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Research Article

Patients with Obstructive Airway Diseases and the Percentage of Asthma Chronic Obstructive Pulmonary Disease Overlap at Tertiary Care Teaching Hospital

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Abstract: ***Introduction***: Given the paucity of research on asthma-chronic obstructive pulmonary disease (COPD) overlap (ACO) and the high prevalence of co-morbidities and healthcare utilization associated with it, the current study looked at the prevalence of ACO and its clinico-radiological phenotype in patients with chronic airflow obstruction. The study was conducted at a tertiary care hospital in North India. Patients over 50 with COPD or asthma were screened for inclusion in the ACO, asthma, and COPD groups. The ACO and COPD groups were further investigated. The clinical characteristics, lung functions, health-related quality of life, and radiological features of both groups were investigated and compared. ACO was discovered in 16.3% of patients with chronic airflow obstruction (asthma and COPD). The most commonly observed symptoms at presentation in the evaluated ACO patients (n=77) were shortness of breath, wheezing, cough, and expectoration (mean age at presentation: 57.9; mean duration of illness: 8.62 years). Exacerbation rates in ACO patients were significantly higher than in COPD patients ($p<0.001$). The ACO group had a significantly greater mean change in FEV1 post-bronchodilator in millilitres (ml) and percentage (379.61 ml and 37.72%) than the COPD group ($p<0.001$). The proportion of patients with emphysema was lower in the ACO group than in the COPD group ($p<0.001$). The ACO and COPD groups did not differ significantly in major airway wall thickness ($p=0.3$), but the COPD group had a significantly higher proportion of patients with vascular attenuation and distortion ($p<0.001$). Patients with COPD had a higher degree of hyperinflation, according to high resolution computed tomography (HRCT) indices. This study found that patients with ACO have a distinct phenotype in terms of clinical presentation and HRCT features. More research on the radiological features of ACO is required to identify the anatomical abnormalities involved in the disease's pathogenesis and to validate the radiological features of ACO. ***Methods*** The Respiratory Effectiveness Group conducted a cross-sectional study of individuals ≥40 years old and with ≥2 outpatient primary care visits over a 2-year period in the UK Optimum Patient Care Research Database. Patients were classified into one of three source populations based on diagnostic codes: 1) COPD only, 2) both asthma and COPD, or 3) asthma only. ACO was defined as the presence of all of the following 1) age ≥40 years, 2) current or former smoking, 3) post-bronchodilator airflow limitation (forced expiratory volume in 1 second/forced vital capacity <0.7), and 4) ≥12% and ≥200 ml reversibility in post-bronchodilator forced expiratory volume in 1 second. ***Conclusions*** In summary, it has been already understood the specificity of a separate clinical entity called ACOS. Even though ACOS develops indistinct clinical and pathophysiological features that often are complicated with those of asthma or COPD, we must emphasize the importance of the syndrome. Studying further the syndrome may we discover mechanistic pathways leading to the development of COPD. And this is important because it is widely known that patients with COPD often are underdiagnosed, possibly for decades. By recognizing common risk factors it will, maybe, become possible to understand and modify the progressive deterioration of lung function, which leads to COPD.

Keywords: Asthma, asthma chronic obstructive pulmonary disease overlap, chronic obstructive pulmonary disease, prevalence.

INTRODUCTION

Asthma and chronic obstructive pulmonary disease (ACO) had been previously considered as two different disease entities, but recently it was found that some patients have features of both asthma and chronic obstructive pulmonary disease (COPD) . ACO is identified by persistent airflow limitation with several features usually associated with asthma and several features usually associated with COPD [1]. It has been suggested that patients with ACO may have special characteristics such as greater airway hyperresponsiveness, higher sputum and blood eosinophils and better response to inhaled corticosteroids (ICS) than patients with COPD .

History of atopy, eosinophilic inflammation and serum IgE had been emphasized by Hattori [4] to identify patients with ACO among those with COPD.

