Chest Heart Journal
Vol. 41, No. 2, July 2017

ORIGINAL ARTICLE

Phenotypic Characteristics of Asthma COPD Overlap Syndrome in Patients attended at a Tertiary Care Hospital in Dhaka City.

AKMR Bari[1], MK Anam[1], MMK Ruble[2], MA Hossain[3], SMA Razzaque[4], M Kamal[5], BK Biswas[6]

Abstract:

Background: *Asthma-COPD overlap syndrome (ACOS) has been recently described by international guidelines. Chronic obstructive pulmonary disease (COPD) is a heterogeneous disease in which the clinical presentation and prognosis vary according to the phenotype.* ***Methods:*** *To identify patients with ACOS, a cohort of well-characterized patients with COPD. Evaluated the presence of specific characteristics associated with asthma in this COPD cohort, divided into major criteria (bronchodilator test > 400 mL and 15% and past medical history of asthma) and minor criteria (blood eosinophils > 5%, IgE > 100 IU/mL, or two separate bronchodilator tests > 200 mL and 12%). ACOS defined by the presence of one major criterion or two minor criteria. Baseline characteristics, health status (COPD Assessment Test [CAT]), BMI, airflow obstruction, dyspnea, and exercise capacity (BODE) index, rate of exacerbations.* ***Results:*** *Regarding symptoms, sputum production was found 44(58.7%) in ACOS group and 58(55.2%) in non ACOS group. Dyspnea (mMRC scale > 2) was found 34(45.3%) in ACOS group and 50 (47.6%) in non ACOS group. Mean FEV_1 % predicted was found 62.3±17.8 % in ACOS group and 60.7±19.9 % in non ACOS group. Mean FVC % predicted was found 85.7±18.3 % and 86.7±22.5 % in ACOS group and non ACOS group respectively. Mean FEV_1/FVC was found 54.6±11.1 in ACOS group and 53.1±11.4 in non ACOS group. Majority 41(54.7%) had II mild stage in ACOS group and 50(47.6%) in non ACOS group. Majority 49(65.3%) patients had bode index 0-2 in ACOS group and 64(61.0%) in non ACOS group.* ***Conclusion:*** *Long-acting muscarinic antagonist was statistically significant between ACOS group and non ACOS group. Majority patients had bronchodilator reversibility in ACOS group. Serum IgE- Immunoglobulin E was found significantly higher in ACOS group than non ACOS group.*

Keywords: *Asthma, COPD, Overlap Syndrome.*

[Chest Heart Journal 2017; 41(2) : 138-144]

Introduction:

Asthma-COPD overlap syndrome (ACOS) has been recently described by international guidelines. A stepwise approach to diagnosis using usual features of both diseases is recommended although its clinical application

1. Associate Professor, Respiratory Medicine, Shaheed Suhrawardy Medical College, Sher-E-Bangla Nagar, Dhaka.
2. Assistant Professor, Respiratory Medicine, Shaheed Suhrawardy Medical College, Sher-E-Bangla Nagar, Dhaka.
3. Assistant Professor, Medicine, Shaheed Suhrawardy Medical College, Sher-E-Bangla Nagar, Dhaka.
4. Associate Professor, Respiratory Medicine, Shaheed Tajuddin Ahmed Medical College, Gazipur.
5. Junior Consultant, Medicine, Shaheed Suhrawardy Medical College Hospital, Sher-E-Bangla Nagar, Dhaka.
6. Associate Professor, Respiratory Medicine, NIDCH, Dhaka

Correspondence to: Dr. A.K.M. Rafiqul Bari, Associate Professor, Respiratory Medicine, Shaheed Suhrawardy Medical College, Sher-E-Bangla Nagar, Dhaka. Cell: 01715-108931, e-mail: rafiqul.bari@yahoo.com

Submission on: 17 May 2017 Accepted for Publication: 27 July 2017

Available at http.//www.chabjournal.org

is difficult.[1] Chronic obstructive pulmonary disease (COPD) is a heterogeneous disease in which the clinical presentation and prognosis vary according to the phenotype. In the last years, one of the phenotypes of COPD, that is recognized as the Asthma-COPD Overlap (ACO) has received increasing attention.[2]

