Prevalence of Asthma COPD Overlap (ACO) among the Patients of Obstructive Airway Diseases visiting in Tertiary Care Center in Mandhana, Kanpur, Uttar Pradesh

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Abstract

Asthma-COPD overlap (ACO) has been applied to the condition in which patients have persistent airflow limitations with several features associated with asthma and several features associated with COPD.ACO is a new clinical entity in respiratory medicine that poorly defined and poorly understood among clinicians and associated with poor disease control, higher morbidity and mortality than patients with asthma and COPD alone.

The aims of present study were to estimate the prevalence of ACO and to evaluate the risk factors for the development of ACO in patients with obstructive airways disease.A cross-sectional study was conducted on 200 patients withobstructive airways disease attending the,Department of Pulmonary Medicine, Rama Medical College Hospital and Research Centre, Mandhana , Kanpur, Uttar Pradesh. Patients were enrolled based on past clinical history, clinical examinations and spirometry and were diagnosed with Asthma, COPD, orACO as per the Global Strategy For Asthma Management And Prevention Updated GINA guideline 2024 (GINA

guidelines 2024)[1] and Global initiative for Chronic Obstructive Lung Disease (GOLD guideline 2024)[2].

Out of 200 patients, 82 (41%) patients were diagnosed with asthma, 70 (35%) patients with COPD, and 48 (24%) patients with ACO. Out of these 48 ACO patients,23 having predominantly Asthma symptoms, and 25 havingCOPD symptoms predominantly. ACO patients were younger than COPD patients but older than asthma patients, with male (70.83%) preponderance among ACO patients. AmongCOPD patients, history of childhood asthma; in contrast, among asthma patients, smoking and biomass fuel exposure was significantly associated with ACO development.ACO is a distinct clinical entity that presents with more respiratory symptoms as compared to asthma and COPD, but it is still under diagnosed, which can be attributed to a knowledge gap among clinicians about the correct diagnosis of ACO.We found that the prevalence of ACO was 24% among patients of obstructive airways disease in this study.Among COPD patients, concomitant allergic symptoms, and among asthma patients, concomitant exposure to noxious particles (smoking or biomass fuel) plays acrucial role in the development of ACO.

Keywords: Asthma, COPD, Asthma COPD Overlap

Introduction

Asthma and Chronic Obstructive Pulmonary Disease (COPD) have characteristic clinical features. In asthma, both symptoms and airflow limitations characteristically change over time and intensity. These variations are often triggered by several factors like an allergen, exercise, irritant exposure, weather change, or viral respiratory tract infection[1].COPD is characterized by persistent respiratory symptoms and airflow limitations because of the airway and alveolar

anomalies caused by significant exposure to noxious particles or gases[2]. Tobacco smoking is the most prominent risk factor of COPD, and biomass fuel exposures, as well as air pollution are other important risk factors.However, some patients present with clinical features of both asthma and COPD. This presentation of patients has led to the introduction of the term "asthma-COPD overlap" (ACO), which may be a description of a set of clinical features instead of a definition of a single entity [1][2].ACO is probably not one disease, nor even a syndrome from a clinical perspective, the diagnosis of patients with the characteristic of both asthma and COPD is determining to guide the clinical care of ACO patients[1].

ACO patients present in various clinical forms, which are different from classical asthma or COPD presentation because of several different clinical phenotypes of ACO that are likely due to several different underlying mechanisms responsible for ACO development. Therefore, ACO is identified in clinical practice by virtue of its features with both asthma and COPD[3].While clinically and likely, pathologically, these patients remain distinct, but patients of both diseases fall under the ACO umbrella. ACO is considered in patients with persistent airflow limitation older than 40 years of age with either a history of asthma or large bronchodilator reversibility. Whether ACO emerges after gradual shifting during airway remodeling and inflammation in COPD patients or exposure to a noxious stimulus in an asthma patient, or even as a de novo disease with its pathology is yet not confirmed [4].In various epidemiological studies, ACO's prevalence rates have ranged between 9% and 55% of those with either diagnosis, with variation by gender and age[5–8]. Concurrent doctor-diagnosed asthma and COPD have been reported between 15 and 32% of patients with one or other diagnosis[9–11]. It is difficult to establish an exact disease burden for ACO when no single definition has been accepted universally.Diagnosis of patients with ACO determines their management because

