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ASTHMA-COPD OVERLAP PREVALENCE AND CHARACTERISTICS IN INDIA

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ABSTRACT

Background: According to Dutch hypothesis Asthma and COPD are the chronic airway diseases with different presentation which was determined by genetic and environmental factors. So Asthma-COPD Overlap (ACO) defined as a different entity by GINA and GOLD report. But the exact prevalence of the disease is not yet identified due to different diagnostic criteria applied in different studies worldwide. To solve this problem GINA reported a stepwise approach to the diagnosis of ACO. **Aim:** To estimate the prevalence of ACO in Patients who were receiving treatment for COPD. **Methods:** This is a cross sectional study conducted in a tertiary care center. This study included 75 COPD patients who were identified by age ≥ 40 years, chronic respiratory symptoms with airflow limitation ($FEV_1/FVC < 0.7$). ACO patients were diagnosed by the stepwise approach stated by GINA. **Result:** Our study has shown that the prevalence of ACO in COPD patients 36% (n=27). ACO patients were younger (ACO 60.19 years vs 66.44 years, p=0.004), higher Post bronchodilator FEV_1/FVC Ratio (0.61 vs 0.53, p=0.001), higher Absolute Eosinophil Count (239.63 vs 105.75, p=0.004), higher Total Serum IgE (565.48 vs 333.08, p<0.001) than COPD only patients. Raised total serum IgE(>100) and Absolute Eosinophil Count(>300) are the significant biomarkers for ACO diagnosis (IgE p=0.001 & AEC, p=0.016). **Conclusion:** The results of our study shows that the ACO phenotype differs in clinical characteristics of COPD. GINA Stepwise approach is a helpful tool in identifying ACO. IgE and AEC are important biomarkers to differentiate ACO from COPD.

KEYWORDS: COPD, ACO, IgE and AEC.

INTRODUCTION

Obstructive airway diseases mainly confined to either COPD or Asthma. Both these diseases have different spectrum of airway pathology, in which asthma has airflow limitation which is reversible & COPD characterized by fixed airway obstruction usually irreversible. These two are distinct conditions but their clinical features overlap and sometimes difficult to differentiate, classify and diagnose clinically.[1,2]

The Dutch Hypothesis suggest that Asthma and COPD may be considered as different expressions of a single disease entity.[3,4] This overlapping characteristics were most often seen in asthmatic patients who were smokers. And also in COPD patients with good post bronchodilator reversibility in lung volumes.[5,6] These overlapping features were called by many names in many studies. Recently GINA and GOLD together defined it as Asthma COPD Overlap (ACO).

The epidemiological studies have reported the prevalence of ACO was between 15% to 55%.[7,8,9] This wide range is due to the different criteria used in different studies. This complicates our understanding of epidemiology and clinical characteristics of this disease.

Although we don't have an exact definition and the diagnostic criteria for ACO, the recent report of the Global Initiative for Asthma (GINA) and the Global Initiative for Chronic Obstructive Lung Disease (GOLD) has highlighted a stepwise approach for the diagnosis of ACO.[10,11]

AIM

To identify the prevalence of Asthma-COPD Overlap and its characteristics in patients who were receiving treatment for COPD.

METHODS AND MATERIALS

This is a single center, cross sectional study conducted in Sir Sunderlal hospital, in Varanasi, from December 2017 to July 2018. The study population mainly from Bihar and eastern Uttar Pradesh. After approval from Institute Ethical Committee, 75 COPD patients who visited our hospital for regular follow up were included in this study. This study included previously diagnosed COPD

patients who were on inhaled medications (non ICS) for atleast one year. We excluded the patients who received systemic steroids in last month, who have history of lung cancer, active pulmonary TB, Heart Failure, ILD, not adherent to previous medications and comorbidities like pulmonary hypertension. All the study subjects gave informed written consent.

Complete history of the patient obtained like age of onset of symptoms, no. of exacerbations in last year, seasonal variations, and diurnal variations, previous inhaler use, family history, etc. Patients who have clinically diagnosed asthma by a doctor atleast once in their lifetime considered as previous diagnosis of asthma in this study.

Patients were evaluated for the Asthma COPD Overlap (ACO) features by the Stepwise approach stated by GINA report 2017[10] (Table 1).

Table 1: Features of Airway diseases.