In respiratory medicine, the term overlap syndrome has been applied both to the association between obstructive sleep apnoea and chronic obstructive pulmonary disease (COPD)[3] and to patients with features of both asthma and COPD (asthma–COPD overlap syndrome [ACOS]).[4,5] Features of both asthma and COPD are common in a significant proportion of adult and elderly patients who present with symptoms of a chronic airways disease. The precise proportion of patients with features of both diseases is highly variable, and prevalence rates between 15% and 55% have been reported depending on the diagnostic criteria applied.[6,7] Notably, concurrent doctor-diagnosed asthma and COPD has been reported in between 15% and 20% of patients.[8,9] Globally, the prevalence of ACOS reported varies greatly due to the different diagnostic criteria used. Different epidemiological studies in which ACOS is defined as patients with COPD diagnosed with asthma before the age of 40 described prevalences of 13% and 17%.[1,10] Using the same definition, a multicenter, cross-sectional, observational study carried out in Spain including 3125 patients with COPD in primary care and specialized centers reported a prevalence of ACO of 15.9%.[11] The prevalence of ACO was determined to be between 1.6 and 4.5% in the general adult population and between 15% and 25 % in the adult population with COPD. Most research of treatments for airways diseases has been restricted to patients who meet standard definitions of either chronic obstructive pulmonary disease (COPD) or asthma, yet to distinguish COPD from asthma in adult patients who have clinical features of both can be challenging. Treatment guidelines provide scant advice on how such patients should be managed. With increasing recognition that asthma and COPD are heterogeneous diseases, attention has been directed to the needs of a group of patients with what is now termed asthma–COPD overlap syndrome (ACOS), particularly in view of the high morbidity in this population.[12]

Materials and Methods:

To identify patients with ACOS, a cohort of well-characterized patients with COPD. COPD was defined by smoking history e”10 pack-years and a postbronchodilator FEV1/FVC < 0.7 after 400 μg of inhaled salbutamol. The main goal of the study is to perform a multidimensional evaluation of patients with COPD to better define its natural history and potential clinical phenotypes. The recruitment period was between August 01, 2017, and January 31, 2018. Shaheed Suhrawardy Medical College Hospital, Dhaka. Patients were divided in to two groups 75 were ACOS and 105 were non ACOS, patients are currently in the follow-up period, but data analyzed in the present study come from the baseline assessments. Demographic and clinical data, evaluated at baselaine included anthropometric data (age, sex, and BMI), previous history of doctor-diagnosed asthma and atopy, comorbidities (Charlson index), smoking history, dyspnea (modified Medical Research Council [mMRC] scale), exacerbations in the previous year, health status by the validated of the COPD Assessment Test (CAT) and Clinical COPD Questionnaire, anxiety and depression (hospital anxiety and depression [HAD] scale), pharmacologic treatments spirometry, exercise capacity (6-min walking distance [6MWD]), and BMI, airflow obstruction, dyspnea, and exercise capacity (BODE) index. All patients signed an informed and written consent form. Patient data were anonymized in a database with a hierarchical access control to guarantee secure information access.

Results:

A total of 180 patients were included, among them 75 patients were ACOS and 105 were non ACOS. The mean age was found 61.5±9.3 years in ACOS group and 63.4±8.9 years in no ACOS group. Female was found 11(14.7%) in ACOS group and 17(16.2%) in non ACOS group. Smoking pack per year was found 52.3±24.3 in ACOS group and 55.5±26.7 in non ACOS group. Active smoker was found 28 (37.3%) in ACOS group and 31(29.5%) in non ACOS group. Mean BMI was found 23.6±2.5 kg/m^2 in ACOS group

Table-I

Sociodemographic and Clinical Characteristics of the population, According to the fulfillment of ACOS criteria

Characteristics	ACOS (n=75)	Non ACOS (n=105)	Pvalue
Age (years)	61.5±9.3	63.4±8.9	0.16^{ns}
Sex (Female)	11 (14.7)	17(16.2%)	0.78^{ns}
Smoking pack (year)	52.3±24.3	55.5±26.7	0.41^{ns}
Active smoker	28 (37.3%)	31(29.5%)	0.62^{ns}
BMI (kg/m^2)	23.6±2.5	22.9±2.7	0.08^{ns}
Symptoms			
Sputum production	44 (58.7%)	58 (55.2%)	0.64^{ns}
Dyspnea (mMRC scale >2)	34 (45.3%)	50 (47.6%)	0.76^{ns}
Charlson index	1.24±1.47	1.28±1.55	0.86^{ns}
FEV_1 % predicted	62.3±17.8	60.7±19.9	0.57^{ns}
FVC % predicted	85.7±18.3	86.7±22.5	0.75^{ns}
FEV_1/FVC	54.6±11.1	53.1±11.4	0.38^{ns}
GOLD stage			
I Mild	13 (17.3%)	18 (17.1%)	0.70^{ns}
II Mild	41 (54.7%)	50 (47.6%)	
III Severe	15 (20.0%)	24 (22.9%)	
IV very severe	6 (8.0%)	13 (12.4%)	
Bode index	1.85±1.72	2.02±1.87	0.53^{ns}
0-2	49 (65.3%)	64 (61.0%)	0.09^{ns}
3-4	21 (28.0%)	22 (21.0%)	
5-6	3 (4.0%)	16 (15.2%)	
7-10	2 (2.7%)	3 (2.9%)	
Long-acting muscarinic antagonist	47 (62.7%)	80 (76.2%)	0.04^{s}
Long-acting ²-agonist	55 (73.3%)	78 (74.3%)	0.88^{ns}
Inhaled corticosteroids	47 (62.7%)	75 (71.4%)	0.21^{ns}
Theophylline	4 (5.3%)	11 (10.5%)	0.21^{ns}

