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Original Research Article

Prevalence of asthma chronic obstructive pulmonary disease overlap in patients attending a tertiary health care centre

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ABSTRACT

Background: The study aimed to assess the magnitude of asthma chronic obstructive pulmonary disease asthma chronic obstructive (ACO) in patients with chronic airway disease.
Methods: The study was conducted as cross-sectional study on patients with chronic airway disease presenting at our institute during the study period of 1 year. Global initiative for asthma management and prevention (GINA) syndromic approach table was used to diagnose patients with chronic airways disease. Syndromic and confirmatory diagnosis of ACO was made based upon clinical features and spirometry respectively.
Results: About 73.6% were diagnosed as chronic obstructive pulmonary disease (COPD) and 26.4% cases were diagnosed as asthma. Overall ACO was present in 20% cases. ACO was significantly associated with advancing age, male gender, and longer duration of smoking ($p<0.05$) in asthma patients whereas in COPD patients ACO was associated with advancing age ($p<0.05$).
Conclusions: Overall one fifth of the patients with chronic airway disease have asthma COPD overlap. The ACO is observed in almost equal proportions in asthma and COPD. ACO prevalence was found to increase with age in patients with asthma and COPD.

Keywords: ACO, Asthma, COPD, GINA, GOLD

INTRODUCTION

Asthma and chronic obstructive pulmonary disease (COPD) have characteristic clinical features, but patients with clinical features of both asthma and COPD are encountered in clinical practice. Asthma, a chronic inflammatory state of the lung with cough and sputum production is often confused with chronic obstructive pulmonary disease (COPD) when present in individuals over the age of 40.[1] In contrast to asthma, COPD although being a chronic inflammatory disease has a persistent airflow limitation.[2] This observation has led to the introduction of the term "asthma-COPD overlap" (ACO), which is entity of a collection of clinical features rather than a definition of a single disease. While ACO is likely not a single disease, not even a syndrome from a clinical or mechanistic perspective, recognition of patients with features of both diseases is important to guide clinical care.[3]

Differentiating between the two had been a challenge in the past, but with significant research being done on this field, the GINA and its COPD counterpart, (GOLD) have laid down the principles by which the two can be differentiated.[1,2] The inflammation in asthma although usually eosinophilic, a neutrophilic Phenotype is also seen. Based on the composition of neutrophil and eosinophil, Asthma can be categorized into neutrophilic asthma, eosinophilic asthma, mixed granulocytic asthma and pauci granulocytic asthma whereas, COPD is predominantly a neutrophilic inflammation.[4,5] The asthma phenotype with neutrophilic inflammation is more often associated with

severe asthma and is poorly responsive to inhaled corticosteroids.[6] People had varied opinion about these phenotypes, as some called this a separate entity with overlap of symptoms between asthma and COPD; while others prefer it as a phenotype of asthma itself.

These findings triggered an age-old debate-the Dutch hypothesis, which states that asthma and COPD are different levels of the same disease spectrum eventually results in the disease.[7] The recent thinking on this subject is that there is an overlap of symptoms between asthma and COPD in certain patients, which has been termed as asthma-COPD overlap syndrome.

Literature suggests that ACO has worst prognosis than asthma or COPD. Frequency of exacerbations, poor disease control, increase admission rate, increased economic burden, and rapidly declining lung functions have been shown to be more in ACO. Hence it is very essential to diagnose and treat ACO at an early stage. Thus, we planned this study to find the prevalence of asthma COPD overlap (ACO) in patients attending tertiary health care centre. The purpose of this study is to assess the magnitude of ACO in patients with chronic airway disease at a tertiary care hospital. This data can be further used to diagnose and treat ACO at an early stage.

METHODS

The present study was conducted as an observational cross-sectional study on patients with chronic airway disease presenting at department of medicine, Pt. J. N. M. medical college and Dr. Bhim Rao Ambedkar memorial hospital Raipur during the study period of 1 year i.e., from 1st January 2019 to 31st December 2019.