Feature	Asthma	COPD
Age of onset	Before age 20 years	After age 40 years
Pattern of respiratory symptoms	Variation in symptoms over time	Persistence of symptoms despite treatment
	Symptoms worsen during the night or early morning	Good and bad days but always daily respiratory symptoms and exertional dyspnea
	Symptoms triggered by exercise, emotional change (including laughter), or exposure to dust/allergens	Chronic cough and sputum preceded by onset of dyspnea, unrelated to triggers
Lung function	Record of variable airflow limitation (spirometry, peak expiratory flow)	Record of persistent airflow limitation (post-bronchodilator FEV1/FVC < 0.7)
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, dermatitis)	Heavy exposure to a risk factor like tobacco smoke and biomass fuels
Time course	No worsening of symptoms over time. Symptoms vary either seasonally or from year to year	Symptoms slowly worsen over time (progressive course over years)
	May improve spontaneously or have a response to bronchodilator immediately or to ICS over weeks	Rapid-acting bronchodilator treatment provides only limited symptom relief
Chest X-ray	Normal	Severe hyperinflation

First, patients who had both three or more features favoring asthma and three or more features favoring COPD (as shown in Table 1) were selected as candidates for ACO. In the next step, patients who also had variable airflow limitation were identified as having ACO.

Serum IgE levels were measured during visit by the Chemiluminescent immunoassay. IgE levels >100 IU/L were considered as raised. Serum Absolute Eosinophils Count (AEC) measured by Autoanalyzer. Pulmonary Function Test has been performed by Vyaire, Germany. Bronchodilator (BD) reversibility response assessed after inhalation of salbutamol 400mcg.

Data analysis

Statistical analysis were done using SPSS 16. Continuous data were expressed in means and Standard Deviation, categorical data were expressed in percentage. Comparison of categorical data were made using the Chi-squared test. Comparison of continuous data between two groups were performed by *T*-test (for normal distribution parameters) and Mann–Whitney U test (for abnormal distribution parameters). P value < 0.05 considered as significant.

RESULTS

Total of 75 Patients included in this Study. Among them Male 43% (n=32) and Female 57% (n=43). Prevalence of ACO in our study population is 36% (n=27).

Table 2: Clinical characteristics.

Characteristics	Total N=75	COPD Only n=48	ACO n=27	p-value
Age (yrs)	64.19 ± 9.142	66.44 ± 8.24	60.18 ± 9.43	0.004
Male Female	32 (42.7%) 43 (57.3%)	24 (50%) 24 (50%)	8 (29.6%) 19 (70.4%)	0.87
Previous diagnosis of asthma, n(%)	17 (22.7%)	0 (0%)	17 (63%)	<0.001
Smokers (>10 pack years), n(%)	38 (50.7%)	25 (52.1%)	13 (48.1%)	0.744
Biomass exposure, n(%)	41 (54.7%)	22 (45.8%)	19 (70.4%)	0.040
h/o Previous exacerbation, n(%)	52 (69.3%)	37 (77.1%)	15(55.6%)	0.052
Seasonal variation, n(%)	34 (45.3%)	9 (18.8%)	25 (92.6%)	<0.001
Hyperinflation, n(%)	53 (70.7%)	38 (79.2%)	15 (55.6%)	0.031
Family h/o asthma, n(%)	23 (30.7%)	2 (4.2%)	21 (77.8%)	<0.001

ACO patients were younger than COPD only patients, and having more seasonal variation history, family history and previous diagnosis of asthma. COPD only patients having more hyperinflation, smoking and biomass exposure history.

Table 3: Comparison of spirometric variables and biomarkers.

Characteristics	Total N=75	COPD Only n=48	ACO n=27	p-value
PostBD FEV_1 FVC	0.56±0.099	0.53±0.10	0.61±0.06	0.001
PostBD increase in FEV_1 %	11±8.69	8.11±7.42	18.33±6.76	<0.001
PostBD increase in FEV_1 volume	155.4±131.27	74.85±58.57	298.59±97.85	<0.001
IgE	416.74±434.81	333.08±447.93	565.48±373.51	<0.001
Raised IgE (>100 IU/L)	55(73.3%)	29(60.4%)	26(96.3%)	0.001
AEC	153±205.11	105.75±168.36	239.63 ±245.18	0.004
Raised AEC (>300 cells/mm^3)	10(13.3%)	3(6.2%)	7(25.9%)	0.016

ACO patients were having better lung function, more post BD variability. Serum total IgE, AEC were raised in ACO patients than COPD only patients.