ACOS-Asthma-COPD overlap syndrome, BMI-Body mass index, FEV_1=Forced expiratory volume$_1$, GOLD = Global Initiative for Chronic Obstructive Lung Disease FVC-Forced vital capacity; s=significant; ns=not significant; P value reached from unpaired and Chi square test.

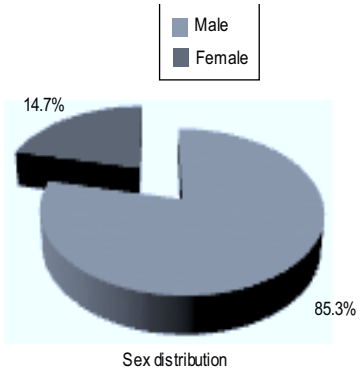

Fig.-1: *Sex distribution of ACOS patients*

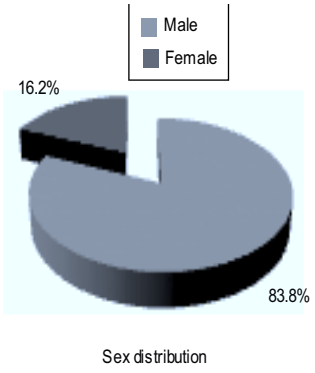

Fig.-2: *Sex distribution of Non ACOS patients*

and 22.9±2.7 kg/m^2 in non ACOS group (Table I). Regarding symptoms, sputum production was found 44(58.7%) in ACOS group and 58(55.2%) in non ACOS group. Dyspnea (mMRC scale > 2) was found 34(45.3%) in ACOS group and 50 (47.6%) in non ACOS group (Table I). Mean charlson index was found 1.24±1.47 in ACOS group and 1.28±1.55 in non ACOS group. Mean FEV_1 % predicted was found 62.3±17.8 % in ACOS group and 60.7±19.9 % in non ACOS group. Mean FVC % predicted was found 85.7±18.3 % and 86.7±22.5 % in ACOS group and non ACOS group respectively. Mean FEV_1/ FVC was found 54.6±11.1 in ACOS group and 53.1±11.4 in non ACOS group (Table I). Regarding GOLD stage, majority 41(54.7%) had II mild stage in ACOS group and 50(47.6%) in non ACOS group. Majority 49(65.3%) patients had body index 0-2 in ACOS group and 64(61.0%) in non ACOS group. Fourty seven (62.7%) patients had long-acting muscarinic antagonist in ACOS group and 80(76.2%) in non ACOS group. Fifty five (73.3%) patients had long acting ²-agonist in ACOS group and 78(74.3%) in non ACOS group. Fourty seven (62.7%) patients had inhaled corticosteroids in ACOS group and 75(71.4%) in non ACOS group. Four (5.3%) patients had theophylline in ACOS group and 11(10.5%) in non ACOS group (Table I). Long-acting muscarinic antagonist was statistically significant ($p<0.05$) between two groups (Table I). Majority 28(37.3%) patients had bronchodilator reversibility in ACOS group and majority 94(89.5%) patients had no bronchodilator reversibility in non ACOS group. Diagnosis of asthma was found 17(22.7%) in ACOS group and not found in non ACOS group. Fourty nine (65.3%) patients had IgE serum < 100 in ACOS group and 21(20.0%) in non ACOS group. Mean serum IgE was found 207.2±217 in

Table-II

Differential Characteristics of Patients with COPD Fulfilling the Criteria for ACOS

