ORIGINAL ARTICLE

Prevalence of ACOS in the ethnic Kashmiri population and the exacerbation rate in this subset of COPD patients

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ABSTRACT

Background: COPD is now recognized as a disease with varied phenotypes with considerable overlap between bronchial asthma and one of the phenotypes namely asthma COPD-overlap syndrome (ACOS). The differentiation between asthma and chronic obstructive pulmonary in the early stage of the disease is extremely important for the adoption of appropriate therapeutic measures.

Aims and Objectives: The present study was undertaken to study the prevalence of ACOS in the ethnic Kashmiri population and the exacerbation rate in this subset of COPD patients.

Materials and methods: This was a prospective study undertaken to study the frequency of ACOS among patients of obstructive airway disease in our ethnic population. Patients suspected of obstructive airway disease were subjected to a pulmonary function test (PFT) according to ATS/ERS guidelines. Airflow obstruction was defined by a post-bronchodilator FEV1/FVC ratio of <0.7. Besides, sputum eosinophilic count, complete blood count, and serum IgE levels were done in all patients.

Subsequently, patients were characterized into three groups based on the results of pulmonary function tests into COPD, asthma, and ACOS. The data was analyzed using Pearson's chi-square t-test, odds ratio with a confidence interval(CI) 95%, and p-value of <0.05 was considered to be statistically significant.

Results: The prevalence of ACOS in the present study was 17.7%. Our study included 130 stable patients of obstructive airway disease, which were assessed for the presence of asthma-COPD overlap syndrome, as per the criteria given by GES EPOC Spanish guidelines. Out of 130 patients, 23 patients (17.7%) were found to have asthma-COPD overlap phenotype, 48 patients (37%) were asthmatics and 59 patients (45%) were COPD patients. Out of 23 patients with asthma COPD overlap syndrome only 3 patients (13%) were having < 2 exacerbations/year and 20 patients (87%) were having ≥ 2 exacerbations /year. (p value<0.0001)

Conclusion: Asthma COPD overlap (ACOS) patients represent a sizeable proportion of patients with obstructive airway disease and have more frequent exacerbations as compared to patients of asthma or COPD alone.

Keywords: COPD, Asthma-COPD overlap, Exacerbation
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INTRODUCTION

Chronic obstructive pulmonary disease (COPD) and asthma are heterogeneous and the most common obstructive airway disease worldwide.[1] Asthma is characterized physiologically by reversible airflow obstruction and has an episodic course with a generally favourable prognosis, responding well to anti-inflammatory treatment. In contrast, COPD is typically caused by tobacco smoking and is characterized by incompletely reversible airflow limitation that results in a progressive decline in lung function leading to premature death.[2]

COPD has now been recognized as a disease with many

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phenotypes which behave differently in terms of clinical course and response to therapy. The widely accepted COPD phenotypes include 1). Chronic bronchitic 2). Emphysematous 3). Asthma COPD overlap 4). Frequent exacerbator and 5). Rare exacerbator.[3,4]. Asthma-COPD overlap (ACO) is the term used for a subset of patients demonstrating features of both asthmas and COPD[3] the prevalence of ACO varies widely from 15% to 55% in various studies.[5] The wide variation in the prevalence rate may be due to different sets of criteria used to define ACO by different authors.

Patients with ACO have a high risk of exacerbation, hospitalization, and reduced quality of life as compared to patients with COPD alone.[6] Therefore, it becomes very important to identify a subset of individuals with features suggestive of ACO among patients with obstructive airway disease so that early and appropriate management is provided to improve the outcome. In our population, the reported prevalence of spirometrically defined COPD among individuals > 40 years is highest as compared to most of the states of our country.[7] Limited studies are available that tried to know the prevalence of ACO in India.[8] The present study was aimed to know the prevalence of ACO among patients with chronic airflow limitation who reported to the outpatient pulmonary clinic of our institute.

METHODS

Study design

This was a single-center prospective observational study that was conducted over two years. The study protocol was approved by the local ethics committee.

Study population

Patients attending the Out patient clinic with a known or suspected history of obstructive airway disease based on history, physical examination, and laboratory parameters were enrolled for the study. Enrolled patients were subjected to spirometry examination and assessment of post bronchodilator response. (if previous spirometry not available). Patients who fulfilled the following criteria were included in the study: Ratio of forced expiratory volume in the first second (FEV1) to forced vital capacity (FVC) of < 0.7 and age more than equal to 40 years. Patients who were not able to perform spirometry, pregnant patients, patients with lung disease other than COPD or asthma, and those who refused to provide consent were excluded from the study.

