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DOI: 10.4103/ejop.ejop_4_21

# Characteristics of asthma–chronic obstructive pulmonary disease overlap among chronic obstructive pulmonary disease and asthma patients: Based on one center cross-sectional study

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**Abstract:**

**BACKGROUND:** Asthma-chronic obstructive pulmonary disease overlap (ACO) is a disease characterized by persistent airflow obstruction with several features of both asthma and chronic obstructive pulmonary disease (COPD).

**AIM:** The aim was to find patients who meet ACO criteria among COPD and asthmatics.

**MATERIALS AND METHODS:** This cross-sectional study included outpatients who applied to our pulmonology outpatient clinic with the previous diagnosis of asthma and COPD in 2019. These participants were evaluated to determine whether they met criteria of ACO. The diagnostic criteria in Global Initiative for Asthma (GINA)-Chronic Obstructive Lung Disease (GOLD), Spanish, and American Thoracic Society (ATS) Guidelines were used as the diagnostic assessment for ACO.

**RESULTS:** There were 156 men (56%) and 123 women (44%) with a mean age of  $56.7 \pm 15.6$ . Of the 279 patients analyzed, 25 (9%) met the ACO diagnostic criteria; 137 (49.1%) had COPD, and 117 (41.9%) had asthma. 5.5% of COPD and 12.7% of asthma patients were given the diagnosis of ACO. Eighty eight percent of ACO patients met the diagnostic criteria of GINA-GOLD, whereby 64% of them met Spanish, and 68% met ATS Guideline Criteria. Patients with ACO were of older age, had more comorbidities, higher rates of smoking, and worse spirometry parameters when compared with asthmatics ( $P < 0.01$ ,  $P < 0.01$ ,  $P = 0.017$ , and  $P < 0.01$ , respectively). ACO patients had a higher rate of female gender, higher mean age and more allergic symptoms than COPD patients (all  $P < 0.01$ ).

**CONCLUSION:** There were more patients who were given the diagnosis of ACO in asthma group when compared with COPD group. Clinicians may consider the diagnosis of ACO in smokers and older asthmatics and in COPD patients with atopic symptoms.

**Keywords:**

Asthma, asthma-chronic obstructive pulmonary disease overlap, chronic obstructive pulmonary disease, prevalence

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**Received:** 08-04-2021

**Revised:** 28-04-2021

**Accepted:** 10-05-2021

**Published:** 12-08-2021

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**How to cite this article:** Turan O, Polat F, Kara AG, Sözmen K. Characteristics of asthma–chronic obstructive pulmonary disease overlap among chronic obstructive pulmonary disease and asthma patients: Based on one center cross-sectional study. *Eurasian J Pulmonol* 2021;23:122-7.

## Introduction

Asthma and chronic obstructive pulmonary disease (COPD) are airway diseases characterized by airflow limitation but with different clinical features. Asthma-COPD overlap (ACO) syndrome (ACOS), which includes features of these two diseases, was first mentioned in literature at the beginning of 21<sup>st</sup> century and has been used as an important concept in many guidelines since that time.<sup>[1,2]</sup> The definition, termed ACO, was first specified by the Global Initiative for Asthma (GINA) and the Global Initiative for Chronic Obstructive Lung Disease (GOLD), as the condition being characterized by persistent airflow limitation combined with some characteristics of both asthma and COPD.<sup>[3]</sup>

There have been different definitions and the diagnostic criteria with respect to ACO in many guidelines without any exact consensus in this regard since 2000. The most common characteristics found in these guidelines include persistent airflow limitation, with a history of childhood asthma, and with reversibility in the pulmonary function tests.<sup>[4]</sup> However, no set definition of ACO has been established despite the existence of several diagnostic criteria.<sup>[5]</sup>

ACO is of clinical significance because patients with ACO usually describe more severe symptoms and exacerbations than those with either asthma or COPD alone.<sup>[1]</sup> The prevalence of ACO has been reported with rates varying between 15% and 55% in different trials.<sup>[6]</sup> However, there are only a few randomized controlled studies about the prevalence of ACO in the literature.

Our aim was to determine the patient population who meet the diagnosis criteria of ACO in patients with asthma and COPD.

