Research Article

Asthma COPD overlap syndrome in patients of chronic obstructive pulmonary disease

Nezar R. Tawfike*, Mohamed A. Abd Elhakim, Zainab H. Saeed*, and Rofaida N. Eldin Helmy[*]**

* Department of chest diseases, Faculty of Medicine, Minia university, Egypt

** Department of clinical pathology, Faculty of Medicine, Minia university, Egypt

Abstract

Introduction: Although asthma and chronic obstructive pulmonary disease (COPD) differ in origin, they share similar physiological features and may clinically co-exist as so-called asthma–COPD overlap syndrome (ACOS). Patients with ACOS experience more rapid decline in lung function, frequent exacerbations, have poorer health-related quality-of-life (HRQoL) outcomes, and may require a different treatment and early introduction of inhaled corticosteroids (ICS) could be justified **This study aimed to:** Compare between COPD patients who fulfill the criteria of ACOS and those COPD patients without such features as regard the clinical and functional parameters. **Patient and methods:** 60 stable COPD patients were divide into two groups: group A (pure COPD) and group B (ACOS). ACOS was diagnosed when compatible with any of the following two diagnostic criteria: Post-bronchodilator FEV/FVC <70% and either history of bronchial asthma before age of 40 years old or reversibility of FEV1 after bronchodilator ≥ 200 ml and 12% plus wheezy chest in the last year. The two groups were compared as regard clinical and functional parameters. **Results:** There was no significant difference between ACOS patients and pure COPD patients as regard sex, age, smoking history, dyspnea, exacerbations or most PFTs. ACOS patients had more atopic manifestations, higher FVC postbronchodilator and higher CAT(COPD Assessment test) score. **Conclusion:** This study demonstrated that there was no significant difference between ACOS and COPD pateints except for history of atopy and higher CAT score in ACOS pateints.

Key words: ACOS, Asthma, COPD, CAT

Introduction

Asthma and chronic obstructive pulmonary disease (COPD) are two major obstructive airway diseases. They are characterized by chronic inflammation and airway remodeling, but they differ in the patterns of inflammation, the structures affected and the prime anatomic site at which pathological changes occur[1]**.** Although their pathogeneses differ in origin, they share similar physiological features and may clinically co-exist as so-called asthma–COPD overlap syndrome (ACOS)[2,3]. A joint project of Global Initiative for Asthma (GINA) and Global Initiative for Chronic Obstructive Lung Disease (GOLD) provides a clinical description of asthma–COPD overlap syndrome (ACOS) as follows[4]**.** Patients with ACOS experience more rapid decline in lung function, frequent exacerbations, have poorer health-related quality-of-life (HRQoL) outcomes,

and require a large amount of medical resources compared to patients with asthma or COPD alone[5,6]**.** In 2007, the Canadian guidelines for COPD recognized that patients with COPD and an asthma component may require a different treatment and early introduction of inhaled corticosteroids (ICS) could be justified [7]**.** This specific and differential treatment justifies the efforts to identify the subgroup of patients with ACOS from the large population of patients with COPD.

As a result, this outcast syndrome has become an active area of research.

Aim of work:

Compare between COPD patients who fulfill the criteria of ACOS and those COPD patients without such features as regard the clinical and functional parameters.

Patients and methods

This cross-sectional study was performed on 60 stable COPD patients randomly selected from patients who sought medical advice in the outpatient clinics of Chest department of Minia Cardiothoracic University Hospital during the period from September 2015 to September 2016.

Inclusion criteria: patients over 40 years old with clinical and functional diagnosis of COPD based on GOLD, 2016 citeria[8].

Exclusion criteria: patients with acute exacerbation of COPD at the time of the study, congestive heart failure, patients with any obvious abnormal lung parenchymal lesions on chest radiograph like interstitial pneumonias, air space shadows, fibrocystic lesions, patients with lung cancer or with infectious diseases including lung tuberculosis.

All subjects were subjected to the following: detailed history taken from patients or their relatives, The grade of dyspnea was determined by using the modified Medical Research Council (mMRC) dyspnea scale, detailed general and local chest examination, **CAT** (COPD Assessment test) [9], plain chest X-ray (PA view), arterial blood gas analysis (ABG), Routine laboratory investigations including (CBC, Renal and liver function tests, C-Reactive Protein) and spirometry. COPD severity was defined as mild when post-bronchodilator FEV1 ≥ 80% predicted, moderate when post-bronchodilator FEV1 from 50-79% predicted, severe when post-bronchodilator FEV1 from 30-49% predicted, very severe when post-bronchodilator FEV1 <30% predicted.[8] COPD combined assessment for severity according to [8] was assessed in all patients.