Sputum examination for eosinophil count and serum IgE levels (immunoglobulin E) was performed in all the participants apart from routine laboratory tests that included complete blood count, liver function test, kidney function test, and chest radiograph.

Sputum collection and processing

Sputum sample for eosinophil count was produced spontaneously or induced by nebulization with 3% hypertonic saline (in case of failure to produce sputum spontaneously). Sputum samples were collected in a sterile container and processed within two hours of expectoration. The sputum was considered adequate if the volume of the sputum collected was >2 mL, presence of squamous cell ≤80% with at least 200 inflammatory cells per slide.

Processing of sputum was done according to set guidelines.[9] Sputum samples were visually separated from saliva with the help of blunt forceps. A phosphate-buffered saline solution was prepared with dithio-threitol (DTT) [Sigma-Aldrich, Brazil] at 0.1% concentration and added to an equal volume of sputum, and the mixture was briefly stirred with a vortex mixer. DTT is a sulfhydryl reagent that produces mucolytic by breaking di-sulfide bonds those crosslink glycoprotein fibers. Drops of this mixture were then spread over the glass slides, and the slides were air-dried, fixed, and stained with Leishman stain.

Cell counts were performed with a light microscope at 1,000×magnification. At least 200 cells were counted by two investigators blinded to patient classification. The cell count was expressed as a percentage.

Definition of ACO

In this study, ACO was defined based on the Spanish criteria.[10] Those who fulfilled two major or one major plus two minor criteria were labeled as having Asthma COPD overlap. The major criteria included a positive bronchodilator test (increase in FEV1 15% and ≥400ml over baseline), eosinophilia in sputum (≥3%), and a personal history of asthma. The minor criteria included a high total IgE (>100 IU/ml), personal history of atopy, and a positive bronchodilator test (increase in FEV1 ≥12% and ≥200ml over baseline) on two or more occasions.

Data collection

Data regarding age, gender, smoking status, and frequency

of exacerbation were recorded from all the participants. An exacerbation was defined as any of the following events occurring within the past 1 year as a result of worsening of symptoms: change of regular treatment, administration of antibiotics and/or systemic steroids, unscheduled/ emergency room visit, or hospitalization. A severe exacerbation was defined as that requiring hospitalization.

Statistical analysis

Continuous variables were expressed as mean and standard deviation or median (interquartile range) where ever appropriate. Categorical variables were expressed as number and percentage and the difference between them was calculated by using Pearson's Chi-square test or Fischer exact test. A p-value of < 0.05 was considered to be statistically significant. The analysis was done by using SPSS version 25 (Armonk, NY:IBM Corp).

RESULTS

A total of 130 patients were included in the study. The most common obstructive lung disease observed in our cohort was COPD reported in 45.4% of the participants followed by Asthma in 36.9% and ACO in 17.7%. The majority of the patients belonged to an age group of more than 60 years with a median age of 62 years. No significant difference was observed in terms of age between the groups. More than half of the participants (58.5%, n=76) were males and the remainder were females. However, in a subgroup of patients with ACO majority belonged to the female sex (52.2%). The majority of the patients were current smokers as compared to ex-smokers (73.8% vs 26.2%). Significant proportion of patients with ACO (87%, n=20) and COPD (81.4%, n=48) were current smokers as compared to patients with asthma (58.3%, n=28). Patients with ACO had significantly more frequent exacerbations as compared to patients with COPD and asthma.