Characteristics	ACOS(n=75)	Non ACOS(n=105)	Pvalue
Bronchodilator reversibility			
No BDR	28 (37.3%)	94 (89.5%)	
Minor (>200 mL and >12%)	24 (32.0%)	11 (10.5%)	0.001^s
Major (>400 mL	and >15%)	23 (30.7%)	0 (0.0)
Diagnosis of asthma	17 (22.7%)	0 (0.0)	0.001^s
IgE serum >100	49 (65.3%)	21 (20.0%)	0.001^s
IgE serum	207.2±217	115.9±275	0.001^s
Eosinophils blood > 5%	25 (33.3%)	7 (6.7%)	0.001^s
Eosinophils blood >3%	39 (52.0%)	28 (26.7%)	0.001^s
Eosinophils blood	3.59±2.3	2.45±1.37	0.001^s
Chronic bronchitis	46 (61.3%)	62 (59.0%)	0.758^{ns}

IgE- Immunoglobulin E
s=significant; ns=not significant
P value reached from unpaired and Chi square test

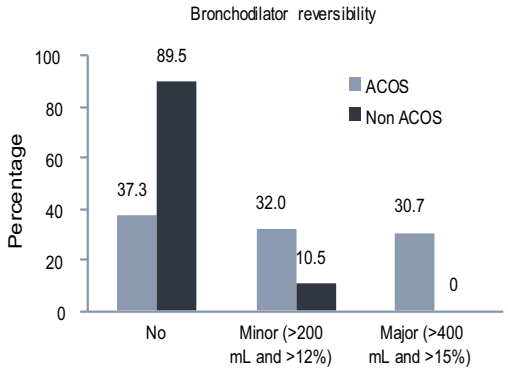

Fig.-3: *Bronchodilator reversibility of the patients.*

ACOS group and 115.9±275 in non ACOS group. Eosinophils blood > 5% was found 25(33.3%) in ACOS group and 7(6.7%) in non ACOS group. Eosinophils blood >3% was 39(52.0%) in ACOS group and 28(26.7%) in non ACOS group. Mean eosinophils blood was found 3.59±2.3 in ACOS group and 2.45±1.37 in non ACOS group. The difference were statistically significant ($p<0.05$) between two groups (Table II).

Discussion:

In present study observed that the mean age was found 61.5±9.3 years in ACOS group and 63.4±8.9 years in no ACOS group. Female was found 11(14.7%) in ACOS group and 17(16.2%) in non ACOS group. Smoking pack per year was found 52.3±24.3 in ACOS group and 55.5±26.7 in non ACOS group. Active smoker was found 28 (37.3%) in ACOS group and 31(29.5%) in non ACOS group. Mean BMI was found 23.6±2.5 kg/m^2 in ACOS group and 22.9±2.7 kg/m^2 in non ACOS group. Regarding symptoms, sputum production was found 44(58.7%) in ACOS group and 58(55.2%) in non ACOS group. Dyspnea (mMRC scale > 2) was found 34(45.3%) in ACOS group and 50 (47.6%) in non ACOS group. Mean charlson index was found 1.24±1.47 in ACOS group and 1.28±1.55 in non ACOS group. Mean FEV_1 % predicted was found 62.3±17.8 % in ACOS group and 60.7±19.9 % in non ACOS group. Mean FVC % predicted was found 85.7±18.3 % and 86.7±22.5 % in ACOS group and non ACOS group respectively. Mean FEV_1/FVC was found 54.6±11.1 in ACOS group and 53.1±11.4 in non ACOS group. Similar observation was found Baarnes et al.[13] mean age was found 63.0±10.5 years in COPD group and 56.2±11.7 years in non COPD group. Mean FEV_1 (% pred) was found 71.1±19.1 in COPD group and 92.5±17.5 in non COPD group. Regarding GOLD stage, majority 41(54.7%) had II mild stage in ACOS group and 50(47.6%) in non ACOS group. Majority 49(65.3%) patients had bode index 0-2 in ACOS group and 64(61.0%) in non ACOS group. Fourty seven (62.7%) patients had long-acting muscarinic antagonist in ACOS group and 80(76.2%) in non ACOS group. Fifty five (73.3%) patients had long acting ²-agonist in ACOS group and 78(74.3%) in non ACOS group. Fourty seven (62.7%) patients had inhaled corticosteroids in ACOS group and 75(71.4%) in non ACOS group. Four (5.3%) patients had teophylline in ACOS group and 11(10.5%) in non ACOS group. Long-acting muscarinic antagonist was statistically significant ($p<0.05$) between two groups.