In this study, we diagnosed ACOS when compatible with any of the following two diagnostic criteria:

1- Post-bronchodilator FEV/FVC <70% and history of bronchial asthma before age of 40 years old)[2].

2- Post-bronchodilator FEV/FVC <70% and reversibility of FEV1 after bronchodilator ≥ 200 ml and 12% plus wheezy chest in the last year [10].

According to this method, the 60 patients were classified into 2 groups:

Group A: patients with COPD alone (Pure COPD), and **Group B**: patients with ACOS. So, the two groups were compared as regard clinical and functional parameters.

Results

Table (1): Demographic data of the studied groups (Group A with pure COPD, Group B with ACOS)

Variable	Group A Pure COPD	Group B ACOS	p value
Number (%)	36 (60%)	24 (40%)	
Age (years) Mean± SD	63.05±7.64	60.13±9.43	0.21
Sex Number (%) Male Female	29 (80.5%) 7 (19.5%)	18(75%) 6 (25%)	0.61
Smoking Number (%) Non smokers Smokers	9 (25%) 27 (75%)	8 (33.3%) 16 (66.7 %)	0.49

Table (2): Clinical characteristics of the studied groups

Variable	Group A	Group B	p value
MMRC Grade Grade I Grade II Grade III Grade IV	 2 (5.5%) 11(30.5%) 22(61.2%) 1(2.8%)	 2 (8.3%) 9 (37.5%) 12 (50%) 1(4.2%)	0.82
Wheezing	22 (61%)	16 (66%)	0.91
Number of exacerbations last year Range Mean± SD	 0-4 1.50±1.18	 0-4 2.04± 1.33	0.06
CAT score Range Mean± SD	 8-30 18.75±4.08	 8-35 24.79±7.36	**0.001***
+ve family history	5 (13.8%)	7 (29.2%)	0.19
History of Atopy	2(5.5%)	7 (29%)	**0.02***
Combined ICS/LABA	18(50%)	15(62.5%)	0.34
LABA only	6 (16.7%)	0	0.07

Table (3): PFTs and GOLD classification of the studied groups

Variable	Group A	Group B	p value
FEV1 % predicted Prebronchodilator Mean± SD	37.69±17.79	36.33±12.39	0.74
FEV1 % predicted Postbronchodilator Mean± SD	39.33±18.50	47.25±15.40	0.07
FVC % predicted Prebronchodilator Mean± SD	55.50±17.78	53.66±12.28	0.66
FVC % predicted Postbronchodilator Mean± SD	56.64±17.69	68.63±13.93	0.005*
FEV1.Change (ml) Mean± SD	50.27±94.06	250.41±164.75	0.0001*
FEV1%Change Mean± SD	4.65±9.69	29.75±19.25	0.0001*
FEF25-75 % predicted Prebronchodilator Mean± SD	31.30±15.92	31.95±14.92	0.70
FEF25-75 % predicted Postbronchodilator Mean± SD	35.89±18.32	36.50±11.34	0.52
GOLD stage **II** **III** **IV**	 10 (27.8%) 9 (25%) 17 (47.2%)	 10 (41.7%) 9 (37.5%) 5 (20.8%)	0.09

Table (4): COPD combined assessment of severity of studied groups

Variable	Group A	Group B	p value
Class A	2 (5.5%)	2(8.3%)	0.95
Class B	8(22.2%)	4(16.7%)	0.73
Class D	26 (72.3%)	18(75%)	0.81

Discussion

Recognizing and understanding the Asthma-COPD overlap syndrome may offer new insight into the mechanisms and treatment of chronic airway inflammatory diseases. There is no generally agreed term or defining features for this category of chronic airflow limitation[11].

According to the criteria used in this study, the demographic data showed that there was no significant difference between ACOS patients and pure COPD patients as regard sex, age, smoking history and this comes in agreement with Nguyen et al., [12] and Suzuki et al.,[13].

On the other hand, Hardin.,[2] and Barrecheguren et al.,[14] observed that ACOS patients are usually younger, more frequently females and they have had lower smoking exposure compared to COPD patients.

