

ORIGINAL ARTICLE

Asthma, asthma-COPD overlap syndrome, and chronic obstructive pulmonary disease in Turkey

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ABSTRACT

BACKGROUND: Asthma, asthma-chronic obstructive pulmonary disease overlap syndrome (ACOS), and chronic obstructive pulmonary disease (COPD) are the most common pulmonary diseases worldwide characterized by chronic airway inflammation and airway obstruction. There isn't enough information about the new diagnosed asthma, ACOS, and COPD outpatients among the Turkish population. We aimed to describe the disease characteristics of outpatients with new diagnosed asthma, ACOS, and COPD.

METHODS: New diagnosed asthma, ACOS, and COPD outpatients were retrospectively evaluated at Samsun Medical Park Hospital, Department of Pulmonary Medicine, between May 2012 and July 2017.

RESULTS: In total of 108 outpatients were included in the study. The main age was 56.6±14.7 years and male to female ratio was 95/13. Most common symptoms were dyspnea (32.5%) and cough (27.8%). Bronchodilator reversibility was positive in 52(48.1%) of the patients. The most common group of outpatients was ACOS (31.5%). Eleven patients (10.1%) had pulmonary comorbidities including lung cancer (N.=7), interstitial lung diseases (N.=2) and bronchiectasis (N.=2). 3(3%) patients were newly diagnosed both with lung cancer and COPD at the same time in outpatient clinic.

CONCLUSIONS: ACOS is the most common type of obstructive lung disease and it can be defined with age >40 years, smoking, postbronchodilator FEV₁/FVC <70% of expected and postbronchodilator FEV₁ value can raise over 70% due to high reversibility rates. Lung cancer is the most common pulmonary comorbidities in COPD patients. The outpatients with new diagnosed COPD who is over the age of 40 and smoker should be screened for lung cancer.

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KEY WORDS: Asthma - Chronic obstructive pulmonary disease - Comorbidity - Obstructive lung diseases.

Asthma, chronic bronchitis, and emphysema are the most common pulmonary disease worldwide characterized by chronic airway inflammation and airway obstruction. Airway obstruction is usually variable in asthma, while it is progressive and persistent in patients with chronic obstructive pulmonary disease (COPD) which includes; chronic bronchitis and emphysema. However, some of the patients presenting

with symptoms of chronic airway diseases have clinical features of both asthma and COPD.¹ Furthermore, both diseases have overlapping pathological and functional characteristics. Although such patients are commonly described as “asthmatic bronchitis” or “asthmatic form of COPD” in the US, the term “asthma-COPD overlap syndrome” (ACOS) is recently being used to describe these patients.²⁻⁴ Currently,

there is not enough data about the new diagnosed asthma, ACOS, and COPD outpatients in Turkey. We aimed to evaluate disease characteristics of outpatients with new diagnosed asthma, ACOS, and COPD.

Materials and methods

Patient selection

New diagnosed asthma, ACOS, and COPD outpatients were retrospectively evaluated in Samsun Medical Park Hospital, Department of Pulmonary Medicine, between May 2012 and July 2017. Inclusion criteria were as follows:

- patients who have not previously been diagnosed with asthma, COPD, and ACOS;
- symptomatic patients (cough, sputum, dyspnea, wheezing);
- presence of airway obstruction in spirometry ($FEV_1/FVC \leq 70\%$ of expected);
- patients who had never used bronchodilators before;
- abnormal chest auscultation consistent with obstructive lung disorders.

Spirometry

The basal and postbronchodilator forced vital capacity (FVC), forced expiratory volume in the 1st second (FEV_1), and FEV_1/FVC values were measured using the MIR MiniSpir PC-Based USB Spirometer by the same physician (S.O.) following a 30-minute resting period in an outpatient clinic. The test must be performed in a seated position, when the nose is clamped and nasal respiration is hindered. The patients performed the forced expiratory maneuver at least three times and the maximum FEV_1 value was recorded as the basal value. Bronchodilator reversibility levels were evaluated as the absolute change in FEV_1 and the percentage of change from the initial FEV_1 , calculated as:

$$FEV_1\% \Delta_{init}: \text{post } FEV_1 - \text{pre } FEV_1 / \text{pre } FEV_1 \times 100$$

(according to American Thoracic Society guidelines), and bronchodilator reversibility is defined as a drug-induced increase in FEV_1 of ≥ 200 mL and $\geq 12\%$ baseline. Results are presented as means \pm standard deviation of means.

