European Journal of Molecular & Clinical Medicine

ISSN 2515-8260 Volume 10, Issue 02, 2023

Original Research Article

To Study the Magnitude of Asthma-COPD Overlap (ACO) among Patients Diagnosed as Asthma and COPD

[1]Ch. Praveen Kumar, [2]V Sai Krishna Rao, [3]Abhilash Reddy K

[1]Assistant Professor, Department of Pulmonary Medicine, Chalmeda Anand Rao Institute of Medical Sciences, Karimnagar, Telangana, India
[2,3]Post Graduate, Department of Pulmonary Medicine, Chalmeda Anand Rao Institute of Medical Sciences, Karimnagar, Telangana, India

Corresponding Author:
Abhilash Reddy Kandula (abhilashreddykandula87@gmail.com)

Abstract

Introduction: Asthma-COPD overlap (ACO) is known by many names in many countries and a universal consensus has not yet been reached on this subject regarding its definite clinical pattern and diagnosis. However, the GINA and GOLD committees have together established a guideline, by which a clinician can arrive at a diagnosis of Asthma-COPD overlap syndrome [1,2].

Aim/Objectives: Assessment of patients diagnosed to have Asthma or Chronic Obstructive Pulmonary Disease (COPD) fulfilling current criteria for ACO.

Materials and Methods: The study was a Cross-sectional study done in Chalmeda Anand Rao Institute of Medical Sciences, Karimnagar, Telangana. From November 2019 to May 2021 and 107 patients were included in the study.

Results: Of the 65 pre-study asthma patients, only 62 (96%) confirmed as asthmatics, 1 (1.7%) as COPD and 2(2.3%) were confirmed to be ACO. Likewise of the 35, pre-study diagnosis of COPD patients, only 20 (58%) confirmed as COPD, 9 (25%) confirmed as Asthma patients and 6 (17%) confirmed ACO patients. There were 7 ACO patients however only 1 of them was confirmed to be ACO, 5 confirmed as Asthma and 1 confirmed to be COPD.

Conclusion: The prevalence of ACO was established in the study population; 17.2% from COPD and 2.8% from Asthma. Overall, it was 5.4% of all obstructive airway diseases, obtained from our study population.

Keywords: GINA (Global Initiative for Asthma Management and Prevention), GOLD (Global initiative for chronic obstructive lung disease), PSDA (Pre-Study Diagnosis of Asthma), PSDC (Pre-Study Diagnosis of COPD)

Introduction

Asthma, a chronic inflammatory state of the lung with cough and wheezing is often confused with Chronic Obstructive Pulmonary Disease (COPD) when present in individuals over the age of 40 years [1]. In contrast to Asthma, COPD although being a chronic inflammatory disease has a persistent airflow limitation [2]. Differentiating the two had been a challenge in the past, but with significant research being done on this field, the Global Initiative for Asthma Management and Prevention (GINA) and its COPD counterpart, Global Strategy for Diagnosis, Management, and Prevention of COPD (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

ISSN 2515-8260 Volume 10, Issue 02, 2023

recognized [3]. Based on the composition of neutrophils and eosinophils, Asthma can be categorized into neutrophilic asthma, eosinophilic asthma, mixed granulocytic asthma and pauci granulocytic asthma [4]. Whereas, COPD is predominantly a neutrophilic inflammation [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 to call it as a phenotype of asthma itself.

'The Dutch hypothesis', which states that Asthma and COPD are different levels of the same disease spectrum as overlapping mechanisms may be present, in the gene-environment reaction that eventually results in the disease [7]. The recent thinking on this subject is that there is at least an overlap of symptoms between asthma and COPD in certain patients, which has been termed as 'Asthma-COPD overlap Syndrome'. GINA have however renamed the term as Asthma-COPD overlap, ACO because it encompasses a cluster of patients with varying degrees of overlap.

