



STUDY OF CLINICAL, RADIOLOGICAL AND PULMONARY FUNCTION CHARACTERISTICS OF PATIENTS HAVING ASTHMA COPD OVERLAP

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ABSTRACT

As there is no gold standard for the diagnosis of ACOS one cannot be absolutely sure that newly diagnosed COPD patients with BDR and/or self-reported wheezing always have ACO. However, in spite of that, the present study may provide important knowledge with regard to identification of patients with possible ACO among new patients diagnosed with COPD.

In this study, 100 syndromically defined ACOS patients were studied in a tertiary care teaching hospital. Detailed history was taken with respect to demographic characteristics, clinical symptoms, grade of dyspnoea, past history of smoking, duration of smoking, frequency of exacerbations. Complete blood count and a chest x-ray were done. Their lung functions were studied. Results show that majority of the patients classified as ACO had breathlessness and wheezing as major symptoms, had positive smoking history with high number of exacerbations and more than 50% of the patients had an obstructive pattern along with significant bronchodilator response in pulmonary function tests.

The majority of patients with COPD are diagnosed and managed in primary care, and as wheezing and BDR are easy to detect characteristics also in primary care, our findings may offer substantial guidance for general practitioners to screen for possible ACOS among their patients with COPD, although further diagnostic work-up is likely to be needed.

KEYWORDS : asthma, COPD, Asthma-COPD overlap

INTRODUCTION

Asthma-COPD overlap (ACO) has been recognized as a condition characterized by the coexistence of some clinical features of both asthma and COPD, with the disease severity and clinical course differing from those of other chronic airway diseases.^(1,2)

Although a consensus on the exact definition and the diagnostic criteria of ACO remains elusive, 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.^(1,2)

This study aims to prospectively identify patients with ACO using a stepwise approach, as in the GINA/GOLD report, among outpatients receiving medical treatment for COPD or Asthma:

MATERIALS AND METHODS

This is a prospective observational study carried out at a tertiary care centre in Bhavnagar from September 2016 to August 2017.

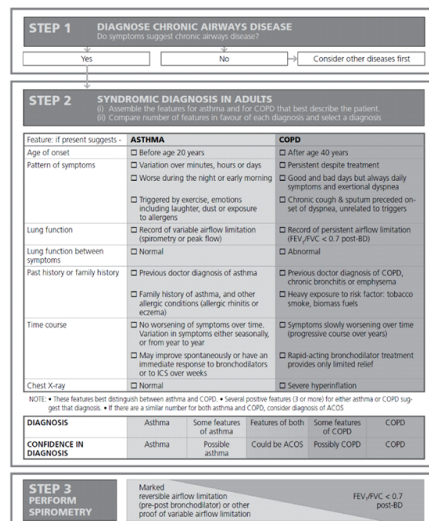
Patients who were diagnosed with Chronic airway obstruction by any physician or presented with the same clinical features, as defined in the GOLD/ GINA ACO guidelines were considered.^(1,2)

Patients who had three or more features favoring asthma as well as three or more features favoring COPD, as shown in Table 1, were selected as candidates for ACO. Detailed history was taken which included age, sex, symptoms, smoking history, exacerbation history, history of allergy and any significant past history of respiratory or cardiac condition.

Complete blood count and a Chest X-ray (PA) was obtained. All patients were subjected to Spirometry (FVC Maneuver). Spirometry tests were performed at baseline and 15 min after the inhalation of 400 g salbutamol, according to the American Thoracic Society ATS & ERS guidelines of acceptability and reproducibility in sitting position.⁽³⁾

STATISTICAL ANALYSIS

The Data Analysis was done with SPSS software version 23 (evaluation copy) and was considered significant if p value is < 0.05.