ACO patients experience more frequent and severe respiratory exacerbations[12], despite their younger age and reduced lifetime smoking history[13–15]. These patients have a rapid decline in lung function with higher mortality[9, 15]and greater use of healthcare resources[12, 16] compared with patients bearing features of asthma or COPD. There is a crucial need for more research on the ACO to guide better recognition with safe and effective treatment of ACO patients.We have conducted this study with the aims to find the prevalence of Asthma COPD Overlap (ACO) in patients of obstructive airways disease, as well as toStudy the risk factors forthe development of ACOin patientswithobstructive airways disease.

Material and methods

A cross-sectional study was conducted on 200 patients with obstructive airways disease attending theDepartment of Pulmonary Medicine, Rama Medical College Hospital and Research Centre, Mandhana, Kanpur.Patients of either sex,age≥18 years, having an obstructive airway disease based on history, clinicalexamination, and spirometry were enrolled for study after obtaining informed written consent.Patients having co-morbidities likeHeart disease, Tuberculosis, bronchiectasis,carcinomalung, interstitial lung disease were excluded.

Patients having childhood-onset of disease or onset of disease before 40 years of age, family history of asthma and allergy, personal history of asthma and allergy in childhood, history of diurnal variation of cough, history of wheezing, postnasal drip, sneezing, skin allergy, symptoms triggered by exposure to dust or allergen, blood and sputum eosinophilia, chest x-ray (PA view) within normal limit, spirometry with post-bronchodilator reversibility were diagnosed with asthma[1].Patients having the onset of disease after 40 years of age, history of cough with expectoration without diurnal variation, negative family history of asthma and allergy and no

personal history of asthma and allergy, history of active/passive smoking, history of biomass fuel exposure, chest x-ray (PA view) suggestive of hyperinflation and changes of COPD, on spirometry no post-bronchodilator reversibility were diagnosed with COPD[2].Patients presented with three or more features of both asthma and COPD were diagnosed with asthma COPD overlap (ACO) on basis of the Global Strategy For Asthma Management And Prevention Updated guideline 2024 (GINA guidelines 2024) [1].

Statistical methods

The collected data were entered on Microsoft Excel. Graphs and tables were generated using Microsoft Word and Excel. The statistical analysis used mean, median, standard deviation (SD), and unpaired t-Test for numerical data while Pearson Chi-square for the categorical data with IBM SPSS Version 22. The p-value of <0.05 was considered statistically significant (S), and $p<0.01$ was considered highly significant (HS).

Results

In the current study, out of 200 patients, 82 (41%) patients were diagnosed with asthma, 70 (35%) patients were diagnosed with COPD, and 48 (24%) patients were diagnosed with ACO. (Table1). In105 asthma patients (asthma and ACO in asthma), 23 (21.90%) patients were diagnosed with ACO in asthma, and in 95 COPD patients (COPD and ACO in COPD), 25 (26.32%) patients were diagnosed with ACO in COPD. (Table 2) The mean age of ACO patients (62.77±8.52 years) was more than the asthma patients (44.58±11.07 years) but less than the COPD patients (66.41±6.90 years). The mean age of onset of diseases in ACO patients (32.06±14.31 years) was more than the asthma patients (17.89±7.75 years) but less than the COPD patients (46.13±4.90 years). Out of 48 ACO patients, 14 (29.17%) were females, and 34