DISCUSSION

Asthma COPD Overlap was diagnosed by so many criteria in previous literatures. So the exact prevalence of the disease could not be identified.

Even in the same population prevalence differs if the diagnostic criteria changes.[12,13,14] Jo YS et al, found that by using modified Spanish criteria the prevalence was 31% and by the Platino criteria that was 48% in same population. Recent GOLD and GINA reports suggested a stepwise approach to diagnose ACO which is widely accepted, hence we decided to use this tool to assess the magnitude of ACO in our study.

In our study, the prevalence data for ACO among COPD patients was 36%. Among the population who had airway obstruction, the prevalence of ACO was between 3.1% and 55.5%.[13,15-17] In patients with COPD, the prevalence of ACO ranged from 4.2% to 66.0%.[9,18-23] Our study results were well within this range. In a meta-analysis, Alshabanat et al, reported that prevalence of ACO was 27% and 28% in the population- and hospital-based studies, respectively.[18]

In our study 70.4% of the ACO patients were female and 29.6% were male. The prevalence of ACO was found to be more in Female (N = 19) compared to Male (N = 8). This is similar to a study done in the US, by Vaz Fragoso et al, in which they found that 67% of their ACO patients were female.[24] Our study result is contrast to another study done by Montes de Oca M et al, In which they have reported that 65% of the ACO patients were male[25] & Park HJ et al, in which they have reported that 95% males with ACO.[26] This may be due to the alterations in the smoking habits in the population.

In our study ACO patients were younger than COPD patients (Mean age ACO=60.19±9.43 years vs COPD Only=66.44±8.249 years, p=0.004). This is similar to various studies all over the world.[23,27-30]

In India Rahul Sharma et al, reported that the mean age of patients in ACO was 63 years.[31] This is similar to our study 60.19±9.43years. But they found male predominant.

In our study all the patients of previous doctor diagnosed asthma who treated as COPD later have ACO. Previous studies also stated that significant proportion of asthma patients could be diagnosed as having ACO later in their life.[25,32,33] In our study all the patients of ACO having either smoking history or biomass exposure history. Previous studies also stated that smoking or biomass exposure should be present for the diagnosis of ACO.[34]

In our study the post-BD FEV_1/FVC Ratio is significantly higher in ACO patients than COPD Only patients. This is similar to the study done by Izquierdo-Alonso JL et al, in which the post-BD FEV_1/FVC Ratio is significantly higher in COPD-Asthma Phenotype than Emphysema Phenotype.[35]

In our study ACO group has significantly higher serum Absolute Eosinophil count (p=0.004) & serum total IgE(p<0.001) than COPD Only group. In our study the patients who has raised serum Absolute Eosinophil counts (>300 cells) and raised serum total IgE (>100) were significantly more in ACO group than COPD Only group(AEC: p=0.001 & IgE: p=0.016).

This is similar to the study done by Suzuki M et al, they described that ACO as the combination of bronchodilator reversibility, blood eosinophilia (peripheral blood eosinophil count of >300 cells), and/or atopy (the presence of specific serum IgE to at least 1 of the 14 common inhaled allergens) in Hokkaido cohort study.[36] Kitaguchi et al, compared the clinical features of COPD patients with asthmatic symptoms with those of COPD patients without asthmatic symptoms. The peripheral eosinophil counts significantly higher in the COPD with asthma group.[37]

In India Rahul Sharma et al, reported that serum total IgE and Eosinophil counts are significantly higher in ACO patients.[31] This is similar to our study.

CONCLUSION

This study highlights that history of the COPD patients should be evaluated thoroughly for overlapping features. The stepwise approach should be used for the diagnosis of ACO universally in any population to estimate the exact prevalence and characteristics.

Our study showed the prevalence of ACO in Indian population is 36%. And ACO patients were younger and have better lung function. Previous diagnosis of Asthma, family history of asthma, seasonal variation were the features favoring ACO.

We suggest the use of serum IgE, Absolute Eosinophils count as biomarkers for ACO. They may be the therapeutic targets in future in this population.

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