RESULT

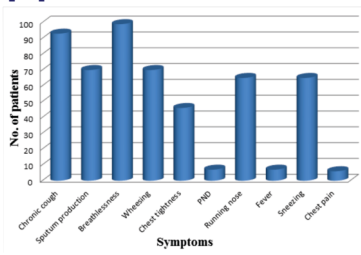
The study included a total of 100 patients enrolled out of which there were 76 males (76%) and 24 females (24%) with age ranging from 40 to 86 (mean age 56.42 ± 10.54)

Table 5.1 Age Wise Distribution of Patients

Age Group (in years)	40-50	51-60	61-70	71-80	81-90	Total
Percentage of (N=100)	38	30	22	9	1	100

Among symptoms, breathlessness (99%) was the most common complaint followed by chronic cough (93%), sputum production (70%), wheezing (70%), running nose (65%), sneezing (65%), chest tightness (46%), paroxysmal nocturnal dyspnoea (PND) (7%), fever (7%) and chest pain (6%).

Figure 5.1: Symptom Profile of Patients



48% of patients had grade 1, 39% had grade 2 and 12% had grade 3 dyspnoea. There were no patients having grade 0 and grade 4 dyspnoea.

History of smoking tobacco or other substances (74%) and exposure to airborne pollutants; domestic biomass fuel exposure or occupational exposure (63%) were found to be the major risk factors in this patient group.

25% were Active Smokers while 49% were Ex-Smokers (cessation of more than 6 months) and 26% patients were never smokers (< 100 cigarettes or bidis/day).

Table 5.5 Smoking Status

Smoking Status	Current smoker	Ex smoker	Never smokers	Total
Percentage of N = 100	25	49	26	100

Among those with smoking history, 66% of smokers had total duration of smoking of more than 10 pack years and 34% had less than 10 pack years.

In this study, acute exacerbations experienced in last year was 2.74 ± 2.302 (Mean \pm SD)

Table 5.6 Acute Exacerbations Profile of Patients

Parameters	AE in a year when Untreated	AE in a year on treatment	AE in last year	AE leading to Hospitalizations
Mean \pm SD	8.68 \pm 7.072	3.63 \pm 3.098	2.74 \pm 2.302	1.73 \pm 1.254

Table 5.8 Eosinophilic Count % of Total Peripheral Leukocyte Count of Patients

Eosinophil count (%)	< or = 6	> 6
Percentage of (N=100)	92	8

The mean eosinophilic count (% of the total leukocyte count (TLC)) was found to be 3.11 ± 2.799 . Only 8% subjects showed eosinophilia (>6% of TLC) and the rest 94% were in the normal range of eosinophils.

Figure 5.3 Radiological Features Analysis of Patients

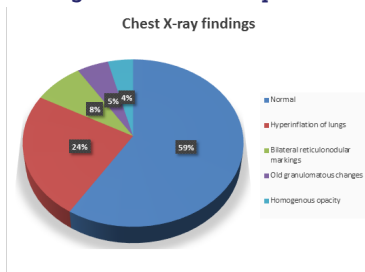


Table 5.9 Pulmonary Function Test (Spirometry) of Patients

Spirometric Parameter	Mean \pm SD	Median
FVC pre %	68.41 \pm 23.134	65.00
FVC post%	78.21 \pm 22.410	76.00
Improvement in FVC Post bd%	16.47 \pm 13.257	14.00
FEV pre%	55.53 \pm 25.937	47.00

FEV post %	65.32 \pm 26.626	59.00
Improvement in FEV Post bd%	21.07 \pm 13.576	19.00
FEV 1/FVC Pre ratio	60.1186 \pm 12.07961	60.3350
FEV 1/FVC Post ratio	61.9957 \pm 13.75364	61.3950
FEF 25-75 pre%	26.20 \pm 18.568	20.00
FEF 25-75 post %	32.48 \pm 23.026	25.00
Improvement in FEF 25-75 post%	25.73 \pm 22.227	22.00
PEFR pre%	38.17 \pm 19.821	35.00
PEFR post%	47.95 \pm 23.028	43.00
Improvement in PEFR post bd%	31.46 \pm 33.451	24.00

*Data is represented as % Mean \pm SD.

