Original Article

An Assessment of Various Phenotypes of Chronic Obstructive Pulmonary Disease

Devendra Singh, Ramakant Dixit, Neeraj Gupta, Hasha Thankam Somson, Akhilesh Verma, Himanshu Mittal
Department of Respiratory Medicine, JLN Medical College, Ajmer, Rajasthan, India

Abstract

Context: Chronic obstructive pulmonary disease (COPD) is a multifactorial and heterogeneous disease. To approach this heterogeneity, an attempt to group patients with similar characteristics that could be associated with a differential clinical outcome has been done by using the term clinical phenotype. **Aim:** This study aimed to classify phenotypes of COPD, assess and compare demography, assess and compare functional status and comorbidities. **Patients and Methods:** A hundred stable COPD patients were studied to identify various phenotypes of COPD, clinical assessment (modified Medical Research Council grading), functional assessment (6-min walk test), spirometry (fraction of exhaled breath nitric oxide, diffusing capacity for carbon monoxide) and radiological assessment (high-resolution computerized tomography, echocardiography) and screening for obstructive sleep apnea by Berlin questionnaire. Chi-square test/Fisher's exact test was used for the analysis of qualitative data. **Results:** The mean age of subjects was 60.8 ± 9.2 years with male-to-female ratio 9:1. Out of total 100 COPD patients, 45% had emphysema phenotype, 15% had COPD with bronchiectasis, and 20% each had asthma COPD overlap and chronic bronchitis. COPD phenotype was most common in age group 56–65 years. Emphysema patients (48.6%) were underweight and obesity was found to be most common in chronic bronchitis (30%). Emphysema patients (91%) had maximum exacerbation during the past 1 year with mean 6-min walk distance (158.7 m) and mean forced expiratory volume in 1% was 37.5. **Conclusion:** This is the first study in India which provides comparative categorizations of the phenotypic subgroups of COPD on various parameters.

Keywords: Asthma chronic obstructive pulmonary overlap, chronic obstructive pulmonary, emphysema, phenotype

Introduction

Chronic obstructive pulmonary disease (COPD) is a multifactorial and heterogeneous disease and not every patient responds to all available drugs.[1] Identifying various phenotypes are essential to approach this heterogeneity. This can pave the way for personalized treatment of a patient.

A group of patients having similar characteristics with differential clinical outcomes is termed as clinical phenotype.[2] Determination of the phenotypes is utmost important to understand the epidemiology and pathogenesis of COPD.

Therefore, we planned this study to screen the stable COPD patients to determine the distinct phenotype among COPD, their relative proportion, and most relevant clinical and other characteristic among them.

Access this article online

Quick Response Code:

Website: www.ijrc.in

DOI: 10.4103/ijrc.ijrc_31_21

Patients and Methods

This study was carried out after approval from ethical committee. A total of 100 patients with COPD were recruited during the study period. All stable patients with symptoms and signs of COPD diagnosed clinically with chest high resolution computed tomography (HRCT) and spirometry, willing to participate with necessary investigations and those who met the global initiative for chronic obstructive lung disease (GOLD) criteria for COPD for severity of disease were included in this study.

Address for correspondence: Dr. Devendra Singh, Department of Respiratory Medicine, JLN Medical College, Ajmer, Rajasthan, India.
E-mail: drrdev@gmail.com

How to cite this article: Singh D, Dixit R, Gupta N, Somson HT, Verma A, Mittal H. An assessment of various phenotypes of chronic obstructive pulmonary disease. Indian J Respir Care 2021;10:305-11.

Received: 22-02-2021 **Revised:** 14-05-2021
Accepted: 17-07-2021 **Published:** 13-09-2021

Patients with other coexisting chronic lung disease other than COPD, any systemic disease causing pulmonary hypertension other than COPD, those with acute exacerbation, pneumothorax, those with active respiratory infection in the past 6 weeks were excluded from the study.

The clinical diagnosis of COPD was based on history, physical findings and confirmed by spirometry (forced expiratory volume in 1 [FEV1]/forced vital capacity [FVC] <0.7). Patients were evaluated for respiratory symptoms such as cough, shortness of breath, and wheezing episode. Assessment of dyspnea was done by modified Medical Research Council (mMRC) Dyspnea Scale and grading was done accordingly. All patients were subjected to measurement of fractional exhaled nitric oxide (FeNO) level. This was done by using FeNO–HYPAIR (GERMANY) to evaluate asthma component in COPD patient. The 6-min walk test and body mass index (BMI), airflow obstruction, dyspnea, and exercise (BODE) index were recorded in all patients. Diffusion capacity of lung diffusing capacity of the lungs for carbon monoxide (DLCO), was measured as the single breath DLco by COSMED pulmonary function equipment attached with Q-box in all eligible study patients.