In Sugimoto et al.[14] study reported that a total of 70 ACOS cases were identified. There were 58(83%) male patients, the mean age was 70.0±11.0 years. Sugimoto et al. study conducted a case-control study using 32 patients with ACOS exacerbations (ACO Sex) and 38 controls which had no exacerbations. Asthma severity was a significant risk factor for ACOS-ex. The age, sex, Body Mass Index, GOLD stage and smoking status adjusted odds ratio for moderate and severe persistent as compared with mild intermittent were 5.24(95% CI, 1.27-21.6, $p<0.05$) and 12.9 (95% CI, 1.10-149.9, $p<0.05$), respectively. de Marco et al.[15] study revealed that the subjects with current asthma alone were younger (mean±SD 33.6±7.2 years) and more likely to be women than subjects in the other groups (table 2), while subjects with COPD were the oldest (36.0±6.5 years). Smoking was more frequent among subjects with ACOS or COPD. Among lifetime smokers, the prevalence of heavy smoking (~*15 pack-years) was 51.5% for subjects with COPD alone (median (interquartile range) 16.8 (15.9) pack-years), and it ranged from 27.1% (healthy 9.8 (13.8) pack-years) to 35.1% (ACOS 10.3 (20.1) pack-years) in the other groups ($p<0.001$). In study of Cosio et al.[1] observed that Patients with ACOS defined by one major criteria or two minor criteria were not different by age (P=0.170) or sex (P=0.076) but there were significant differences by blood eosinophils (P <0.01) and IgE (P< 0.05). As expected from a population with COPD, patients were predominantly male, with predominantly mild to moderate disease assessed by lung function or BODE and with high prevalence of respiratory symptoms. Out of all comparisons, no statistically significant differences between patients with ACOS and those without ACOS were found, although there was a trend for higher disease severity in patients without ACOS (proportion of patients with BODE index e"5 was 6.7% vs 19.5%). Similarly, no differences in comorbidities were found between both groups, other than past diagnosis of asthma. The treatments that these patients were receiving

by the time of recruitment were similar for inhaled therapies in both groups, except for long-acting antimuscarinic agents (LAMAs) that were less frequently used in the ACOS group. Seventy-nine patients (63.2%) in the ACOS group were receiving inhaled corticosteroids. Oral theophylline was also prescribed significantly less frequently in the ACOS group (P < .05). In a sensitivity analysis, the significant differences observed when comparing ACOS to patients without ACOS in use of LAMA and theophylline were rendered non significant when stratifying by GOLD severity spirometry thresholds mild and moderate (I and II) vs severe and very severe (III and IV), with P values for LAMA 0.081 and 0.188, while 0.115 and 0.249 for theophylline.

In current study revealed that the majority 28(37.3%) patients had no bronchodilator reversibility in ACOS group and 94(89.5%) in non ACOS group. Diagnosis of asthma was found 17(22.7%) in ACOS group and not found in non ACOS group. Fourty nine (65.3%) patients had IgE serum < 100 in ACOS group and 21(20.0%) in non ACOS group. Mean serum IgE was found 207.2±217 in ACOS group and 115.9±275 in non ACOS group. Eosinophils blood > 5% was found 25(33.3%) in ACOS group and 7(6.7%) in non ACOS group. Eosinophils blood >3% was 39(52.0%) in ACOS group and 28(26.7%) in non ACOS group. Mean eosinophils blood was found 3.59±2.3 in ACOS group and 2.45±1.37 in non ACOS group. The difference were statistically significant (p<0.05) between two groups. Cosio et al.[1] study showed Fourty six (36.8%) patients had no bronchodilator reversibility in ACOS group and 633(89.7%) in non ACOS group. Diagnosis of asthma was found 28(31.2%) in ACOS group and not found in non ACOS group. Seventy (65.4%) patients had IgE serum < 100 in ACOS group and 88(19.8%) in non ACOS group. Mean serum IgE was found 206.6±232 in ACOS group and 115.7±273 in non ACOS group. Eosinophils blood > 5% was found 39(32.5%) in ACOS group and 34(5.2%) in non ACOS group. Eosinophils blood >3% was 61(50.8%) in ACOS group and 174(26.7%) in non ACOS group. Mean eosinophils blood was found 3.56±2.2 in ACOS group and 2.40±1.38 in non ACOS group. The difference were statistically significant (p<0.05) between two group. Following the proposed ACOS criteria, 66 patients would be diagnosed with ACOS by fulfilling one major criterion (28 patients with previous diagnosis of asthma and 39 with a bronchodilator response to albuterol higher than 15% or 400 mL) and 59 patients with two minor criteria. A Venn diagram with squares proportional to the weight of the major criteria in this population and with circles showing the overlap between minor criteria was built. In contrast, there is increasing awareness of the role of eosinophils in some types of patients with COPD, and blood eosinophilia has been identified as a surrogate marker of response to steroids in patients with COPD.[16]