Ethical statement

The study was performed in accordance with the ethical principles of the Good Clinical Practice Guidelines (GCP) and with applicable local regulatory requirements. The protocol was approved by local ethics review boards. All the patients have read the patient information form about the study procedure, and written informed consents were obtained.

Results

The total of 108 outpatients were included in the study. Demographic characteristics of patients are presented in Table I. The mean age was 56.6 ± 14.7 years and male to female ratio was 95/13. Most common symptoms were dyspnea (32.5%) and cough (27.8%). 6 (5.5%) of patients had other/non-specific symptoms including sweating and weight loss. The diagnosed groups of patients and reversibility rates are presented in Table II. Bronchodilator reversibility was positive in 52 (48.1%) of patients. The most common group of patients was ACOS (31.5%). The demographic and spirometric features of patients with

TABLE I.—Patients' characteristics.

Characteristics	Values
Age, years (range)	56.6 \pm 14.7 (21-84)
Sex, M/F	95 (88%)/13 (12%)
BMI, kg/m ² (range)	26.9 \pm 5.4 (17.3-54)
Smoking status	
Non-smoker	15 (13.9%)
Current smoker	57 (52.8%)
Ex-smoker	36 (33.3%)
Symptoms	
Dyspnea	35 (32.5%)
Cough	30 (27.8%)
Consultation	15 (13.9%)
Cough with sputum	13 (12%)
Wheeze	9 (8.3)
Other	6 (5.5%)
Pulmonary comorbidities	11 (10.1%)
Baseline spirometry results	
FVC	
Mean \pm SD, mL (range)	3051 \pm 1141 (1110-5920)
%pred \pm SD (range)	77.0 \pm 23.1 (35-155)
FEV_1	
Mean \pm SD (range)	1934 \pm 776 (620-4050)
%pred \pm SD (range)	60.9 \pm 20.4 (23-130)
FEV_1/FVC	
%pred \pm SD (range)	63.0 \pm 7.0 (40.5-70)

BMI: Body Mass Index; FVC: forced vital capacity; FEV_1 : forced expiratory volume in 1st second.

TABLE II.—Diseases groups and reversibility results.

Types	N. (%)
Asthma	29 (29.9%)
ACOS	34 (31.5%)
Chronic bronchitis	27 (25%)
Emphysema	15 (13.9%)
Mix	3 (2.8%)
Reversibility	
Yes	52 (48.1%)
No	56 (51.9%)

ACOS: asthma-COPD overlap syndrome.

asthma, ACOS, chronic bronchitis, emphysema and mix type are shown in Table III. 11(10.1%) of patients had pulmonary comorbidities including lung cancer (N.=7), interstitial lung diseases (N.=2), and bronchiectasis (N.=2). Four of the patients had previously diagnosed lung cancer and they had newly diagnosed COPD. 3(3%) patients were newly diagnosed both with lung cancer and COPD at the same time in outpatient clinic (Figure 1). The bronchodilator reversibility test results of patients with asthma, ACOS, chronic bronchitis, emphysema and mix type are shown in Table IV. The common characteristics of ACOS patients were age >40 years, smoking,

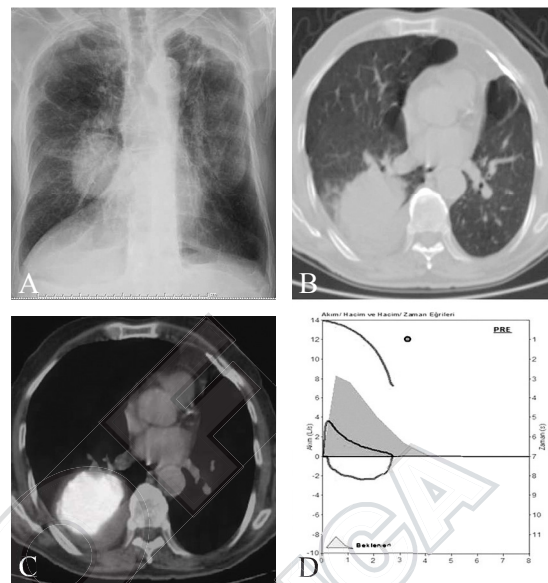


Figure 1.—A-D) A 73-year-old male patient was diagnosed with concurrent COPD and lung cancer. Chest radiography, ¹⁸F-DG-PET/CT scan and spirometric flow-volume curves show the pulmonary mass and airway obstruction.