Table 5.10 Chronic Airflow Obstruction Profile of Patients FVC – Forced vital capacity, FEV1 – Forced expiratory volume

FEV1/FVC post bd ratio	More than 70	Less than 70
Number (%) of patients	33	67

Table 5.11 Bronchodilator (BD) Reversibility in Patients

Improvement in FEV1 post-BD in %	More than 12	Less than or equal to 12
Number (%) of patients	74	26

FEV1 – Forced expiratory volume, post% - post bronchodilator % of predicted, BD - bronchodilator

Table 5.12 Classification of Chronic Airflow Obstruction (Fev1/Fvc Post Bd Ratio < 70) Patients According To Severity

Severity	Mild COPD	Moderate COPD	Severe COPD	Very Severe COPD	Total N= 67
Gold Category	GOLD 1	GOLD 2	GOLD 3	GOLD 4	
Fev1 Post bd (%)	>80	50 - 79	30 – 49	< 30	
Number Of Patients(N%)	8 (11.9)	23- (34.3)	32 (47.8)	4 (6)	67 (100)

Table 5.13 Bronchodilator (Bd) Reversibility in Patients with Chronic Airflow Obstruction (Fev1/Fvc Post Bd Ratio in % < 70%) Patients

Improvement In Fev1 Post-Bd in %	More Than 12	Less Than Or Equal To 12	Total N = 67
Total Number Of Patients (N %)	54 (80.6)	13 (19.4)	67 (100)

Table 5.14 Pulmonary Function Test Pattern of Patients

Pattern	Number Of Patient N (N %)
Normal	26
Obstructive With No Significant Bdr	13
Obstructive With Significant Bdr	54
Restrictive	7
Total	100

Bdr – Bronchodilator Response

DISCUSSION

This study identified 100 ACO patients using the stepwise approach, based on the features stated in the GINA/GOLD ACO report and their clinical, radiological features were studied.^(1,2)

Majority of the patients in the study were males (76%) and females were (24%). Jinhee Kim et al⁽⁴⁾ also reported more number of males than females in their study. 53% of the patients belonged to urban areas and 47% belonged to rural

areas with an average age of 56.42 ± 10.54 years. A large no. of patients (68%) fall in the younger age groups from 40-60 years as compared to(32%) in the older age groups of 60-90, with the highest incidence (38%) being in the 40-50 age group.

J.-W. Bai et al⁽⁶⁾ supports this finding of patients with ACO tending to have earlier ages of onset.

Majority of the patients in this study had complaints of breathlessness or dyspnoea (99%) followed by cough (93%), sputum production (70%), wheezing (70%), running nose (65%), sneezing (65%), and chest tightness (46%).

However, Camilla Boslev Baarnes et al⁽⁶⁾ found cough was the most prevalent symptom among the enrolled subjects, followed by dyspnoea and sputum production.

On evaluation of dyspnoea according to the mMRC classification, most patients were found to have grade 1 dyspnoea (48%) followed by grade 2 dyspnoea (39%) and grade 3 dyspnoea was documented only in 12% of the patients. No patients were found to have either grade 0 or grade 4 dyspnoea.

The mean ± SD mMRC grade in this study group was found to be 1.64 ± 0.692. This was found to be high as supported by the various studies shown below.

Table 6.2 Mmrc Grade of ACO patients in Various Studies

Studies	Camilla Boslev Baarnes et al N = 264	Maria Montes de Oca et al N = 35	Hiromasa Inoue et al N = 90	Present study N = 100
mMRC grade (Mean ± SD)	2.2 ± 0.8	1.7 ± 1.3	1.0 ± 1.0	1.64 ± 0.692

History of smoking tobacco or other substances was found in 74% of patients and Exposure to airborne pollutants ; domestic biomass fuel exposure or occupational exposure in about 63% of patients. The mean pack years of smoking in this study group was 25.25 ± 19.43.

In this study, 25% were Active Smokers while 49% were Ex-Smokers and 26% patients were never smokers.