Sample size was calculated using the formula:

n= $Z^2p(1-p)/d^2$

Where, n=sample size, Z=confidence interval at 95%, p=estimated prevalence, d=desired level of precision

For our study, p=20% (from previous study)=0.2, d=7%=0.07

Thus, sample size was estimated to be 125.

Patients with chronic airway disease belonging to age range of 18 to 60 years were included whereas exclusion criteria were patients with left ventricular failure, structural lung diseases, pulmonary Tuberculosis and bronchiectasis.

After obtaining ethical clearance from Institute's ethical committee, GINA syndromic approach table was used to diagnose patients with chronic airways disease.[1] All the patients diagnosed to be suffering from chronic airway disease were enrolled and written consent was obtained from them.

Table 1: Features distinguish asthma and COPD.

Features	Asthma	COPD
Age of onset (years)	Before age 20	After age 40
Pattern of symptoms	Variation over minutes, hours or days	Persistent despite treatment
	Worse during the night or early morning	Good and bad days but always daily symptoms and exertional dyspnea
	Triggered by exercise, emotions including laughter, dust or exposure to allergens	Chronic cough and sputum preceded onset of dyspnea, unrelated to triggers
Lung function	Record of variable airflow limitation (spirometry or peak flow)	Record of persistent airflow limitation (FEV1/FVC<0.7 post-BD)
Lung function between symptoms	Normal	Abnormal
Past history or family history	Previous doctor diagnosis of asthma	Previous doctor diagnosis of COPD, chronic bronchitis or emphysema
	Family history of asthma, and other allergic conditions (allergic rhinitis or eczema)	Heavy exposure to risk factor: tobacco smoke, biomass fuels
Time course	No worsening of symptoms over time. Variation in symptoms either seasonally, or from year to year	Symptoms slowly worsening over time (progressive course over years)
	May improve spontaneously or have an immediate response to bronchodilators or to ICS over weeks	Rapid-acting bronchodilator treatment provides only limited relief
Chest X-ray	Normal	Severe hyperinflation

Stepwise approach to diagnosis of ACO was used which included:

Step 1-For diagnosis of chronic airway disease

Clinical history was obtained in detail. History regarding previous treatment with inhaled medications, smoking tobacco and/or other substances abuse, exposure to environmental hazards, e.g., airborne pollutants was obtained and entered in questionnaire. Also, previous prescriptions relating to diagnosis of asthma or COPD if any was also obtained. Further all the patients were subjected to detailed physical and systemic examination. Radiology (CXR or CT scan) was performed and findings were noted.

Step 2-Syndromic diagnosis of asthma-COPD overlap (ACO)

If the patient has ≥3 features of both asthma or COPD from GINA syndromic approach, asthma COPD overlap (ACO) was suspected.

Step 3-Confirmation of asthma COPD overlap (ACO) by spirometry

Spirometry was done to confirm chronic airflow limitation and presence of asthma, COPD and ACO.

Table 2: Distinguish between asthma, COPD and ACO by spirometry finding.

Spirometric variable	Asthma	COPD	Overlap
Normal FEV1/FVC pre- or post-BD	Compatible with asthma	Not compatible with diagnosis (GOLD)	Not compatible with diagnosis
Post-BD FEV1/FVC<0.7	Indicates airflow limitation; may improve	Required for diagnosis by GOLD criteria	Usual in asthma- COPD overlap (ACO)
FEV1 ≥80% predicted	Compatible with asthma (good control, or interval between symptom)	Compatible with mild COPD	Compatible with mild ACO
FEV1, <80% predicted	Compatible with asthma. A risk factor for exacerbations	Indicates severity of airflow limitation and risk of exacerbations and mortality	Indicates severity of airflow limitation and risk of exacerbations and mortality
Post-BD increase in FEV1 >12% and 200 mL from baseline (reversible airflow limitation)	Usual at some time in course of asthma; not always present	Common in COPD and more likely when FEV1 is low	Common in ACO, and more likely when FEV1 is low
Post-BD increase in FEV1 >12% and 400mL from baseline	High probability of asthma	Unusual in COPD	Compatible with diagnosis of ACO