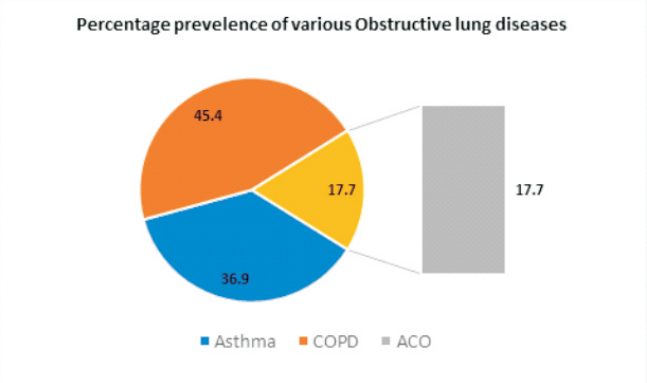


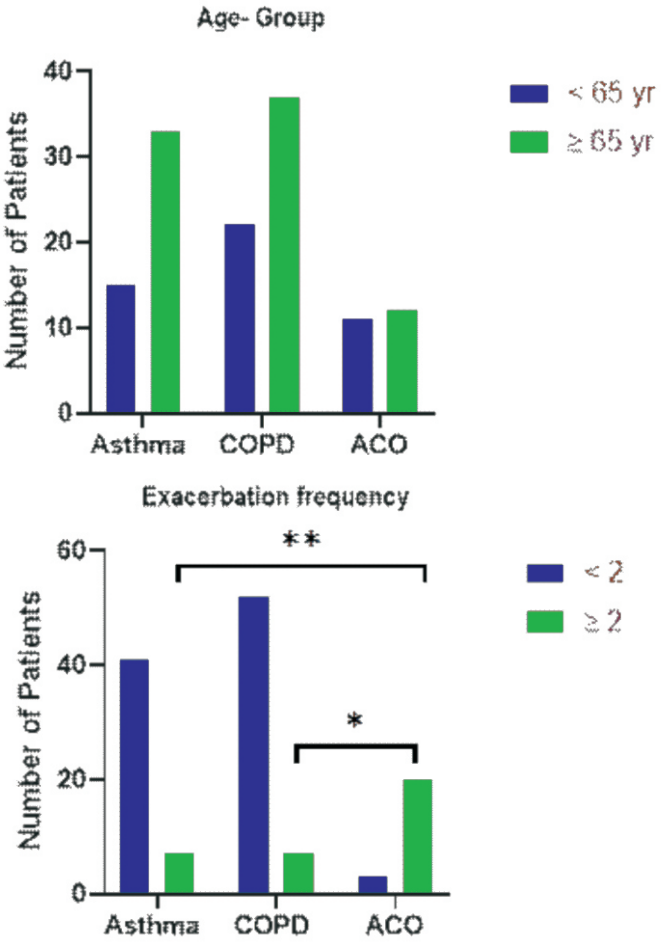
Table 1: Clinical characteristic of patients

Characteristic	Asthma (n=48)	COPD (n=59)	ACO (n=23)
Age category, no. (%)			
< 60 yr	15(31.25)	22(37.29)	11(47.83)
≥ 60 yr	33(68.75)	37(62.71)	12(52.17)
Gender, no. (%)			
Male	25 (52.1)	40 (67.8)	11 (47.8)
Female	23 (47.9)	19 (32.2)	12 (52.2)
Smoking status, no. (%)			
Current smoker	28 (58.3)	48 (81.4)	20 (87)
Former smoker	20 (41.7)	11 (18.6)	3 (13)
Number of exacerbations			
< 2	41 (85.4)	52 (88.1)	3 (13)
≥ 2	7 (14.6)	7 (11.9)	20 (87)

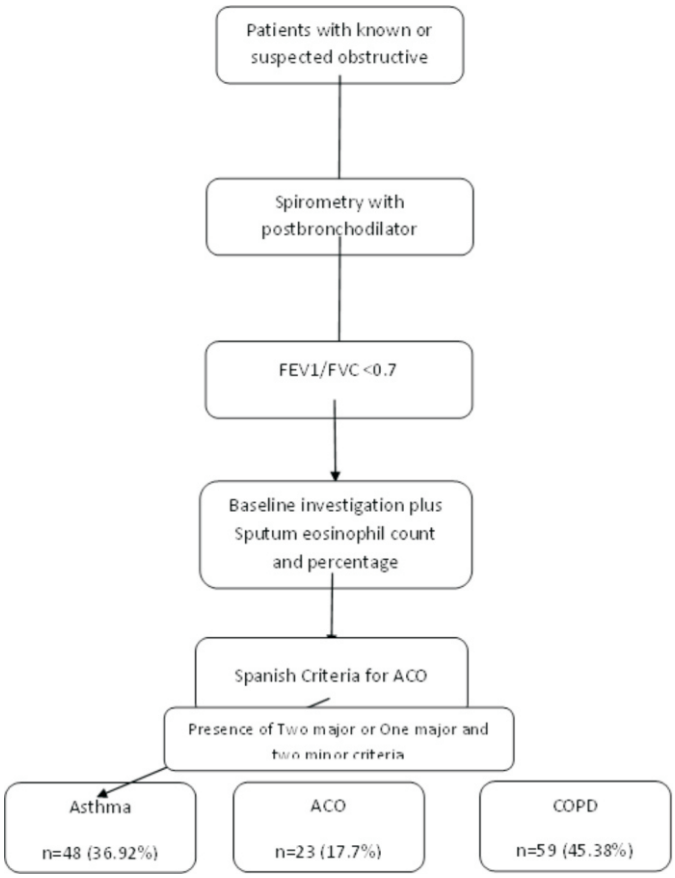
p value for Age group COPD vs ACO = 0.378, Asthma vs ACO= 0.180, COPD vs Asthma= 0.523