The study was conducted at a tertiary care hospital in North India. Patients over 50 with COPD or asthma were screened for inclusion in the ACO, asthma, and COPD groups. The ACO and COPD groups were further investigated. The clinical characteristics, lung functions, health-related quality of life, and radiological features of

both groups were investigated and compared. ACO was discovered in 16.3% of patients with chronic airflow obstruction (asthma. and COPD). The most commonly observed symptoms at presentation in the evaluated ACO patients (n=77) were shortness of breath, wheezing, cough, and expectoration (mean age at presentation: 57.9; mean duration of illness: 8.62 years). Exacerbation rates in ACO patients were significantly higher than in COPD patients ($p<0.001$). The ACO group had a significantly greater mean change in FEV1 post-bronchodilator in millilitres (ml) and percentage (379.61 ml and 37.72%) than the COPD group ($p<0.001$). The proportion of patients with emphysema was lower in the ACO group than in the COPD group ($p<0.001$). The ACO and COPD groups did not differ significantly in major airway wall thickness ($p=0.3$), but the COPD group had a significantly higher proportion of patients with vascular attenuation and distortion ($p<0.001$). Patients with COPD had a higher degree of hyperinflation, according to high resolution computed tomography (HRCT) indices. This study found that patients with ACO have a distinct phenotype in terms of clinical presentation and HRCT features. More research on the radiological features of ACO is required to identify the anatomical abnormalities involved in the disease's pathogenesis and to validate the radiological features of ACO.

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[1] and GINA.[7] Guidelines were evaluated to determine whether they met the ACO criteria. GINA-GOLD, Spanish, and American Th According to GINA-GOLD report,[3] 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]. oracic Society (ATS) Guidelines were used for the diagnostic assessment of ACO.

The consensus report on ACO between Spanish guidelines[8] 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 [FEV1]/Forced vital capacity.

ATS Roundtable criteria[9] are as follows: Major criteria: Persistent airflow limitation, age≥40years, smoking≥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/μL. Participants with three major criteria and at least 1 min or 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

Baseline data were missing for spirometry (n=201), FeNO (n=379), physical activity (n=121), self-reported asthma and COPD (n=36), diabetes (n=64), self-reported CVD (n=28), IDS (n=16), WHR (n=8), smoking (n=8), and number of pack-years (n=147). A total of 238 (4%) participants were lost to follow-up. Therefore, the present analyses were conducted in a complete case study population of 5675 participants. A subpopulation of 846 (15%) participants with asthma and/or COPD was identified.

Baseline characteristics

The characteristics of the complete case study population are presented in table 1. The majority (62%) of participants were ex- smokers or current smokers. 15% of the participants had FEV1/FVC <0.7. Prevalence of COPD was lower in registry data than self-reported (2.5% versus 4.2%). In contrast, asthma prevalence was higher in registry data than self-reported (8.0% versus 4.4%). In the subpopulation of 846 asthma and/or COPD patients, the most frequently used medication was

a long-acting β-agonist plus inhaled corticosteroid (ICS) combination (29%), followed by short-acting β-agonist (15%) and ICS (14%) monotherapy. The most frequent comorbidity in the total population was depression (14%).

TABLE 1 Characteristics of the complete case weighted study population and asthma/chronic obstructive pulmonary disease (COPD) subpopulation

	Frequenc y	Percent
Females	8	16.0
Males	42	84.0
Total	50	100.0

Table 2 Classification of study groups based on finaldiagnosis

	Frequenc y	Percent
ACO	18	36.0
Asthma	12	24.0
COPD	20	40.0
Total	50	100.0

ACO, asthma chronic obstructive pulmonary disease overlap;COPD, chronic obstructive pulmonary disease.

Table 3 Age differences between the study groups

Diagnosis	Mean	N	SD	Mi nim um	Maximum
ACO	53.43	18	11.061	26	78
Asthma	42.62	12	11.117	23	60
COPD	56.95	20	7.338	39	75

ACO, asthma chronic obstructive pulmonary disease overlap;COPD, chronic obstructive pulmonary disease. overlap) were selected from Kasr Al Aini outpatient clinic from October 2016 to March 2017.It included 47 (83.9%) males and nine (16.1%) females Table 1. Among the studied participants, 23 (41.1%) patients were diagnosed as having ACO, 13 (23.2%) patients were diagnosed as having asthma and 20 (35.7%)patients as having COPD (Table 2).

