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TO DETERMINE THE PREVALENCE OF ACO AMONG COPD PATIENTS, DEFINE THEIR DEMOGRAPHIC, FUNCTIONAL CHARACTERISTICS, AND ASSESS THE NEED INHALED CORTICOSTEROID (ICS)

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ABSTRACT

Background: Asthma-COPD overlap (ACO) shares features of both asthma and COPD.

Materials and Methods: A prospective observational study was conducted with 170 stable COPD patients. Spirometry measurements were used to obtain FEV1 values. Eosinophilic inflammatory markers, including total eosinophil count, serum IgE, sputum eosinophil counts, and FeNO, were measured and analysed. ACO diagnosis was made using the criteria outlined by Sin et al. The study compared the severity of symptoms, frequency of exacerbations, and eosinophilic inflammation markers between the ACO and COPD groups.

Results: ACO prevalence was 26.9%. No significant differences in gender, age group, or smoking index and respiratory symptoms between the two groups, with both groups predominantly male and in the age range of 50 to 60 years. Exacerbations and family history of atopy were more common in the ACO group ($p = 0.045$, $p < 0.001$, respectively). Sputum eosinophils, total eosinophil count, and bronchodilator reversibility were significantly higher in the ACO group ($p = 0.005$, $p < 0.001$, $p < 0.001$). No differences were found in FeNO or serum IgE levels .

Conclusion: ACO should be considered a distinct entity in COPD management due to its higher exacerbation risk and need for more aggressive treatment. A family history of atopy is a key factor in its development, while elevated eosinophilic markers emphasize the role ICS in treatment .

KEYWORDS: Asthma COPD overlap , Chronic obstructive pulmonary disease, Asthma, Inhaled corticosteroids

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) and asthma are distinct conditions with different causes, symptoms, and treatment approaches. COPD, primarily linked to smoking and environmental factors, causes chronic respiratory symptoms, airway inflammation, and airflow obstruction, usually in individuals over 40.[1] Asthma, on the other hand, is characterized by episodic, reversible symptoms, often linked to allergies, and can affect people of all ages.[2]

Asthma-COPD overlap (ACO) is a heterogeneous condition characterized by persistent airflow limitation that shares features of both asthma and COPD.

The overlap between COPD and asthma makes it difficult to differentiate between the two, particularly in adult patients, as they share similar symptoms and clinical features. The complexity of airway diseases complicates their management, often leading to suboptimal treatment. Patients with ACO are often excluded from studies focused on either disease. Despite extensive research, there remains uncertainty about whether ACO should be considered a separate entity. As a result, its prevalence of ACO in COPD patients varies widely, ranging from 12.6% to 55.7 %, due to differing definitions and criteria used in studies. [3]

The objectives of our study are to determine the prevalence of ACO among COPD patients, define their demographic and functional characteristics, and assess the need for changes in therapy, with a particular focus on inhaled corticosteroids (ICS).

MATERIAL AND METHODS

Study Design And Setting

This study was a prospective observational study, conducted among stable COPD patient attending the outdoor in the department of respiratory medicine after getting clearance from institutional ethical committee (37618-31 JLN Medical college ,Ajmer) for a period of two years.