(70.83%) were males.The most common presenting symptom of ACO patients was cough (91.67%) followed by breathlessness (89.58%), expectoration (83.33%), seasonal variation of symptoms (79.17%), postnasal discharge (52.08%) and history of wheeze (95.83%). History of childhood asthma was present in 62 (75.61%) of asthma patients, 8 (11.43%) of COPD patients, and 26 (54.17%) of ACO patients. Family history of asthma and allergy was present in 26 (31.71%) of asthma patients, 6 (8.57%) of COPD patients, and 11 (22.92%) of ACO patients. The mean absolute eosinophil count(AEC) in blood in ACO patients (543.71±64.61) was higher than in COPD patients (199.31±46.22) but lesser than in asthma patients (663.32±74.76). Bronchodilator reversibility on spirometry was present in 91.46% of patients with asthma, 4.29% of patients with COPD, and 6.25% of patients with ACO. In the present study, 10 (12.20%) patients with asthma, 43 (61.43%) patients with COPD, and 30 (62.50%) patients with ACO were exposed to biomass fuel. The mean year of exposure to biomass fuel was 2.40±0.70 years in asthma patients, 18.91±2.52 years in COPD patients, and 19.40±3.11 years in ACO patients. One hundred and seven (53.50%) patients had a history of smoking. Out of 107 patients, 8 (9.76%) patients of asthma, 60 (85.71%) patients of COPD, and 39 (81.25%) patients of ACO had a history of smoking. In asthma, 8 (100%) were active smokers, in COPD, 57 (95%) were active smokers, and three (5%) were passive smokers, and in ACO, 35 (89.74%) were active smokers, and four (10.26%) were passive smokers. The mean pack-year of smoking in asthma patients was 3.75±0.71, in COPD patients was 19.21±3.25 and in ACO patients was 18.20 ±2.85.

Discussion

In the current study, the mean age of ACO patients (62.77±8.52 years) was more than the mean age of asthma patients (44.58±11.07 years) but less than the COPD patients (66.41±6.90 years). Thus, we found that ACO patients were younger than COPD patients but older than asthma patients. These results were comparable with the studies conducted by Alshabanat et al[12], De Marco et al[17], Kumbhare et al[18], Kobayashi et al[19], Inoue et al[7], Sharma et al[20], Ekerljung et al[21], Krishnan et al[11].Out of 48 patients diagnosed with ACO, 14 (29.17%) were females, and 34 (70.83%) were males. The prevalence of ACO was more in males than females. Similar results were found by Cosio et al[22]and Krishnan et al[11] which showed male predominance in ACO patients with 81.6% and 60% of males respectively. In contrast, Ekerljung et al[21], Senthilselvan et al[23] in their study found that the proportion of females was significantly higher than males in ACO patients. Zeki et al[24] found male predominance till the age of 75 years and then female predominance in ACO patients.

In our study, out of 200 patients, 82 (41%) patients were diagnosed with asthma, 70 (35%) patients were diagnosed with COPD, and 48 (24%) patients were diagnosed with ACO. The prevalence of ACO in patientswithasthma and COPD was 24%. These results were comparablewith the studies done by Krishnan et al[11], in which they found a 20% prevalence of ACO in a total of 2165 patients with asthma and COPD. On the contrary, in a study done by Uchida et al[10] prevalence of ACO among asthma and COPD patients ranged from 0.9% to 11.1%. The prevalence of ACO varies widely due to differences within the definition, population characteristics, and study design used in various studies.

Out of 105 asthma patients (asthma and ACO in asthma), 23 (21.90%) patients were diagnosed with ACO in asthma, and out of 95 COPD patients (COPD and ACO in COPD), 25

(26.32%) patients were diagnosed with ACO in COPD. Thus, the prevalence of ACO in asthma was 21.90%, and ACO in COPD was 26.32%. These results were comparable with the study done by Hosseini et al[25], in which the prevalence of ACO in asthma was 26.5% and in COPD was 29.6%. Leung et al[4] found in a cohort of COPD patients, the prevalence of ACO ranged from 6% to 55%, and in a cohort of asthma patients, ACO prevalence ranged from 10% to 31%.Kiljander et al[26] in a cross-sectional study on 190 asthma patients, found the prevalence of ACO to be 27.4%.Ekerljung et al[21] found that the prevalence of ACO was 18.1% in 138 asthma patients. Hardin et al[27] found in their study that the prevalence of ACO patients ranged from 13% to 21.7% in the COPD group. Suzuki et al[28], in their study on 140 COPD patients, found that the prevalence of ACO was 28.6%. In a systemic review and meta-analysis done by Alshabanat et al[12], including 17 studies, the prevalence of ACO was 27% among COPD patients.In the present study, a history of childhood asthma was present in 54.17% of ACO patients, 75.61% of asthmapatients, and 11.43% of COPDpatients. Childhood asthma was a risk factor for COPD development and had a strong association with ACO development; this result was in concordance with the study done by Shirtcliffe et al[29], who concluded that childhood asthma emerged with the strongest association for GOLD- defined COPD. De Marco et al[17] concluded in their study that early-onset asthma progressed to fixed airflow obstruction leading to ACO.In the present study, family history of asthma and allergy was present in 22.92% of ACO patients, 31.71% of asthma patients, and 8.57% of COPD patients. Theseresults showed that a family history of allergy was more associated with asthma than COPD and ACO patients. This result was in concordance with the study done by London et al[30], Putcha et al[31], Sharma et al[20].In the current study, the most common presenting symptom of ACO patients was cough (91.67%) followed by breathlessness (89.58%), expectoration (83.33%), seasonal