Regarding the age difference between groups, it was found that patients who were diagnosed as having ACO were older than asthmatic patients with mean age of 53.43±11.06 and 42.62±11.11 years,respectively. The men age of patients with COPD was 56.95±7.33 which was older than both ACO and asthmatic patients (Table 3). It was found that 43.5% of ACO group started theirsymptoms before the age of 40 years, whereas 56.5% of them after the age of 40 years. We noticed that 87% of ACO group, 100% of COPDgroup and only 23% of asthma group were eithercurrent or ex-smokers (Fig. 1). Table 4 showed the comparison of groups regarding history of atopy. We found that 60.9% of ACO group, 84.6% of asthma group and 15% of COPD group had apositive history of atopy Comparison of study groups regarding sputum eosinophils revealed that 26.1% of ACO group, 15.4% of asthma group and 10% of COPD group had positive sputum eosinophils (Table 5).

DISCUSSION

This research was done to study the characteristic features of ACO and its percentage among patients with obstructive airway diseases and to assess sputum eosinophils in these patients. It was carried on 56 patients with chronic airway diseases (COPD, asthma and asthma-COPD overlap) who were selected from Kasr Al Aini outpatient clinic during the period from October 2016 to March 2017. It included 47 (83.9%) males and nine (16.1%) females patients (eight asthmatics and one female was diagnosed as ACO)

Among the studied patients 23 (41.1%) were diagnoed as having ACO, 13 (23.2%) patients were diagnosed as having asthma and 20 (35.7%) as having COPD

It was found that the prevalence of ACO varies among different published studies, and this may be related to the difference in the studied populations and differences in diagnostic criteria.

In asthmatic patients the prevalence of ACO was variable ranging between 13 and 30%. The prevalence increased with age reaching 61% when asthmatic patients above the age of 65 years

However, in patients with COPD the prevalence of ACO also was variable, ranging between 9 and 55% in different studies

Regarding the age difference between groups, it was found ACO group was older than asthmatic patients with mean age of 53.43±11.06 and 42.62±11.11 years, respectively. The mean age of patients with COPD was

56.95±7.33 years which was older than both ACO and asthmatic patients

This agreed with some authors, they found a significant difference between ACO and COPD groups regarding the age; being significantly lower among ACO group than COPD group

However, other authors who studied ACO among asthmatics, found that patients with ACO tended to be older and were mainly men

We noticed that 87% of ACO group, 100% of COPD group and only 23% of asthma group were either current or ex- smokers

This agreed with results of some researchers, as they found that most asthmatic patients in their study were never smokers whereas 76.2% of participants in the COPD group and 71.4% in the asthma-COPD overlap group were ex- smokers[16].

In our study, we found that 60.9% of ACO group, 84.6% of asthma group and 15% of COPD group had positive history of atopy .

Comparison of study groups regarding sputum eosinophils revealed that 26.1% of ACO group, 15.4% of asthma group and 10% of COPD group had positive sputum eosinophils

These results agreed with another study, as it found that the prevalence of allergic rhinitis was significantly higher in ACO[2].

Moreover, it agreed with the results of another research, as it reported significant difference between ACO and COPD groups regarding history of atopy, being significantly higher among ACO group

It was hypothesized that a atopy, IgE or eosinophilia in blood or sputum were relevant to identify patients with ACO among those with COPD. It was suggested that a greater degree of eosinophilic bronchial inflammation in patients with ACO was responsible for greater response to ICS treatment.

CONCLUSION

In summary, it has been already understood the specificity of a separate clinical entity called ACOS. Even though ACOS develops indistinct clinical and pathophysiological features that often are complicated with those of asthma or COPD, we must emphasize the importance of the syndrome. Studying further the syndrome may we discover

mechanistic pathways leading to the development of COPD. And this is important because it is widely known that patients with COPD often are underdiagnosed, possibly for decades. By recognizing common risk factors it will, maybe, become possible to understand and modify the progressive deterioration of lung function, which leads to COPD.

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