Several published studies have concluded that ACO has worse prognosis than Asthma or COPD. Frequency of exacerbations, poor disease control, increased admissions, increased economic burden, and rapidly declining lung functions have been shown to be more in ACO in certain studies. Hence it is essential to diagnose and treat ACO at an early stage.

Materials and Methods

This study was designed to be a cross sectional study. Patients who were visiting pulmonary medicine outpatient department, CAIMS, Karimnagar on a regular basis for management of Bronchial Asthma or COPD were observed and analyzed, if they had characteristic features suggestive of ACO, as defined by GINA guidelines.

The study patients were randomly selected from the OPD appointment list. After informed consent, the study proforma was administered. Their Spirometry, IgE, % of peripheral eosinophils were documented. GINA syndromic approach table was used to re visit diagnosis in these patients.

Inclusion criteria

- All patients attending the pulmonary medicine OPD with a prior diagnosis of Asthma and COPD, were included.

Exclusion criteria

- Age less than 18 years.
- Other pulmonary morbidities such as Bronchiectasis, Pulmonary TB sequelae, Lung malignancy, Interstitial Lung disease etc.
- Patients who had been diagnosed within 6 months.

Results

For further discussion and in order to avoid confusion, the original Asthma patients who were included in the study are here after known as "Pre-Study Diagnosis of Asthma (PSDA)". The original COPD patients who were included in the study are here after known as "Pre-Study Diagnosis of COPD (PSDC)". After application of the GINA-GOLD syndromic approach tool for ACO, a new set of Asthma, COPD and ACO are diagnosed. They will be known as 'Confirmed Asthma', 'Confirmed COPD' and 'Confirmed ACO'.

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Table 1: Baseline Characteristics of Pre-Study Diagnosis of Asthma (PSDA) patients

Parameter	Value
1. Gender	Males: 24 (41.5%) Females: 41 (58.5%)
2. Age Group	18 to 40 years: 25(38.1%) 41 to 60 years: 28 (42.4%) 61 to 80 years: 12 (18.6%) Above 80 years: 1 (0.9%)
3. Smoking history	3 (4.49%)
4. Biomass fuel exposure	16 (24.5%)
5. Family history of Asthma	19 (29.6%).
6. Allergic Rhinitis	55 (85.35%)
7. Spirometry	FEV1/FVC <0.7: 23 (35.3 %) FEV1/FVC >0.7: 42 (64.7%)
8. Significant reversibility	19(29.6%)
9. Regular follow-up	61 (93.4%)
10. Hyperinflation in X ray	8 (12%)

Table 2: Baseline Characteristics of COPD patients

Parameter	Value
1. Gender	Males: 30 (85.3%) Females: 5 (14.6%)
2. Age Group	18 to 40 years: 0 41 to 60 years: 9 (26.1%) 61 to 80 years: 25 (71.34%) Above 80 years: 1 (2.5%)
3. Smoking	27 (77.71%)
4. Biomass fuel exposure	5 (12.74%)
5. Family history of Asthma	3 (7.6%)
6. Allergic Rhinitis	7 (21%)
7. Spirometry	FEV1/FVC <0.7: 27 (75.8 %) FEV1/FVC >0.7: 8 (24.2%)
8. Significant reversibility	8 (22.82%)
9. Regular follow-up	32 (90.5%)
10. Hyperinflation in X ray	24 (69.4%)

Study results after re categorizing diagnosis (as per GINA-GOLD syndromic approach tool)

The total number of Pre-study diagnosis of Asthma patients were 65 and the number pre-study diagnosis of COPD patients were 35, 7 patients who had a pre-study diagnosis of ACO based on some other criteria were also included to verify their diagnosis.

Of the 65 pre-study asthma patients, only 62 (96%) of them were confirmed Asthmatics. 1 (1.7%) were confirmed to be COPD and 2(2.3%) were confirmed to be ACO.

Likewise of the 35, pre-study diagnosis of COPD patients who were enrolled in the study, only 20 (58%) were confirmed COPD, 9 (25%) of them turned out to be confirmed Asthma patients and 6 (17%) of them were confirmed ACO patients.

