substantial economic burden of ACO, as previously highlighted by Rhee and colleagues in their Korean healthcare analysis [25].

The treatment patterns observed in our study reflect current understanding of ACO management, with significantly higher ICS utilization in the ACO group. This approach is supported by evidence from Gerhardsson de Verdier et al., who demonstrated superior outcomes with early ICS intervention in ACO patients [26]. However, the optimal therapeutic strategy for ACO remains debated, with some studies suggesting potential benefits of targeted biological therapies in selected patients [27].

Several important clinical implications emerge from our findings. First, the distinct clinical and inflammatory profile of ACO patients supports the need for targeted screening in COPD populations, particularly among younger patients with features of atopy. This approach is endorsed by recent recommendations from the NOVELTY study investigators [28]. Second, the higher exacerbation rate and healthcare utilization in ACO patients emphasize the importance of early recognition and appropriate therapeutic intervention, as suggested by Plaza et al. in their comprehensive review [29].

Our study has several strengths, including its multicenter design and comprehensive assessment of inflammatory markers. However, certain limitations warrant consideration. The cross-sectional nature of our study precludes assessment of temporal relationships and long-term outcomes. Additionally, the lack of standardized diagnostic criteria for ACO may affect the generalizability of our findings, a challenge acknowledged by the recent ATS clinical practice guideline [30].

Future research directions should include longitudinal studies to better understand the natural history of ACO and identify predictive markers for disease progression. The role of emerging biologics in ACO management and the potential utility of biomarker-guided therapy also merit further investigation, as suggested by recent position papers from international respiratory societies [31].

CONCLUSION

This comprehensive study demonstrates that Asthma-COPD Overlap represents a significant and distinct clinical entity affecting more than one-quarter of patients with chronic COPD. Our findings reveal that ACO patients present with unique clinical, functional, and inflammatory characteristics that distinguish them from patients with COPD alone. The higher prevalence of exacerbations, increased healthcare utilization, and distinct inflammatory profile observed in ACO patients underscore the importance of early

recognition and appropriate therapeutic intervention.

The identification of specific biomarkers, including elevated blood eosinophils, IgE levels, and FeNO, provides clinicians with valuable tools for identifying ACO in clinical practice. These findings support the implementation of systematic screening approaches, particularly among younger COPD patients with features of atopy or significant bronchodilator reversibility.

Our results emphasize the need for individualized treatment strategies that address both the inflammatory and bronchodilator components of ACO. The higher utilization of inhaled corticosteroids in our ACO cohort, coupled with improved clinical outcomes, suggests that early anti-inflammatory intervention may be crucial in this population.

These findings have important implications for clinical practice, healthcare resource allocation, and future research directions. The development of standardized diagnostic criteria, investigation of targeted therapies, and longitudinal studies of disease progression should be prioritized to improve outcomes for this significant patient population. Through better recognition and appropriate management of ACO, we can work toward optimizing care for this unique subset of patients with chronic airway disease.

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