Table 6.4 Smoking Status of Patients in Various Studies

Studies	Hyonsoo Joo et al	Maria Montes de Oca et al N = 35	Hiromasa Inoue et al N = 93	Present study N = 100
Current smokers(%)	23.8	40	15.1	25
Ex- smokers (%)	76.2	57.1	84.9	49
Never smoked (%)	0	2.9	0	26

David M. Mannino et al⁽⁷⁾ stated that current or former smoking status was consistently associated with ACO. Hiromasa Inoue et al⁽⁸⁾ reported ACO patients were having lower number of pack-years.

Table 6.5 Acute Exacerbation Profile in Various Studies

Studies	Maria Montes de Oca et al N = 35	Hiromasa Inoue et al N = 93	Present study N = 100
Number of exacerbations, past year, mean (SD)	0.4 ± 1.0	0.570	2.74 ± 2.302
Hospitalisation due to exacerbation past year,	3	-	1.73

The above findings are consistent with previous study findings

that ACO patients having a high number of exacerbations and hospitalizations due to the same.

In the **PLATINO Study**, which was a population-based study in five Latin American countries, individuals with ACO had more respiratory symptoms, worse lung function and were 2.1 times more likely to experience an exacerbation and 4 times more likely to become hospitalized than those with COPD alone.⁽⁴²⁾

Spirometry-confirmed COPD (chronic obstruction) was defined as having an FEV₁/FVC <0.70, based on post-bronchodilator lung function.

Bronchodilator response was the mean percentage improvement in FEV₁ from baseline and significant bronchodilator response was the percentage with a significant response (> 12% and > 200ml in FEV₁ or FVC).⁽⁷⁾

Pulmonary function tests (Spirometry) showed 67% of patients having FEV₁/FVC ratio less than 0.7. Out of these 67% patients, 8 (11.9%) patients had FEV₁ between > 80 % (Mild COPD/ GOLD 1), 23 (34.3%) patients had FEV₁ between 50-80 (Moderate COPD/ GOLD 2), 32(47.8%) patients had FEV₁ between 30-50 (Severe COPD/ GOLD 3) and 4 (6%) patients had FEV₁ below 30 % (Very Severe COPD/ GOLD 4).

Hiromasa Inoue et al⁽⁸⁾ noted that the distribution of patients in each GOLD stage was also significantly different between the ACO and the COPD groups; the ACO group had fewer patients classified as severe similar to our study

54% of all the patients, had FEV₁/FVC ratio less than 0.7 plus significant bronchodilator response (> 12% and > 200ml in FEV₁).

7% of all the patients had Restrictive pattern and 26 % had normal pulmonary function tests.

David M. Mannino et al⁽⁷⁾ found 44.2% of those with ACO had obstruction and an additional 17.8% had restriction.

In the study by Menezes et al⁽⁴²⁾ comparable to our study, they found a higher degree of reversibility, but no difference in estimated life-time tobacco exposure. Furthermore, in support of our findings, their patients with ACO were slightly younger, lower FEV₁ patients, and experienced more dyspnoea.

There was no significant raised eosinophil count in this study group and the most common Chest X-ray finding was found to be normal (59%) followed by hyperinflation of both lung fields (24%).

This study has several limitations like being a single centered study. The sample size was only 100 patients which is small. This study used the fixed ratio (FEV₁/FVC < 0.70) rather than the lower limit of normal (LLN) to define obstruction. Our definitions of ACO, COPD, and asthma are not the same as those of previous studies. The absence of stringent criteria for the diagnosis of asthma and COPD in clinical practice adds to the potential for this diagnostic bias.

CONCLUSION

This study reports that clinically diagnosed ACO patients were mostly males, belonged to middle age groups, had breathlessness, wheezing, chronic cough with sputum production and rhinitis and sneezing as the major symptoms, suffered from high mMRC grades of dyspnoea, had positive smoking history with low pack years, tend to be ex-smokers, with increased exacerbations and also hospitalizations due to it.

The pulmonary function tests revealed majority of the patients having chronic obstruction but with moderate severity of

obstruction. Also, a majority of these patients had significant positive bronchodilator response. X-ray chest PA reporting for most patients was found to be normal followed by findings of hyperinflation of lung fields. However, no significant eosinophilia was seen in the patients.

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