postbronchodilator FEV₁/FVC <70% of expected and postbronchodilator FEV₁ value can raise over 70% due to high reversibility rates.

TABLE III.—Patients' characteristics by group.

Characteristics	Asthma	ACOS	Chronic bronchitis	Emphysema	Mix
Age, years	40.5±13.3	57.5±10.3	64.4±8.0	69±7.8	67.3±10.7
Sex, M/F	20/9	32/2	25/2	15/0	3/0
BMI, kg/m ²	26.6±4.2	28.5±6.2	27.3±5.5	22.9±4.1	26.3±4.7
Smoking status					
Non-smoker	9 (31%)	3 (8.8%)	3 (11.1%)	0	0
Current smoker	19 (65.5%)	19 (55.9%)	10 (37%)	7 (46.7%)	2 (66.7%)
Ex-smoker	1 (3.5%)	12 (35.3%)	14 (51.9%)	8 (53.3%)	1 (33.3%)
Baseline spirometry results					
FVC					
Mean±SD, mL	3574±1310	3059±1204	2805±752	2732±930	1706±215
%pred±SD	81.2±20.3	76.1±24.4	78.7±25.7	71.2±21.8	61±20.9
FEV ₁					
Mean±SD	2370±849	1903±782	1761±508	1639±732	1100±176
%pred±SD	64.7±16.3	58.9±20	64.6±23.8	53.4±21.5	50±18.7
FEV ₁ /FVC					
%pred±SD	66.4±4.2	61.6±7.2	64.0±6.4	57.6±9.2	64.2±2.4

TABLE IV.—The reversibility and postbronchodilator results of groups.

Characteristics	Asthma	ACOS	Chronic bronchitis	Emphysema	Mix
Reversibility	21 (72.4%)	29 (85.2%)	0	1 (6.6%)	1 (33.3%)
Change, mL	298±195	365±151	104±59	88±50	160±62
Change, %pred	19.1±11.4	23.2±14.1	6.4±4.1	6.2±3.3	14±3.4
Postbronchodilator values					
FEV ₁ , %pred	76.2±16.4	70.5±20.9	68.4±24.3	56.4±21.6	55.6±19.6
FEV ₁ /FVC, %pred	71.4±5.4	66.8±9.1	64.9±7.9	57.4±11.5	65.9±6.8

Discussion

Airway obstruction is variable in asthma, while it is progressive and persistent in chronic bronchitis and emphysema. However, some of the patients presenting with symptoms of chronic airway diseases have clinical features of both asthma and COPD. The group with ACOS phenotype was characterized by definitely irreversible airway obstruction accompanied by symptoms and signs of reversibility.¹ Most common symptoms were exertional dyspnea and with cough or without sputum in outpatients. Interestingly, 13.9% of patients with airway obstruction were referred other clinics with pulmonary/non-pulmonary symptoms. Around 5.5% of patients were suffered from sweating and weight loss due to obstructive lung diseases. Bronchodilator reversibility was positive in 548.1% of patients. In this study, most common group was ACOS(31.5%) in outpatients. In our recent study, we have described the most common disease ACOS with rate of 29.8% in Turkish patients with obstructive lung disease.¹ Our results consistent with literatures, and the prevalence of ACOS in the asthma/COPD population ranged between 4.4% and 38.3%, depending on the definition used.^{5, 6} Various guidelines have also described the significance of asthma component in COPD patients or has the same symptoms of asthma. The terms “asthmatic bronchitis” or “asthmatic form of COPD” were used to describe such patients in the USA, and the term “asthma-COPD overlap syndrome” is recently being used. A lot of diagnostic criteria were described for ACOS patients from basic to complex definitions. Basically, “asthmatic smokers with COPD” fulfill the profile of patients with ACOS.⁷ Soler-Cataluna *et al.* have described the “COPD-asthma overlap” phenotype with presence of at least two of the major and minor criteria: Major criteria were very high reversibility test ($FEV_1 \geq 15\%$; ≥ 400 mL), eosinophilia in sputum, history of asthma. Minor criteria have included positive reversibility test ($FEV_1 \geq 12\%$; ≥ 200 mL), increased IgE, history of atopy. The major criteria for ACOS described by Louie *et al.* in 2013 included both asthma and COPD diagnosed in the patient by the same doctor, presence or history of atopy