There were 7 ACO patients who were also included in the study to verify the diagnosis according to GINA-GOLD syndromic approach guidelines, however only one of them was confirmed to be ACO, 5 of them were confirmed as Asthma and 1 of them was confirmed to be COPD.

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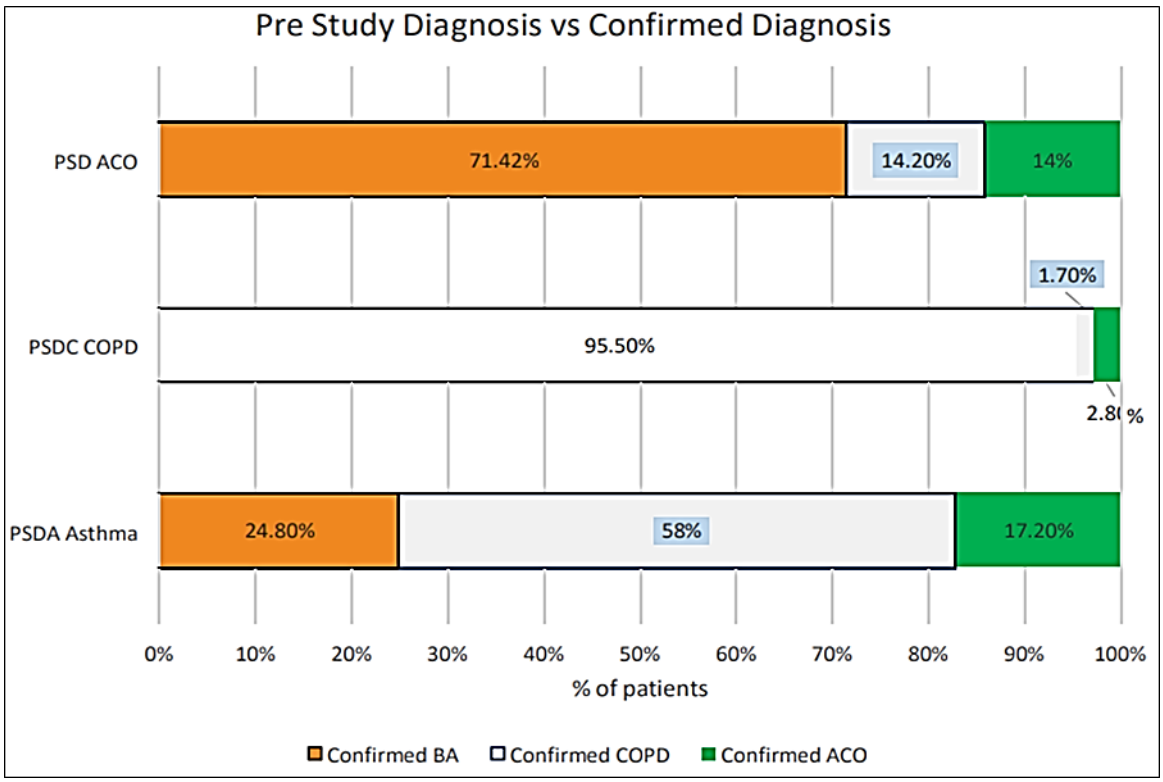
Table 3: Tabulation of Initial diagnosis against Final diagnosis

Pre-study Diagnosis	Confirmed diagnosis			Total
	Asthma	COPD	ACO	
Asthma	62	1	2	65
	93.93	11.54	41.67	81.30
COPD	9	20	6	35
	5.38	87.50	56.25	17.90
ACO	5	1	1	7
	0.69	0.96	2.08	0.80
	76	22	9	107



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 [8]. By some of the earlier criteria the prevalence of ACO was over reported. Over the years there have been multiple studies with different criteria which was discussed earlier. Jo YS *et al*., compared the prevalence rate obtained from different criteria from the same population. The prevalence varied from 31% by using modified Spanish Criteria to 48% using the Platino criteria [9]. 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.