variation of symptoms (79.17%), postnasal discharge (52.08%), history of wheeze (95.83%); Thus, ACO patients presented with more frequent respiratory symptoms as compared to asthma and COPD patients. Similar results were found by Miravitles et al[32], De Marco et al[33], Hardin et al [34], Sharma et al[20], Vaz Fragoso et al[14], Ekerljung et al[21], Senthilselvan et al[23], Morgan et al[35], as they also concluded that ACO patients had the highest proportion of respiratory symptoms when compared with patients of asthma and COPD. In the present study,the mean absolute eosinophil count in blood in ACO patients (543.71±64.61) was higher than in COPD patients (199.31±46.22) but lesser than in asthma patients (663.32±74.76). This result was in concordance with the study done by Kobayashi et al[19], Suzuki et al[28], Inoue et al[7], Sharma et al[20].In the present study, 10 (12.20%) patients withasthma, 43 (61.43%) patients withCOPD, and 30 (62.50%) patients of ACO were exposed to biomass fuel. The mean year of exposure to biomass fuel was 2.40±0.70 years in asthma patients, 18.91±2.52 years in COPD patients, and 19.40±3.11 years in ACO patients. There was a significant difference in the mean year of exposure to biomass fuel between asthma patients and ACO patients, but no significant difference was found between COPD patients and ACO patients. We have found that there was higher biomass fuel exposure among ACO patients. This result was in concordance with the study conducted by Morgan et al[35], which also found that ACO was higher in patients with household exposure to biomass fuel smoke. Biomass fuel exposure was found to be an important risk factor for the development of ACO in patients with asthma in our study.

In this study, 107 (53.50%) patients had a history of smoking. Out of 107 patients, 8 (9.76%) patients of asthma, 60 (85.71%) patients of COPD, and 39 (81.25%) patients of ACO had a history of smoking. In COPD patients, 57 (95%) were active smokers, and three (5%) were passive smokers, in ACO patients, 35 (89.74%) were active smokers, and four (10.26%) were

passive smokers. So, active and passive smoking bothplayed an important etiological role in the ACOpathogenesis [36]. The mean pack-year of smoking among active smokers in asthma patients was 3.75±0.71, in COPD patients was 19.21±3.25, and in ACO patients was 18.20±2.85. The mean pack-year of smoking was significantly higher in ACO patients than asthma patients, but no significant difference was found between ACO patients and COPD patients. A similar result was found by Alshabanat et al[12],they found no significant difference between ACO and COPD patients in terms of smoking status. Kiljander et al[26] found that age $\geq$ 60years and smoking history $\geq$ 20 pack-years were the best predictors of ACO in asthma. Kobayashi et al[22], Inoue et al[9] found that ACO patients had a shorter smoking history and a lower number of pack-years than COPD patients.Ekerljung et al[21] reported that smoking was present in 71% of ACO patients, 48% of asthma patients, and 74% of COPD patients. Zeki et al[24] reported that pack-year smoking was an important risk factor for ACO.Krishnan et al[11]found that smoking was a major risk factor for ACO development. Our study suggests that smoking was an important risk factor for the development of ACO in asthma patients because tobacco smoking among asthma patients might trigger increased neutrophilic inflammation leading to fixed airflow obstruction and the development of ACO.The present study limited by a small sample size taken from a single source.

Conclusion

The study shows that ACO is a distinct clinical entity that presents with more respiratory symptoms as compared to asthma and COPD, but it is still under-diagnosed, which can be attributed to a knowledge gap about the correct diagnosis of ACO among clinicians. The prevalence of ACO varies widely depending upon the study design, diagnostic criteria, and the

study population. Our study found the prevalence of ACO was 24% among asthma and COPD patients, which is quite high. Among COPD patients, concomitant allergic symptoms, and among asthma patients, concomitant exposure to noxious particles (smoking or biomass fuel) plays an important role in the development of ACO. A high index of suspicion should be kept in mind while treating every patient of asthma and COPD based on additional history for the correct diagnosis and better management of ACO.