(*e.g.*, allergic rhinitis), increased IgE, age ≥ 40 , >10 pack years smoking, post-bronchodilator $FEV_1 < 80\%$ pred. and $FEV_1/FVC < 70\%$, while the minor criteria were post-bronchodilator $\geq 15\%$, $\geq 12\%$, and >200 -mL increase in FEV_1 . Despite high reversibility values, post-bronchodilator mean FEV_1 value was $< 80\%$ and FEV_1/FVC value was $< 70\%$.⁸⁻¹³ In present study, we suggested that the ACOS patients can practically diagnosed in outpatient clinic with these criteria; ACOS; >40 years old, smoker, postbronchodilator $FEV_1/FVC < 70\%$ of expected and postbronchodilator FEV_1 value can raise over 70% due to high reversibility rates. In our study, 11(10.1%) of patients had pulmonary comorbidities including lung cancer (N.=7), interstitial lung diseases (N.=2), and bronchiectasis (N.=2). Four of the patients had previously diagnosed by lung cancer and they had new diagnosed COPD. 3(3%) patients were newly diagnosed with both of lung cancer and COPD at the same time in outpatient clinic. The number of patients who is over the age of 40 and has a history of 15 pack/year smoking with airway obstruction was 77(92.5%). 7(9%) of these patients had lung cancer and 3(3.9%) of them newly diagnosed with concurrently COPD and lung cancer.

The prevalence of COPD in lung cancer patients is estimated at 50%, while the estimates of lung cancer prevalence in COPD patients varies based on the population and the severity of COPD but is estimated to be between 3.8 and 8.0%. The risk of lung cancer is estimated to be over twice as high in individuals with airway obstruction, and between 50% and 3.5 times higher in individuals with emphysema.¹⁴⁻¹⁸ There are some studies which also suggests that the common exposures such as tobacco smoke or air pollution could lead to epigenetic modification of bronchial cells and increase risk for the development of either COPD or lung cancer by similar mechanisms. Another possible mechanism is that the inflammation that is present systemically and in the airways of individuals with COPD could predispose to the development of lung cancer. Regardless of the mechanism, the high prevalence of comorbid lung disease in patients with COPD has already inspired trials aimed at studying enhanced lung cancer screening in this population.¹⁹

Conclusions

In conclusion, this article is the first outpatient report about the characteristics of patients who has new diagnosed asthma, ACOS, and COPD in Turkish population. ACOS is the most common type of obstructive lung diseases and it can be defined with >40 years-old, smokers, post-bronchodilator FEV₁/FVC<70% of expected and postbronchodilator FEV₁ value can raise over 70% due to high reversibility rates. Lung cancer is the most common pulmonary comorbidities in COPD patients. The outpatients with new diagnosed COPD who is over the age of 40, and smokers should be screened for lung cancer.