Miravitlles *et al*., reported 6.5% of ACO prevalence among COPD patients [10]. Golpe *et al*., reported a prevalence of 5% in smoking COPD and 21% among biomass fuel COPD [11]. There is other studied which quote the prevalence of ACO from a previous diagnosis of COPD to be between 11.3% to 18.60% [12, 13]. Likewise, from a previous diagnosis of Asthma the prevalence of ACO is around 30% [12, 14].

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In our study, the prevalence data for ACO among COPD patients was similar to most studies done in multinational centres, 17%. While there are only few studies done to assess the prevalence of ACO in Asthma patients, the prevalence rate in our study was 2.8%, lower from, than that of COPD as expected.

ACO was generally found to be gender nonspecific. In a study done in the US, Vac Fragoso *et al*., found that 67% of their ACO patients were females [15]. In another study done by Maria Montes *et al*. 65% of the ACO patients were male [13]. Jung *et al*., reported 95% males with ACO [16]. Generally, the studies have shown that the mean age of diagnosis of ACO was much earlier than COPD [15]. There was not much difference in our study. The number of COPD and ACOS patients in the 60+ age group was almost double the number in the 40-60 age group. The mean age of patients in each of the groups is as follows: Asthma 46 ± 15, COPD 64 ± 9 and ACOS 62 ± 11.

Family history of asthma in the immediate family member had been consistently shown to be a risk factor for asthma development in various literature. A comparison was done between ten studies by Burke W *et al*., sensitivity of the positive family history to predict development of asthma was between 4% to 43%, the positive predictive value was between 11% to 37%, and the negative predictive value was high and between 86% to 97%. Positive family history increases the probability to develop asthma [17]. In our study 29% of Asthma and 25% of ACO had a positive family history of Asthma.

Asthmatics can have a normal spirometry at the time of diagnosis, but presence of an obstruction is essential for the diagnosis of COPD and ACO. The GINA syndromic approach fails in this aspect that patients who were diagnosed to have COPD using this tool, 5.7% of them had no obstruction in spirometry. 35.42% of the patients diagnosed as ACO also had no obstruction. However, this could be explained by the fact that the GINA tool provides much weightage to the clinical nature of the illness compared to the actual spirometry values. Similarly, reversibility of obstruction in a previous known COPD patient would be classified as ACO in most criteria. 16% of COPD patients and 31% of ACOS patients have shown reversibility. Of which the 400ml & 12% reversibility, that is almost diagnostic of asthma was also present in 6 COPD and 2 ACOS patients. This again could be explained by the presence of overlap symptoms.

Significant peripheral blood eosinophilia is associated with high medical care resource use in Asthmatics. Sputum eosinophilia is more important in identifying eosinophilic asthma. Peripheral blood eosinophils were found to be elevated in Asthma and ACO when compared with COPD. But there was no difference between Asthma and ACO

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 [13, 15].

Most studies have shown worse exacerbation rate with ACO (13). In our study ACO had worst disease control, but COPD had the most exacerbations per 100 patient years. Also, COPD had more ICU admissions and NIV/intubations.

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. This study was an eye opener as to how many of our COPD patients were actually Asthma patients, who were misdiagnosed and over treated.

Conclusion

The primary objectives of the study were achieved. The prevalence of ACO was established in the study population; 17.2% from COPD and 2.8% from Asthma. Overall, it was 5.4% of all obstructive airway diseases, obtained from our study population.

This study provides an insight into the prevalence rate in India. ACO per se did not have

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worse disease control, exacerbation rate, admissions, NIV requirement or exercise desaturation compared to COPD. ACO is worse than Asthma in all the above aspects.
This GINA tool apart from being a tool to identify ACO have also helped us to differentiate COPD from very severe Asthma with fixed airway, which is otherwise very difficult and confusing. Further research is needed to refine the diagnostic criteria, which is the need of the hour.

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