## Materials and Methods

This cross-sectional study included outpatients who applied to our pulmonology outpatient clinic with the previous diagnosis of asthma and COPD in 2018. Outpatients who had a confirmed diagnosis of asthma or COPD in hospital data according to GOLD<sup>[1]</sup> and GINA.<sup>[7]</sup> Guidelines were evaluated to determine whether they met the ACO criteria. GINA-GOLD, Spanish, and American Thoracic Society (ATS) Guidelines were used for the diagnostic assessment of ACO.<sup>[3,8,9]</sup>

According to GINA-GOLD report,<sup>[3]</sup> patients with airflow limitations who have both three or more features favoring asthma, and three or more features favoring COPD, meet the criteria for ACO [Appendix 1].

The consensus report on ACO between Spanish guidelines<sup>[8]</sup> shows that diagnosis of ACO is confirmed when a patient (35 years of age or older) is a smoker or ex-smoker of more than 10 pack-years and presents with airflow limitation (postbronchodilator forced expiratory volume in 1 s [FEV<sub>1</sub>]/Forced vital capacity <0.7) and has an objective current diagnosis of asthma. In cases with no asthma diagnosis, significant positive results on a bronchodilator test (FEV<sub>1</sub>  $\geq$  15% and  $\geq$  400 mL) or elevated blood eosinophil count ( $\geq$  300 eosinophils/ $\mu$ L) will also support the diagnosis of ACO.

ATS Roundtable criteria<sup>[9]</sup> are as follows: Major criteria: Persistent airflow limitation, age  $\geq$  40 years, smoking  $\geq$  10 pack-years, air pollution exposure, documented asthma history before 40 years of age, or bronchodilator response (BDR) >400mL; and minor criteria: Documented atopy or allergic rhinitis history, two separate BDR >12% and 200mL, and blood eosinophil count over 300/ $\mu$ L. Participants with three major criteria and at least 1 minor criterion were accepted as ACO according to ATS roundtable criteria.

The demographic data and evaluation parameters about ACO, such as a history of childhood asthma, presence of atopy, eosinophilic status of blood, smoking status, and spirometry values, were collected according to face-to-face meetings and medical records. The patients with incomplete data about the diagnostic criteria of ACO were excluded.

Patients were divided into three groups following evaluation of ACO criteria such as the asthma group, the COPD group, and the ACO group. The characteristics and some parameters of these three groups were compared.

The study was approved by the Institutional Ethics Committee of İzmir Katip Çelebi University Atatürk Training and Research Hospital on October 04, 2018 with the approval number of 2018-KAE-0112. Written informed consent was obtained from all the patients.

## Statistical analysis

Statistical analyses were performed using the Statistical Package for the Social Sciences version 15.0 software (SPSS Inc.; Chicago, IL, USA). The continuity correction Chi-square test and Fisher's exact test were used in the comparison of the frequency rates of categorical variables between groups of asthma/ACO and COPD/ACO. The nonparametric Kruskal-Wallis test was applied for multiple comparisons when the Mann-Whitney *U*-test was used for comparison between the groups. The Pearson correlation was used to assess the strength of the linear relationship between two

variables. A paired sample *t*-test was used to compare the means of the groups. A  $P < 0.05$  was considered statistically significant.

## Results

There were 156 men (56%) and 123 women (44%) with a mean age of  $56.7 \pm 15.6$  in our study. The participants had been followed up with the diagnosis of COPD ( $n = 145$ ) and asthma ( $n = 134$ ). Of these 279 patients included in the analysis, 25 (9%) met the diagnostic criteria for ACO; 137 (49.1%) had COPD and 117 (41.9%) had asthma. There were 5.5% of COPD and 12.7% of asthma patients who were given the diagnosis of ACO. Eighty-eight percent of ACO patients met the diagnostic criteria of GINA-GOLD, whereby 64% of them were Spanish, and 68% of them met ATS Guideline Criteria on ACO. Patient demographics and characteristics are shown in Table 1.

There were 117 patients (41.9%) who had at least one comorbidity. Hypertension (17.9%), chronic heart diseases (8.6%), and diabetes mellitus (8.2%) were the most common comorbidities.

Five COPD patients, one asthma and one ACO patient had a hospitalization story because of their chronic airway diseases in the previous year.

### Characteristics of patients with asthma-chronic obstructive pulmonary disease overlap

The ACO group consisted of 11 (44%) male and 14 (56%) female patients with a mean age of  $54.2 \pm 13.2$ . Twenty-five ACO patients (88%) had a smoking history (mean:  $42.2 \pm 23.8$  pack-years). Dyspnea and cough were the most frequent symptoms in this patient group (both 92%). The mean age of onset of the symptoms was  $34.8 \pm 18$ . Atopic symptoms were also present in 72% of patients with ACO.