Statistical analysis

Microsoft excel was used for data compilation. IBM SPSS software was used for data analysis. Numerical data was expressed as mean±SD whereas categorical data was expressed as frequency and proportion. Student's t test was used to check the significance of difference between two parameters in parametric data. Pearson correlation analysis was performed to check the association between the numerical variables. Chi square test was used to analyses the significance of difference between frequency distribution of the data. P<0.05 was considered as statistically significant.

RESULTS

In present study, mean age of patients with chronic airway disease was 55.10±10.24 years. male predominance for chronic airway disease was observed in present study with male: female ratio of 2.68:1. About 72.8% patients were males whereas only 27.2% cases with chronic airway disease were females.

Out of 125 patients, majority i.e., 92 (73.6%) were diagnosed as COPD whereas only 33 (26.4%) cases were diagnosed as asthma (Figure 1).

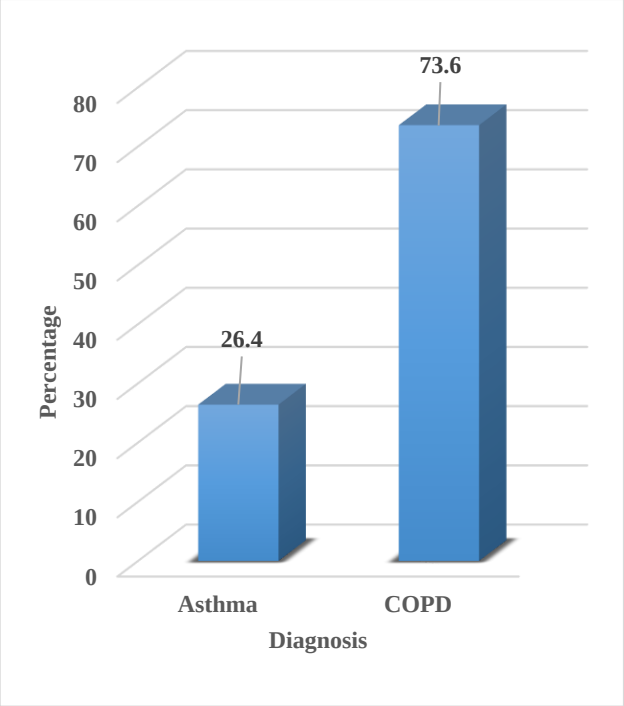

Figure 1: Distribution of patients according to diagnosis.

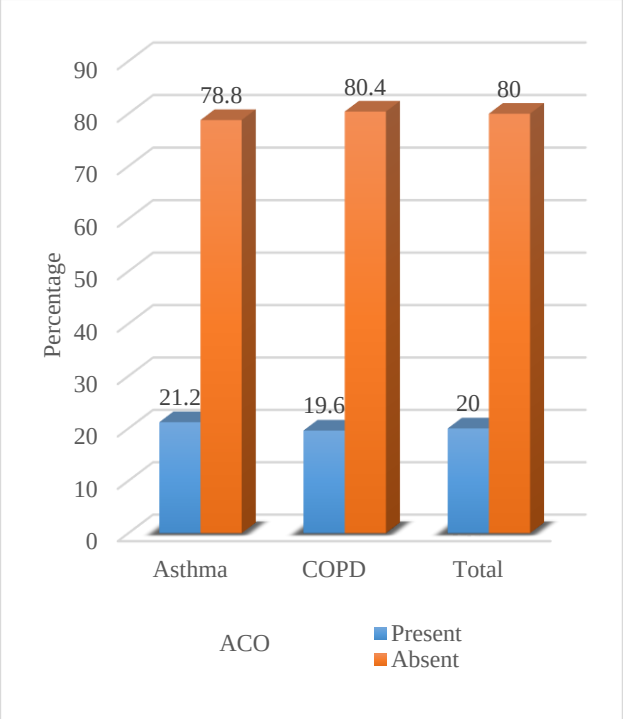

Figure 2: Prevalence of asthma COPD overlap.