Conclusion:

Long-acting muscarinic antagonist was statistically significant between ACOS group and non ACOS group. Majority patients had bronchodilator reversibility in ACOS group. Serum IgE- Immunoglobulin E was found significantly higher in ACOS group than non ACOS group. The study has been conducted on centre with a small sample size. So the study findings are not generalized in large scale and represent in whole country. Further large scale and multi centre study should be conducted to get the whole country scenario.

Reference:

1. Cosio BG, Soriano JB, López-Campos JL, Calle-Rubio M, Soler-Cataluna JJ. Defining the Asthma-COPD Overlap Syndrome in a COPD Cohort. CHEST 2016; 149(1): 45-52.
2. Alexa N, Marc M. Diagnostic Criteria for the Asthma-COPD Overlap (ACO) Still Room for Improvement. Int J Pul & Res Sci. 2017; 1(4): 555-569.
3. Ioachimescu OC, Teodorescu M. Integrating the overlap of obstructive lung disease and obstructive sleep apnoea: OLDOSA syndrome. Respirology 2013; 18: 421–31.
4. Zeki AA, Schivo M, Chan A, Albertson TE, Louie S. The asthma-COPD overlap syndrome: a common clinical problem in the elderly.J Allergy (Cairo) 2011; 2011: 861926.
5. GINA-GOLD. Diagnosis of diseases of chronic airflow limitation: asthma, COPD

and asthma-COPD overlap syndrome (ACOS), 2014.http://www.goldcopd.org/asthma-copd-overlap.html (accessed May 5, 2015).

6. Marsh SE, Travers J, Weatherall M, et al. Proportional classifications of COPD phenotypes [published correction appears in Thorax. 2014; 69(7): 672] Thorax. 2008; 63(9):761-767.
7. Weatherall M, Travers J, Shirtcliffe PM, et al. Distinct clinical phenotypes of airways disease defined by cluster analysis. Eur Respir J. 2009; 34(4): 812-818.
8. Kauppi P, Kupiainen H, Lindqvist A, et al. Overlap syndrome of asthma and COPD predicts low quality of life. J Asthma. 2011;48 (3): 279-285.
9. Andersén H, Lampela P, Nevanlinna A, Säynäjäkangas O, Keistinen T. High hospital burden in overlap syndrome of asthma and COPD. Clin Respir J. 2013; 7(4): 342-346.
10. Hardin M, Silverman EK, Barr RG, Hansel NN, Schroeder JD, et al. The clinical features of the overlap between COPD and asthma. Respir Res 2011; 12: 127.
11. Barrecheguren M, Román-Rodríguez M, Miravitlles M. Is a previous diagnosis of asthma a reliable criterion for asthma-COPD overlap syndrome in a patient with COPD? Int J Chron Obstruct Pulmon Dis 2015; 10: 1745-1752.
12. Bateman ED, Reddel HK, van Zyl-Smit RN, Agusti A. The asthma–COPD overlap syndrome: towards a revised taxonomy of chronic airways diseases? Lancet Respir Med 2015; 1-10.
13. Baarnes CB, Kjeldgaard P, Nielsen M, Miravitlles M and Ulrik CS. Identifying possible asthma–COPD overlap syndrome in patients with a new diagnosis of COPD in primary care. Primary Care Respiratory Medicine 2017; 27: 2-6.
14. Sugimoto Y, Yamamoto T, Nakano H, Nakazato M, Takayama M. Risk factors for exacerbation of asthma-copd overlap syndrome. Respirology (2017) 22 (Suppl. 3); 88–278.
15. de Marco R, Marcon A, Rossi A, Antó JM, Cerveri I, Gislason T, Heinrich J, Janson C. Asthma, COPD and overlap syndrome: a longitudinal study in young European adults. Eur Respir J 2015; in press.
16. Bafadhel M, McKenna S, Terry S, et al. Blood eosinophils to direct corticosteroid treatment of exacerbations of chronic obstructive pulmonary disease: a randomized placebo controlled trial. Am J Respir Crit Care Med. 2012;186(1):48-55.