References

- Ozkaya S, Dirican A, Tuna T. The objective evaluation of obstructive pulmonary diseases with spirometry. *Int J Chron Obstruct Pulmon Dis* 2016;11:2009–15.
- Global Initiative for Asthma. Diagnosis of Diseases of Chronic Airflow Limitation: Asthma, COPD and asthma-COPD overlap syndrome; 2015 [Internet]. Available from: <https://goldcopd.org/asthma-copd-asthma-copd-overlap-syndrome/> [cited 2018, Jul 9].
- Nakawah MO, Hawkins C, Barbandi F. Asthma, chronic obstructive pulmonary disease (COPD), and the overlap syndrome. *J Am Board Fam Med* 2013;26:470–7.
- Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global Strategy for the Diagnosis, Management and Prevention of COPD; 2017 [Internet]. Available from: <https://goldcopd.org/gold-2017-global-strategy-diagnosis-management-prevention-copd/> [cited 2018, Jul 9].
- Bonten TN, Kasteleyn MJ, de Mutsert R, Hiemstra PS, Rosendaal FR, Chavannes NH, *et al.* Defining asthma-COPD overlap syndrome: a population-based study. *Eur Respir J* 2017;49:160–2008.
- Kiljander T, Helin T, Venho K, Jaakkola A, Lehtimäki L. Prevalence of asthma-COPD overlap syndrome among primary care asthmatics with a smoking history: a cross-sectional study. *NPJ Prim Care Respir Med* 2015;25:15047.
- Barrecheguren M, Esquinas C, Miravittles M. The asthma-chronic obstructive pulmonary disease overlap syndrome (ACOS): opportunities and challenges. *Curr Opin Pulm Med* 2015;21:74–9.
- Gibson PG, Simpson JL. The overlap syndrome of asthma and COPD: what are its features and how important is it? *Thorax* 2009;64:728–35.
- Miravittles M. The overlap syndrome between asthma and COPD: implications for management. *Hot Topics in Respiratory Medicine* 2011;16:15–20.
- Qaseem A, Wilt TJ, Weinberger SE, Hanania NA, Criner G, van der Molen T, *et al.*; American College of Physicians; American College of Chest Physicians; American Thoracic Society; European Respiratory Society. Diagnosis and management of stable chronic obstructive pulmonary disease: a clinical practice guideline update from the American College of Physicians, American College of Chest Physicians, American Thoracic Society, and European Respiratory Society. *Ann Intern Med* 2011;155:179–91.
- Soler-Cataluña JJ, Cosío B, Izquierdo JL, López-Campos JL, Marín JM, Agüero R, *et al.* Consensus document on the overlap phenotype COPD-asthma in COPD. *Arch Bronconeumol* 2012;48:331–7.
- Louie S, Zeki AA, Schivo M, Chan AL, Yoneda KY, Avdalovic M, *et al.* The asthma-chronic obstructive pulmonary disease overlap syndrome: pharmacotherapeutic considerations. *Expert Rev Clin Pharmacol* 2013;6:197–219.
- Albert P, Agusti A, Edwards L, Tal-Singer R, Yates J, Bakke P, *et al.* Bronchodilator responsiveness as a phenotypic characteristic of established chronic obstructive pulmonary disease. *Thorax* 2012;67:701–8.
- de Torres JP, Bastarrika G, Wisnivesky JP, Alcaide AB, Campo A, Seijo LM, *et al.* Assessing the relationship between lung cancer risk and emphysema detected on low-dose CT of the chest. *Chest* 2007;132:1932–8.
- Mannino DM, Aguayo SM, Petty TL, Redd SC. Low lung function and incident lung cancer in the United States: data from the First National Health and Nutrition Examination Survey follow-up. *Arch Intern Med* 2003;163:1475–80.
- Turner MC, Chen Y, Krewski D, Calle EE, Thun MJ. Chronic obstructive pulmonary disease is associated with lung cancer mortality in a prospective study of never smokers. *Am J Respir Crit Care Med* 2007;176:285–90.
- Wilson DO, Weissfeld JL, Balkan A, Schragin JG, Fuhrman CR, Fisher SN, *et al.* Association of radiographic emphysema and airflow obstruction with lung cancer. *Am J Respir Crit Care Med* 2008;178:738–44.
- Young RP, Hopkins RJ, Christmas T, Black PN, Metcalf P, Gamble GD. COPD prevalence is increased in lung cancer, independent of age, sex and smoking history. *Eur Respir J* 2009;34:380–6.
- Putcha N, Drummond MB, Wise RA, Hansel NN. Comorbidities and Chronic Obstructive Pulmonary Disease: Prevalence, Influence on Outcomes, and Management. *Semin Respir Crit Care Med* 2015;36:575–91.

Conflicts of interest.—The authors certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

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