In present study, overall ACO was present in 25 (20%) cases. Out of 33 patients with asthma, ACO was present in 7 (21.2%) cases whereas out of 92 cases with COPD, ACO was observed in 18 (19.6%) cases.

Table 3: Association of ACO with various factors in cases with asthma.

Variables		ACO		P value
		Present (n=7)	Absent (n=26)	
Age (years)	≤30	0 (0.0)	7 (26.9)	0.007
	31-40	0 (0.0)	11 (42.3)	
	41-50	7 (100)	7 (26.9)	
	>50	0 (0.0)	1 (3.8)	
Gender	Male	6 (85.7)	9 (34.6)	0.016
	Female	1 (14.3)	17 (65.4)	
Residence	Urban	4 (57.1)	7 (26.9)	0.13
	Rural	3 (42.9)	19 (73.1)	
Duration of smoking	<10	1 (14.3)	1 (3.8)	0.004
	11-20	4 (57.1)	6 (23.1)	
	21-30	2 (28.6)	0 (0.0)	
	Occasional	0 (0.0)	1 (3.8)	
	No addiction	0 (0.0)	18 (69.2)	
Family history	Present	2 (28.6)	5 (19.2)	0.59
	Absent	5 (71.4)	21 (80.8)	

ACO was observed in significantly higher proportions of patients with asthma in the age range of 41 to 50 years (100%) ($p<0.05$). Also, ACO was significantly associated with male gender (85.7%), and longer duration of smoking ($p<0.05$).

Table 4: Association of ACO with various factors in cases with COPD.

Variables		ACO		P value
		Present (n=18)	Absent (n=74)	
Age (years)	≤30	2 (11.1)	1 (1.4)	0.041
	31-40	12 (66.7)	40 (54.1)	
	41-50	4 (22.2)	33 (44.6)	
	>50	0 (0.0)	1 (3.8)	
Gender	Male	13 (72.2)	63 (85.1)	0.195
	Female	5 (27.8)	11 (14.9)	
Residence	Urban	10 (55.6)	42 (56.8)	0.927
	Rural	8 (44.4)	32 (43.2)	
Duration of smoking	<10	6 (33.3)	10 (13.5)	0.089
	11-20	9 (50.0)	31 (41.9)	
	21-30	3 (16.7)	30 (40.5)	
	Occasional	0 (0.0)	3 (4.1)	
	No addiction	0 (0.0)	18 (69.2)	
Family history	Present	0 (0.0)	0 (0.0)	NA
	Absent	18 (100)	74 (100)	

ACO was observed in significantly higher proportions of patients with COPD in the age range of 31 to 50 years (88.9%) ($p<0.05$). However, we documented no significant association of ACO with other factors such as gender, duration of smoking, family history and residence ($p>0.05$).

DISCUSSION

ACO is an umbrella term that covers, a set of patients, who have both features of asthma as well as COPD. The degree of dominant symptoms manifestation of one disease over another can be different, yet coexistence of both is what is known as ACO. This includes a wide spectrum of patients that exist in between pure COPD and pure asthma. There are a lot of criteria for diagnosing ACO ever since 2008. Most of them are simple and includes a previous diagnosis of COPD and spirometry evaluation. The prevalence of ACO may vary depending upon criteria used. Jo et al documented 31% prevalence of ACO by using modified Spanish criteria whereas prevalence was 48% using the platino criteria.[8] Due to the lack of consensus across the various groups of respiratory scholars, in 2016 the GINA and GOLD together published a consensus document, proposing a syndromic approach tool to ease and standardize the diagnosis of ACO.[1,2] GINA-GOLD guidelines are widely accepted, hence we decided to use this tool to assess the magnitude of ACO in our study.