There were seven ACO patients (28%) with blood eosinophil counts higher than  $300/\mu\text{l}$ . Forty percent of participants with ACO had a childhood history of

asthma. Reversibility tests were positive in all patients; additionally, 56% of patients had highly positive bronchodilator response ( $>400$  mL and  $> 15\%$  in FEV<sub>1</sub>).

### Comparison of patients with asthma and asthma-chronic obstructive pulmonary disease overlap

There were many more comorbidities in the ACO group compared with asthmatics ( $P < 0.01$ ). Patients with ACO had higher rates of smoking and increased age; the differences of these two parameters were statistically significant between asthmatics and the ACO group ( $P < 0.01$  and  $P = 0.017$ , respectively). ACO patients had poorer spirometry parameters when compared with asthmatic patients, and these were also statistically significant ( $P < 0.01$ ) [Table 2].

### Comparison of patients with chronic obstructive pulmonary disease and asthma-chronic obstructive pulmonary disease overlap

The ACO group had more women (56%) than the pure COPD group (16.8%). ACO patients had more atopic symptoms than compared with ones with COPD. The mean age of COPD patients was higher than the mean of the ACO group. All ACO patients had a positive reversibility test. On the other hand, the reversibility test was positive in only 9.5% of COPD patients. All these parameters were statistically significant ( $P < 0.01$ ) [Table 3].

## Discussion

Although asthma and COPD are heterogeneous entities with different processes, patients with ACO may exhibit clinical features of both diseases. Our study, which identified the frequency of ACO in patients with COPD and asthma, also specified general features of this patient group.

Our results revealed the prevalence of ACO as 5.5% in COPD and 12.7% in asthmatic patients. There are contradictory results regarding this situation described in

**Table 1: Features of patients with asthma, chronic obstructive pulmonary disease, and asthma chronic obstructive pulmonary disease overlap**

Parameters	Asthma ( $n=117$ )	COPD ( $n=137$ )	ACO ( $n=25$ )
Gender (male/female)	30/87	114/23	11/14
Age (mean)	$46.3 \pm 11.3$	$65.9 \pm 19.6$	$54.2 \pm 13.2$
Smoking history (yes/no)	45/72	129/8	22/3
Comorbidities (present/not)	29/88	71/66	17/8
Cough (present/not)	90/27	115/22	23/2
Dyspnea (present/not)	92/25	118/19	23/2
Atopic symptoms (present/not)	98/19	11/126	18/7
FEV <sub>1</sub> (mean, %)	$77.4 \pm 20.6$	$56.2 \pm 20.3$	$61.8 \pm 16.3$
mMRC score	$0.89 \pm 0.6$	$1.65 \pm 0.75$	$1.44 \pm 1.01$

COPD: Chronic obstructive pulmonary disease, ACO: Asthma-COPD overlap, FEV<sub>1</sub>: Forced expiratory volume in 1 s, mMRC: Modified medical research council

the literature. One-third of COPD patients and one-fifth of asthmatics had a diagnosis of ACOS according to one study.<sup>[10]</sup> Wurst *et al.* reported that the prevalence of ACO varied from 12% to 55% among patients with COPD and between 13% and 61% among patients with asthma alone.<sup>[6]</sup> Our study determined that there were more patients with ACO in the asthma patient group when compared with COPD.

Even though there are similarities between asthma and ACO, such as the presence of atopy, diagnosis of childhood asthma, and a positive reversibility test, patients with ACO differ from asthmatics in many ways. Sevimli *et al.* reported that ACO patients had fewer allergic comorbidities and poorer spirometric parameters when compared with those who had asthma alone.<sup>[11]</sup> It was also mentioned that patients in ACO group were older than asthmatics.<sup>[12,13]</sup> A history of smoking is another issue, which was found to be more prevalent in the ACO group.<sup>[14]</sup> In accordance with the literature, patients with ACO were of more advanced age, had many more comorbidities, a higher rate of smoking and worse spirometry parameters when compared with asthmatics due to our results.

In previous reports, patients with ACO tended to have earlier onset ages, lower lung functions, and more allergic symptoms than patients with COPD alone.<sup>[15,16]</sup> ACO patients were found to be significantly younger and have more atopic symptoms than those with COPD in our study, similar to previous reports. Our results also revealed that there was a high rate of female gender and a positive reversibility test in ACO patients compared to those with COPD. Since there are many common basic features in ACO and asthma, increased rate of female gender and positive reversibility test rates in ACO patients were an expected result.