Sample size:
Sample size was calculated at 95% confidence interval to verify an expected 22.6% prevalence of ACOS among all COPD patients as reported by previous study [4] and taking 7% absolute allowable error. Sample size was calculated to be to be minimum 142 subjects, considering 10% non response rate sample size was increased to 170 patients.
Inclusion Criteria:
All stable patients with symptoms and signs of COPD, diagnosed clinically and with chest X-ray and confirmed with Spirometry as per GOLD criteria for COPD were included in this study.
Exclusion Criteria:
Pure Asthmatics.
Patients already on oral steroids.
Comorbidities like IHD, lung cancer, associated bronchiectasis, chest wall deformities, Associated pleural or occupational lung diseases, eosinophilic lung disorders.
Those who were unable to perform spirometry.
One seventy one clinically suspected Stable COPD cases confirmed with spirometry were taken into the study.
Clinical diagnosis of COPD was based on history of chronic cough with or without sputum, dyspnea, chest tightness, along with exposure history related to smoking, occupational history, firewood usage. History of present illness, rhinitis, urticaria, wheezing were noted , past history, occupational history, personal history, treatment history was taken. Physical findings included barrel shaped chest, reduced bilateral breath sound or bilateral presence of rhonchi .Their history of dyspnoea taken and mMRC scale used to assess severity, chest Xray done and findings were noted. Spirometry was performed by using "HELIOS SPIROMETRY 401" as per standard technique [5], and post bronchodilator FEV1/FVC <0.7 confirms the diagnosis of COPD. In patients with FEV1/FVC ≤ 0.7, GOLD grading was done to classify COPD patients based on severity.
Sputum sample and blood sample were collected and fraction of exhaled breath Nitric Oxide (FENO) level was done before the post bronchodilator spirometry in a single sitting. Measurement of FENO level was done by using Medisoft HYPAIR FENO (GERMANY) device for measuring the NO in exhaled air by the conventional method (according to ATS/ERS guideline)[6]. Study subjects were divided into 3 groups (≤25ppb, 26-50ppb and >50ppb) and compared among ACO and COPD patients.
Total Eosinophil count (TEC) was calculated manually using neubars chamber using eosinophil diltuting fluid. TEC ≥ 300 cellsμL-1 were taken as raised [7]
Serum IgE was done on fully automated immunoassay machine based on chemiluminescence method. S.IgE ≥100 IU/mL was counted as raised value of S.IgE . [8]
Similarly Sputum for Eosinophils were seen microscopically on H & E stained smears and counted manually. Sputum for eosinophils > 2.5% was taken as raised in this study. [9]

The above four biomarkers along with demographic features, exacerbations rates were compared among ACO and COPD subjects.
Criteria for diagnosis of ACO in our study (Sin et al 2016) [10]
Major criteria
1.Persistent airflow limitation- post bronchodilator FEV1/FVC < 0.7 or LLN in an individual of 40 years of age or older.
2.At least 10 pack years of tobacco smoke or equivalent indoor or outdoor air pollution exposure.
3.Documented history of Bronchial Asthma before 40 years of age.
4.Bronchodilator reversibility (BDR) >400ml in FEV1.
Minor criteria
1.Documented history of allergic rhinitis or atopy.
2.BDR of FEV1 >200ml & >12% from baseline value on 2 or more occasion in FEV1.
3.Peripheral blood eosinophil count of >300 cells per microlitre.
Presence of 3 major and 1 minor criteria would qualify for diagnosis of ACO.
Statistical analysis
Categorical variables were analysed using the Chi-square test, while continuous variables were analysed with the independent t-test. A p-value < 0.05 was considered significant. Statistical analysis was performed using Epi Info version 7.2.1.0.

RESULTS
Among 171 COPD patients who were screened , ACO was found in 46 patients, making the prevalence of ACO among study subjects to be 26.9%. Among of the COPD Patients were 88% were male (n= 110) and 12% (n=15) were females, Whereas among ACO Patients were 91.3% were male (n=42) and 8.7% were females (n=4).
Table 1 presents the age distribution of the two subject groups. The majority of COPD subjects (44%) were in the 51 to 60 years age range, while 50% of ACO subjects fell within the same range. The age difference between the two groups was not statistically significant.
Among the COPD group, 68% (n=85) were current smokers, followed by 29.6% (n=37) who were ex-smokers. In the ACO group, 67.4% (n=31) were current smokers, and 32.6% (n=15) were ex-smokers (p=0.547). As shown in Table 2, no significant difference was observed in terms of pack years. The majority of subjects in both groups had more than 30 pack years.

Both groups exhibited similar respiratory symptoms, as shown in Table 3, with the majority reporting coughing, followed by rhinitis. A family history of atopy was more prevalent in the ACO group than in the COPD group ($p<0.001$). Exacerbations were significantly more frequent in the ACO group ($p=0.045$), but no significant difference was observed in the severity of dyspnea between the two groups. Markers of eosinophilic inflammation, such as total eosinophil count (TEC) and sputum eosinophils, were significantly higher in the ACO group ($p<0.001$ and $p=0.005$, respectively). However, no differences were observed between the groups in terms of serum IgE and FeNO (Table 5).
Table 4 illustrates bronchodilator reversibility in both groups. The majority of COPD subjects (74.4%) showed no bronchodilator reversibility, whereas 57% of ACO subjects had a reversibility of 200-399 ml, and 13% had >400 ml. None of the COPD subjects exhibited a reversibility of >400 ml.