According to Lancet global health the contribution of chronic airways diseases to the DALYs in India is increased from 4.5% in 1990 to 6.4% in 2016. COPD and Asthma were responsible for 75.6% and 20.5% of the chronic respiratory disease DALYs respectively.[9] In our study out of 125 patients, majority of cases were COPD

i.e., 73.6% whereas 26.4% cases were diagnosed as asthma in patients with chronic airway diseases.

Overall, the prevalence of ACO was documented in 20% cases in our study irrespective of type of chronic airway disease. However, the prevalence of ACO in asthma and COPD was 21.2% and 19.6% respectively. Fu et al reported the prevalence of ACO is 11.1% to 61.0% in Asthma patients and 4.2% to 66.3% in COPD patients.[10] However, Milanese et al reported higher prevalence of ACO (38.1%) in patients with chronic airway diseases.[11] Hosseini et al reported the prevalence of ACO was 21.6% among patients with Asthma and 29.6% among patients with COPD.[12] Vaz Fragoso et al reported 17.4% prevalence of ACO in patients with chronic airway disease.[13] In our study prevalence of ACO was lower than other study due to constraints of age 18-65 as we taken for our study.

In our study, age more than 40 years and more than 30 was significantly associated with ACO in asthma and COPD respectively. However, longer duration of smoking and male gender was significantly associated with ACO in asthmatic patients but not in COPD patients. Kiljander et al revealed ACO prevalence as 27.4% in asthma patients who have a history of smoking. The factors associated with ACO in reference study were smoking 20 packs years and age over 60 years and these were observed to be the best predictors of ACO in the reference study. These risk factors together increased ACO by 6 folds.[14] Menzes et al reported higher mean age in ACO patients is to be related to the development of persistent airways obstruction due to inadequate treatment or on-going insults such as smoking.[15] Similarly, Soriano et al estimated that approximately 23% of patients with COPD having age 50-59 years have ACO, and this value rising to 52% in subjects of 70-79 years.[16]

ACO was generally found to be gender nonspecific. In our study, ACO was significantly higher in asthmatic males as compared to females. In contrast, Vaz Fragoso et al documented higher proportions of patients with ACO to be females.[13] In another study done by Montes et al, 65% of the ACO patients were male.[17] Park et al, on the other hand reported 95% males with ACO.[18]

Overall, there are a lot of population-based studies, disease characterization research, criteria development, morbidity related data, health expenses etc. which are published in increasing numbers over the past few years. Most of the studies have conveyed the idea that ACO have worse outcomes than either asthma alone or COPD alone. They were found to have worse disease control, worse rates of exacerbations and admission, with increased financial demand on the patient.[19]

Overall using GINA syndromic approach to diagnose ACO was fairly simple and less time consuming. Not only it helps us to diagnose ACO, it helps us to differentiate bronchial asthma from COPD with ease.[20] The GINA tool relies lot on the clinical features of the disease process. The drawback is that patients who are poor historians can provide incorrect details. This could explain how patients with 400ml reversibility were labelled as COPD. There were a few such patients in our study who were diagnosed as COPD despite having very significant reversibility, which should definitely be asthma. A significant percentage of the COPD patients had normal FEV1/FVC ratio. We know that normal ratio is not compatible with diagnosis of COPD, but the clinical behavior of the disease would have been very much like COPD.

CONCLUSION

Overall, one fifth of the patients with chronic airway disease have asthma COPD overlap. The ACO is observed in almost equal proportions in asthma and COPD. ACO prevalence was found to increase with age in patients with asthma and COPD. ACO was significantly observed in higher proportion of males as compared to females and longer duration of smoking in patients with asthma but not in COPD. This study provides an insight that outcome of ACO is worse than asthma and COPD alone.

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