**Table 2: Comparison of patients in asthma and asthma chronic obstructive pulmonary disease overlap groups**

Parameters	Asthma (n=117)	ACO (n=25)	P
Comorbidities (present/not)	29/88	17/8	<0.01*
Smoking history (yes/no)	45/72	22/3	<0.01*
Age (mean)	46.3	54.2	0.017*
FEV <sub>1</sub> (mean, %)	77.4	61.8	<0.01*

COPD: Chronic obstructive pulmonary disease, ACO: Asthma-COPD overlap, FEV<sub>1</sub>: Forced expiratory volume in 1 s

**Table 3: Comparison of patients in chronic obstructive pulmonary disease and asthma and asthma chronic obstructive pulmonary disease overlap groups**

Parameters	COPD (n=137)	ACO (n=25)	P
Gender (female/male)	23/114	14/11	<0.01
Presence of atopy (yes/no)	11/126	18/7	<0.01
Age (mean)	65.9	54.2	<0.01
Reversibility test (positive/negative)	13/124	25/0	<0.01

COPD: Chronic obstructive pulmonary disease, ACO: Asthma-COPD overlap

It has been suggested that subjects with ACO have some characteristics which have been known as signs of poor prognosis such as rapid decline in the lung functions and more frequent exacerbations (with high number of hospitalizations) than patients with asthma or COPD alone.<sup>[17]</sup> Our study revealed worse respiratory function test parameters and more chronic diseases in ACO patients when compared with asthmatics, which might be indicators of a poor prognosis.

There were some diagnostic criteria for ACO in many guidelines and studies, but none of them had been entirely accepted and used worldwide as defined diagnostic criteria. As such, there were different results with respect to prevalence from many different studies (Our study revealed that 88% of ACO patients met the diagnostic criteria of GINA-GOLD; 64% of these using Spanish, and 68% of these using ATS Guideline Criteria, which also demonstrates this discrepancy. Consensus provided for ACO criteria will facilitate the diagnostic process.<sup>[18]</sup>

Our study has some limitations. First, the medical history of the patients' childhood was recorded according to their own statements, so these may be misleading. Although the study was performed in a large research hospital, it was a single-center study, which is another limitation.

## Conclusion

There were more patients who were given the diagnosis of ACO in the asthma group when compared with the COPD group. Clinicians may consider the diagnosis of ACO in older patients and asthmatics with a history of smoking, as well as in younger and atopic COPD patients. Our study, which presents clinical features of ACO and its prevalence in the patients with asthma and COPD, appears to be one of the few studies in relation to ACO in Turkey.

## Financial support and sponsorship

Nil.

## Conflicts of interest

There are no conflicts of interest.



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## Appendix

### Appendix 1: Features favoring asthma or chronic obstructive pulmonary disease for evaluating presence of asthma-chronic obstructive pulmonary disease overlap syndrome according to global initiative for asthma-global initiative for chronic obstructive lung disease report<sup>[3]</sup>

Features	Asthma	COPD
Age of onset	Before age 20 years	After age 40 years
Pattern of respiratory symptoms	Variation in symptoms over time Symptoms worsen during the night or early morning	Persistence of symptoms despite treatment Good and bad days but always daily respiratory symptoms and exertional dyspnea
Lung function	Symptoms triggered by exercise, emotional change (including laughter), or exposure to dust/allergens Record of variable airflow limitation (spirometry, peak flow)	Chronic cough and sputum preceded by onset of dyspnea, unrelated to triggers Record of persistent airflow limitation (postbronchodilator FEV <sub>1</sub> /FVC, 0.7)
Lung function between symptoms	Normal	Abnormal
Past history or family history	Previous doctor diagnosis of asthma Family history of asthma and other allergic conditions (allergic rhinitis, dermatitis)	Previous doctor diagnosis of COPD, chronic bronchitis, or emphysema Heavy exposure to a risk factor: tobacco smoke and biomass fuels
Time course	No worsening of symptoms over time. Symptoms vary either seasonally or from year to year May improve spontaneously or have a response to bronchodilator immediately or to ICS over weeks	Symptoms slowly worsen over time (progressive course over years) Rapid-acting bronchodilator treatment provides only limited symptom relief
Chest X-ray	Normal	Severe hyperinflation

COPD: Chronic obstructive pulmonary disease, ACO: Asthma-COPD overlap, FEV<sub>1</sub>: Forced expiratory volume in 1 s, FVC: Forced vital capacity, GINA: Global initiative for asthma, GOLD: Global initiative for chronic obstructive lung disease, ICS: Inhaled corticosteroids