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Table 1: Distribution of patients in Asthma, COPD, and ACO

Diagnosis	Asthma	COPD	ACO	Total	X^2	p-value
N (%)	82 (41%)	70 (35%)	48 (24%)	200(100%)	32.01	0.001

Figure 1: Distribution of patients in Asthma, COPD, and ACO

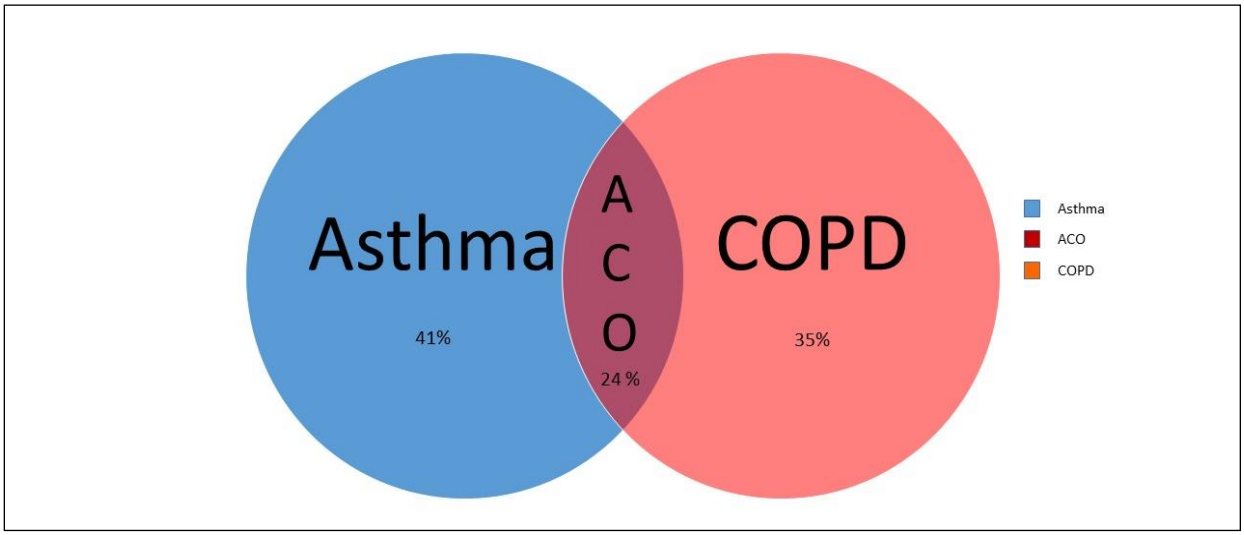

Table 2: Prevalence of ACO in Asthma and ACO in COPD

Diagnosis	Asthma and ACO in asthma (N=105)	COPD and ACO in COPD (N=95)	Total (N=200)	X^2	p-value
ACO	23 (21.90%)	25 (26.32%)	48 (24%)	6.63	0.010