In the present study, there was no significant difference in disease severity when assessed by dyspnea or exacerbations between patients with pure COPD and patients with ACOS. This was in contrast with several general population studies or administrative databases as Menezes et al., [10] and Miravitlles et al.,[15] who observed that ACOS is associated with increased severity, as indicated by more frequent exacerbations. COPD patients recruited in the Menezes et al., study had higher post-bronchodilator FEV1% than the present study with a mean of 82 %. As a result, the rate of exacerbations COPD group in Menezes study was relatively low (5%). This may explain why the rate of acute exacerbations was higher in the ACOS group in Menezes study. Our study comes in agreement with Caillaud et al., Izquierdo-Alonso et al.,[16,17] who observed no statistically significant difference in number of exacerbations between ACOS and pure COPD patients.

In the present study CAT score was significantly higher in the ACOS group than the pure COPD group of patients. This comes in agreement with Suzuki et al., 2015 [13] who found that ACOS patients had higher CAT scores compared to those with COPD when compared 40 ACOS and 100 pure COPD patients. On the other hand, Kobayashi et al.,[18] found no significant difference between 37 ACOS and 220 pure COPD patients as regard CAT score. The much higher number of patients included in that study compared with the present one must be taken into consideration.

The result of the present study comes in agreement with Kurashima et al.,[19] who found that the total CAT scores were significantly higher in patients with ACOS than in patients with pure COPD.

The present study revealed that ACOS patients had more atopic manifestations than pure COPD patients. This comes in the same line with Caillaud et al., study[16] which found that ACOS patients have more atopic features like allergic rhinitis, atopic dermatitis, and atopic asthma than pure COPD patients.

Ji-Young et al.,[20] compared skin prick test (SPT) responses in pure COPD patients and ACOS patients and they observed that the overall positive rate was significantly higher in ACOS than in pure COPD. This reflects some sort of atopy in ACOS patients and this gives some support to our results.

On comparing pulmonary functions between ACOS and pure COPD patients, we observed no statistically significant difference in lung functions except for the post bronchodilator FVC% and in the FEV1% change post bronchodilator which were significantly much higher in the ACOS group than the pure COPD group. This was supported by Kitaguchi et al.,[21] and Miravitlles et al.,[15] who found no significant difference between ACOS and pure COPD patients regarding these parameters. The higher post bronchodilator FVC and the higher FVC % change post bronchodilator in the ACOS group compared with the pure COPD patients in the present study can reflect more benefit of the bronchodilator therapy namely the beta 2 agonists in the ACOS patients [22].

Our results comes in contrast to Menezes et al.,[10] who revealed worse pulmonary functions in ACOS patients than COPD patients. This can be explained by the large number of patients included in that study as they compared 767 COPD patients with 90 ACOS patients.

In our study we observed no significant difference between the two groups as regard using ICS. This comes in contrast with Izquierdo-Alonso., 2013[17] and Rhee et al., 2014[6] who reported that inhaled corticosteroids (ICS) were used more frequently in ACOS patients than in the COPD patients. This may be explained by the fact that most of our patients were classified as class "D" and according to GOLD guidelines, they need ICS in their treatment regardless their phenotype. Longitudinal studies are needed to better examine the response to ICS in ACOS compared to COPD alone.

Conclusion

This study demonstrated that there was no statistically significant difference between ACOS and pure COPD patients except for history of atopy, higher CAT score, higher FVC% post bronchodilator and higher FEV1 % change in the post bronchodilator test in the ACOS group than in the pure COPD one. One of the important findings in this study is the lack of any significant difference between both groups in the rate of acute exacerbations.

Recommendation:

Longitudinal studies are needed to better define the clinical implications of ACOS with respect to the long-term outcome and treatment of ACOS and its sub-phenotypes compared to pure asthma or pure COPD. Higher number of COPD patients are needed to be studied.

References

1. Jeffery PK. (2004) Remodeling and inflammation of bronchi in asthma and chronic obstructive pulmonary disease. Proc. Am. Thorac.Soc; 1: 176–83.
2. Hardin M, Silverman EK, Barr RG, Hansel NN, Schroeder JD, et al., (2011): The clinical features of the overlap between COPD and asthma. Respir Res 12:127.
3. de Marco R, Accordini S, Cerveri I, Corsico A, Anto` JM (2007) Incidence of chronic obstructive pulmonary disease in a cohort of young adults. Am J Respir Crit Care Med 175(1): 32–39.
4. GINA and GOLD. (2015) Diagnosis of diseases of chronic airflow limitation: asthma, COPD and asthma-COPD overlap syndrome (ACOS) (updated 2015). Available from URL:http://www.ginasthma.org/Accessed:13April
5. Rhee CK, Yoon HK, Yoo KH, Kim YS, Lee SW, Park YB et al., (2014) Medical utilization and cost in patients with overlap syndrome of chronic obstructive pulmonary disease and asthma. COPD; 11(2):163–170.
6. Chung JW, Kong KA, Lee JH, Lee SJ, Ryu YJ, Chang JH. (2014) Characteristics and self-rated health of overlap syndrome. Int J Chron Obstruct Pulmon Dis.; 9:795–804.
7. O'Donnell DE, Aaron S, Bourbeau J, et al., (2007) Canadian Thoracic Society recommendations for management of chronic obstructive pulmonary disease 2007 update. Can Respir J; 14 (Suppl B):5B–32B.
8. Global Initiative for Chronic Obstructive Lung Disease (GOLD), (updated 2016). Global strategy for the diag-