DISCUSSION

In our study, the prevalence of ACO among COPD patients was 26.9%, with a higher occurrence in males compared to females. While various studies have reported a wide range of prevalence rates, from 13% [11] to 52% [12], our findings were in accordance with the meta-analysis by A. Alshabanat et al. [13], which reported a pooled prevalence of 27%. Although gender predominance was not significant in many studies [12,13], some studies noted a higher prevalence of ACO in males, possibly due to the higher prevalence of COPD in men. Our study population consisted mostly of elderly individuals, and we found no significant differences in age or smoking index between the COPD and ACO groups. However, these results contradict findings from other studies, which observed that subjects with both COPD and asthma were younger and had fewer pack-years of smoking compared to those with COPD alone [11][14].
Cough and wheezing were the most common symptoms reported by both groups, followed by a history of rhinitis and urticaria. We found no significant difference in respiratory symptoms between the two groups. Conversely, a study by Menezes et al. [14] reported more respiratory symptoms in ACO subjects, while Barrecheguren et al. [15] found that patients with ACOS experienced more wheezing and dyspnea, but similar respiratory symptoms overall. A family history of atopy was more common in ACO patients compared to those with COPD, and this difference was statistically significant. These findings are consistent with previous studies [16, 17]. On the other hand, Ayub et al. [19] found no significant difference between the groups regarding a history of atopy.
Subjects in ACO group experienced more exacerbations compared to the COPD group, a finding consistent with several previous studies [15, 16, 18], including the meta-analysis by Alshabanat et al. [13]. These results highlight the need for more aggressive management in this specific patient population to prevent recurrent exacerbations. The severity of breathlessness, as assessed by the mMRC scale, was similar in both groups, which aligns with the conclusions of Hashimoto S et al. [17], who found no significant difference in mMRC grades between the two groups.
In terms of post-bronchodilator reversibility, most COPD patients (74.4%) had reversibility ≤200 ml, whereas among ACO patients, the majority (54.4%) had reversibility between 200-399 ml, 28.2% had reversibility ≥400 ml, and only a small proportion (17.4%) had reversibility ≤200 ml. This suggests that ACO patients exhibit significantly greater post-bronchodilator reversibility compared to COPD patients. Our observations align with findings from previous studies [15,17, 18, 4] indicates that these subgroup of patients will have good response to bronchodilators.
We observed increased eosinophilic markers, such as high sputum eosinophil levels (>2.5%) and elevated TEC (>300 per μL), in ACO subjects. These results are in accordance with those of previous studies [9, 17], but differ from other studies that found no significant differences in these markers between the groups [19]. Several studies have included elevated blood eosinophil counts as a criterion to distinguish ACO from COPD [19, 10, 20].
In our study, however, we found no significant difference in serum total IgE levels or FeNO between the ACO and COPD groups. This contrasts with the findings of Yusuke Takayama et al. [21], who reported higher FeNO levels in ACO patients compared to those with COPD ($P<0.01$). Similarly, Hashimoto et al. [18] observed significant associations of serum total IgE and FeNO in the non-ACO group, using these markers to differentiate ACO from non-ACO patients and to assess the role of inhaled corticosteroids in treatment. Nonetheless, Barrecheguren et al. [15] found that patients with ACOS exhibited increased reversibility of airflow obstruction, eosinophilic bronchial and systemic inflammation, and a stronger response to inhaled corticosteroids compared to COPD patients, further supporting the role of these biomarkers in managing ACO.

Limitation

A limitation of our study was the lack of CT scan evaluation for all participants. Although we couldn't rule out helminthic infection in all patients, the use of post-bronchodilator reversibility likely excluded it as a cause of peripheral blood eosinophilia. Despite these limitations, our study provides valuable insights into the prevalence and characteristics of ACO, highlighting the need for individualized treatment plans.

CONCLUSION

The present study concludes that the prevalence of ACO among previously diagnosed COPD patients was notably high at 26.9%. Post-bronchodilator reversibility was greater in ACO patients. Elevated eosinophil counts, the presence of sputum eosinophils, and a family history of atopy suggest an atopic/allergic predisposition for the development of ACO, highlighting the role of ICS in management. Increased exacerbations observed in the ACO group emphasize the importance of individualized treatment. However, serum total IgE and FeNO levels did not contribute to the classification of ACO.

Conflicts of Interest: All authors declares no conflicts of interests

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