Figure 2: Prevalence of ACO in Asthma and ACO in COPD

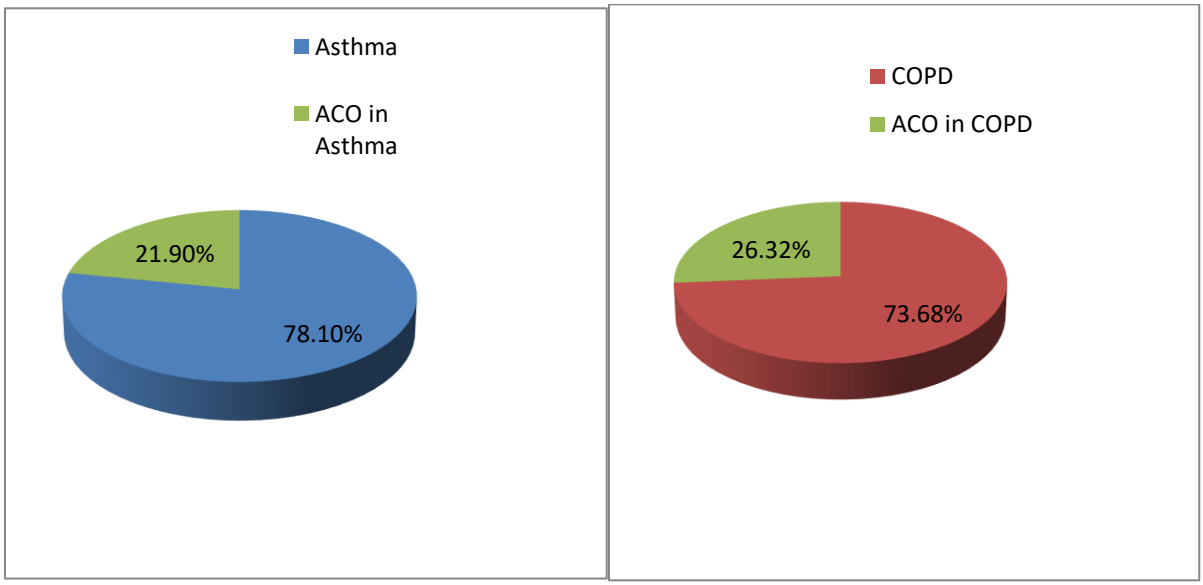

Table 3: Comparison between asthma, COPD and ACO

Characterises		Asthma (N=82)	COPD (N =70)	ACO (N=48)	Asthma VS COPD	Asthma VS ACO	COPD VS ACO
Mean age of presentation (years)	Mean ± SD	44.58±11.07	66.41±6.90	62.77±8.52	0.001	0.001	0.012
Mean age of onset of diseases (years)	Mean ± SD	17.89±7.75	46.13±4.90	32.06±14.31	0.001	0.001	0.001
Gender	Male	32(39.02%	55(78.57%	34	0.001	0.001	0.010

		)	)	(70.83%)			
	Female	50 (60.98%)	15(21.43%)	14(29.17%)			
Chief presenting complaints	Breathlessness	70 (85.37%)	56 (80.0%)	43 (89.58%)	0.022	0.026	0.008
	Dry Cough	69 (84.15%)	50(71.43%)	44 (91.67%)	0.004	0.030	0.015
	Expectoration	33 (40.24%)	54(77.14%)	40 (83.33%)	0.001	0.001	0.017
	Seasonal Variation	38 (46.34%)	4 (5.71%)	37 (79.17%)	0.001	0.054	0.001
	Sneezing	62 (75.61%)	6 (8.57%)	33 (68.75%)	0.001	0.001	0.001
	Postnasal discharge	38 (46.34%)	7 (10.0%)	25 (52.08%)	0.001	0.018	0.018
	Diurnal Variation of cough	78(95.12%)	6(8.57%)	43(89.58%)	0.001	0.027	0.001
	H/o Wheezing	76(92.68%)	5(7.14%)	46(95.83%)	0.001	0.024	0.001
History of childhood asthma	N (%)	62 (75.61%)	8 (11.43%)	26 (54.17%)	0.001	0.001	0.001
Family history of asthma and allergy	N (%)	26(31.71%)	6(8.57%)	11(22.92%)	0.005	0.284	0.056
Post Bronchodilator reversibility	N (%)	75 (91.46%)	3 (4.29%)	3 (6.25%)	0.001	0.001	0.001
Mean Absolute eosinophil count in blood	Mean ± SD	663.32±74.76	199.31±46.22	543.71±64.61	0.001	0.001	0.001
Exposure to Biomass fuel	N (%)	10 (12.20%)	43 (61.43%)	30 (62.50%)	0.001	0.001	0.464
Mean years of exposure to biomass fuel	Mean ± SD	2.40±0.70	18.91±2.52	19.40±3.11	0.001	0.001	0.0458
History of Smoking	Active	8 (100%)	57 (95.0%)	35 (89.74%)	0.001	0.001	0.179
	Passive	0 (0%)	3 (5.0%)	4 (10.26%)			
Total no of mean pack year in active smoker	Mean ± SD	3.75±0.71	19.21±3.25	18.20±2.85	0.001	0.001	0.133