nosis, management, and prevention of COPD Available from URL: http://www.goldcopd.org/
9. Jones PW, Harding G, Berry P, Wiklund I, Chen WH, Kline Leidy N. (2009) Development and first validation of the COPD assessment test. Eur Respir J; 34: 648–654.
10. Menezes AM, Montes de Oca M, Perez-Padilla R, Nadeau G, Wehrmeister FC, Lopez-Varela MV et al., (2014) Increased risk of exacerbation and hospitalization in subjects with an overlap phenotype: COPD-asthma. Chest; 145:297–304.
11. Bujarski S, Parulekar AD, Sharafkhaneh A, Hanania NA. (2015) The Asthma COPD Overlap Syndrome (ACOS). Curr. Allergy Asthma Rep.; 15: 509.
12. Nguyen MS, Nguyen Dang D, Schleich F, Manise M, Corhay JL, Louis R. (2015). "[Asthma-COPD overlap syndrome among patients with stable COPD]." Rev Med Liege. 70(1): 37-43
13. Suzuki T, Tada Y, Kawata N. (2015) Clinical, physiological, and radiological features of asthma–chronic obstructive pulmonary disease overlap syndrome. International Journal of Chronic Obstructive Pulmonary Disease; 10:947-954.
14. Barrecheguren M, Román-Rodríguez M, Miravitlles M. (2015) Is a previous diagnosis of asthma a reliable criterion for asthma–COPD overlap syndrome in a patient with COPD? International Journal of Chronic Obstructive Pulmonary Disease.; 10:1745-1752. doi:10.2147/COPD.S87025.
15. Miravitlles M, Soriano JB, Ancochea J, Munoz L, Duran-Tauleria E, Sanchez G et al., (2013) Characterisation of the overlap COPD-asthma phenotype. Focus on physical activity and health status. Respir Med; 107: 1053–1060.
16. Caillaud D, Chanez P, Escamilla R, Burgel P-R, Court-Fortune I, Nesme-Meyer P, et al., (2016) Asthma–COPD overlap syndrome (ACOS) vs 'pure' COPD: a distinct phenotype? Allergy; DOI:10.1111/all.13004.
17. Izquierdo-Alonso JL, Rodriguez-Gonzalezmoro JM, de Lucas-Ramos P, Unzueta I, Ribera X, Anton E et al., (2013) Prevalence and characteristics of three clinical phenotypes of chronic obstructive pulmonary disease (COPD). Respir Med; 107:724–731.
18. Kobayashi S, Hanagama M, Yamanda S, Ishida M, Yanai M. (2016) Inflammatory biomarkers in asthma-COPD overlap syndrome. International Journal of Chronic Obstructive Pulmonary Disease.; 11:2117-2123. doi:10.2147/COPD.S113647
19. Kurashima K, Takaku Y, Ohta C, Takayanagi N, Yanagisawa T, Sugita Y.(2016) COPD assessment test and severity of airflow limitation in patients with asthma, COPD, and asthma–COPD overlap syndrome. International Journal of Chronic Obstructive Pulmonary Disease.; 11: 479-487. doi:10.2147/COPD.S97343.
20. Ji Young Yhi,Ji-Yong Moon,Sang-Heon Kim, et al., (2015) Atopic characteristics of patients with asthma-COPD overlap syndrome Friday, Hall D1 Foyer (Floor 3) (Coex Convention Center).
21. Kitaguchi Y, Komatsu Y, Fujimoto K, Hanaoka M, Kubo K. (2012) Sputum eosinophilia can predict responseveness to inhaled corticosteroid treatment in patients with overlap syndrome of COPD and asthma. Int J Chron Obstruct Pulmon Dis; 7:283-289.
22. Walker PP[1], Calverley PM. The volumetric response to bronchodilators in stable chronic obstructive pulmonary disease.COPD.2008 Jun;5(3):147-52.doi:10.1080/15412550802092 928