p value for Smoking status COPD vs ACO = 0.595, COPD vs Asthma = 0.006, Asthma vs ACO = 0.009

p value for Exacerbation frequency COPD vs ACO =0.001, ACO vs Asthma=0.001, COPD vs Asthma= 0.682



* /** p value less than 0.05



Flow chart of the Study protocol

FEV1 forced expiratory volume in 1 s; FVC forced vital capacity; ACO, asthma-COPD overlap; COPD, chronic obstructive pulmonary disease.

DISCUSSION

In this observational study, approximately 1 out of 6 patients met the criteria for ACO with a prevalence of 17.7%. The prevalence reported in our study is almost similar to that reported by Marc Miravitles and his colleagues.[11] They analyzed the data from the EPI-SCAN study that included 385 patients, a total of 67 patients (17.4%) met the defined criteria for ACO. However, the prevalence of ACO varies widely, ranging from 0.3 to 5.0% in the general population, 3.2 to 51.4% in patients with asthma, and from 12.6 to 55.7% in patients with COPD. In a recent meta-analysis, that included 27 studies, the pooled prevalence of ACO reported was 2% in the general population, 29.6% among patients with COPD, and 26.5% in patients with asthma.[5] The difference in prevalence could be due to many reasons including the difference in the prevalence of COPD and asthma in the study population, criteria used to diagnose ACO or study sample size. [12,14]

We didn't observe any significant difference in demographic features like age and gender between the groups. Although various studies have reported a significant difference in age between patients with COPD as compared to ACO with ACO being predominantly seen in younger age group, however in most of these studies the mean age of ACO patients was above 60 yrs[11,1518] In our study the median age group of the study population was 62 years with no significant difference between the groups. It was also observed that the majority of the patients with ACO, COPD, and asthma belonged to the age group of more than 60 yr.

.In our study we observed that patients with COPD and asthma had male predominance, whereas more than fifty percent (52.2%) of patients with ACO belonged to the female sex (prevalence 9.23% in females vs 8.46% in males). Our findings were inconsistent with those reported in previous studies.[11,19,21]. In a large population-based study by Anne G Wheaton, a higher prevalence of ACO was reported in females (18.7%) as compared to males (16.7%).[19] Similarly, studies by Roberto et al and Christopher MB et al reported a higher proportion of ACO in females as compared to males.[20,21] However higher prevalence of ACO in males was reported in other studies.[1517]

Our study demonstrated that the percentage of active smokers among ACO was higher than those with COPD or asthma. Kazuyoshi Kurashima et al reported that a smoking history of more than 10 pack-year is an important differentiating marker between patients with ACO and asthma with chronic airflow obstruction.[22] Similarly, Ayal-Roman et al observed that the proportion of active smokers among ACO were greater than among asthmatics (26.8% vs 22.4%).[23] To explain the relationship of smoking with ACO, various authors have postulated that long-term smoking exposure in asthmatics could lead to fixed airflow obstruction and the development of ACO phenotype. [24,25]

Previous studies have reported that patients with ACO had more frequent exacerbation compared to patients with COPD and asthma alone.[6,16,26] In our study, we also observed that the frequency of exacerbation was significantly higher in patients with ACO. In contrast, the study by Hiromasa

Inoue et al didn't observe any significant difference in the frequency of exacerbation in patients with ACO vs COPD. These findings could be due to the younger age group and less intense smoking in patients with ACO.[15]

Limitations of the present study

The low prevalence of ACO in our study could be due to a lack of adequate sample size. Studies with a larger sample size are required to know the exact prevalence of ACO in our population which has the highest reported prevalence of COPD among the majority of the states of our country.

CONCLUSION

In this study, 17.7% of participants had asthma -COPD overlap phenotype. Patients with female gender ,age more than 60 years and active smoking history were more likley to have ACO. Patients with ACO had significantly more frequent exacerbations. Therefore, early diagnosis and appropriate treatment in a subgroup of patients with ACO are key to a better outcome.

Conflict of Interest: None

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Informed consent: Taken

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