All study patients were subjected to assessment by Berlin questionnaires[3] to assess underlying obstructive sleep apnea (OSA) and computed tomography (CT) scan thorax to assess details of underlying pulmonary changes. HRCT findings such as dominancy of emphysema and the presence of bronchial wall thickening were used to classify various phenotypes, especially the chronic bronchitis, associated bronchiectasis, and pulmonary fibrosis.

Criteria of diagnosing and assessing various COPD phenotypes were as below:

Phenotype 1: Emphysema (at least one of the criteria)

I. Pulmonary emphysema proved by CT scan
II. Diffusion test with DLCO/VA, (where VA = alveolar ventilation) values inferior to 80% and thorax radiography suggesting emphysema, according to the criteria described by Miniati *et al*.[4]

Phenotype 2: Chronic bronchitis

I. Habitual coughing and expectoration (chronic bronchitis criteria)
II. Diffusion test with TLco/VA values superior to 80%
III. Absence of pulmonary emphysema demonstrated through imaging techniques, CT, or thorax radiography, according to the previous criteria
IV. Absence of asthma antecedents.

Phenotype 3: "Chronic obstructive pulmonary disease-asthma" overlap

I. Diffusion test with TLco/VA values superior to 80%
II. Absence of pulmonary emphysema demonstrated through imaging techniques, CT, or thorax radiography, according to the previous criteria
III. Personal history of asthma or seasonal variation/rhinitis
IV. Postbronchodilator increase in FEV1 >12% or 200 ml.

Phenotype 4: Chronic obstructive pulmonary disease with bronchiectasis

I. Increased daily sputum production
II. The combination of emphysema and bronchiectasis detectable on HRCT scan.

Based on the above criteria, these four COPD phenotypes were classified and assessed as per aims and objective of this study.

Statistical assessment

Categorical variables were expressed as frequency and percentage and were analyzed using Chi-square test/ Fisher's exact test as applicable. Continuous variables were expressed as means ± standard deviation and were analyzed using one-way ANOVA test. Statistical significance was set at $P < 0.05$. All statistical analysis was done using Epi info version 7.2.1.0, CDC, Atlanta, GA, USA, 2017 statistical software.

Results

There were 100 patients satisfying the eligibility criteria as per study protocol. The mean age of patients was 60.8 ± 9.2 years with most common age group of 56–65 years. There were 90% male and 10% female patients with mean BMI of 19.8 ± 3.8 kg/m^2.

Only 19% patients had biofuel exposure and mean pack years of patients was 25.4 ± 15.4 with maximum patients had 20–40 pack per years. The mean total duration of illness was 5.3 ± 3.8 years. Most common symptoms were breathlessness (90%) followed by cough (89%), 33% had a history of wheeze, and 32% had history rhinitis. The mean distance walked in 6-min walk distance test was 177.4 ± 53.3 m. The mean value of DLco% was 41.03 ± 17.7 and DLco/VA was 73.2 ± 28.6 among study patients. Eighty-three percent of all COPD patients had exacerbation or need for hospital visit during the past 1 year.

Most of the COPD patients (31%) were in quartile-4 and quartile-3 of BODE index with mean BODE index (5.2 ± 2.02). Forty-nine percent patients had mMRC Grade-1 followed by 32% had mMRC Garde-2. According to GOLD staging, 39% patients had GOLD Stage-3 followed by 32% had GOLD Stage-2, 26% patients had GOLD-Stage-4, and only 3% patients had GOLD Stage-1. Seventy-five percent patients had 0–24 FeNO (ppb) at 50 ml/s followed by 19% had 25–50 FeNO (ppb) at 50 ml/s and 6% had >50 FeNO (ppb) at 50 ml/s [Table 1].

We observed that 45% patients had emphysema phenotype followed by 20% had asthma COPD overlap (ACO) type and bronchitis type of phenotype each and 15% had COPD with bronchiectasis [Figure 1].

The mean age of chronic bronchitis phenotype was 54 ± 9.8, emphysema phenotype was 61.8 ± 9.5, ACO phenotype was 63.2 ± 6.8, and COPD with bronchiectasis was 61.4 ± 10.7 (P = 0.575). All COPD phenotypes were more common in males as compared to females (P = 0.007).

Most of the COPD phenotypes (53 patients) were in normal BMI category followed 37 patients having underweight. Among the underweight category (BMI <18.5), the most common phenotype was emphysema (48.6%). The most common phenotype in overweight category (BMI >25) was also emphysema (40%) followed by chronic bronchitis phenotype (30%) (P = 0.091).

Table 1: Characteristics of patients

	Number of patients, *n* (%)
BODE index	
Quartile-1 (0-2)	9 (9)
Quartile-2 (3-4)	29 (29)
Quartile-3 (5-6)	31 (31)
Quartile-4 (7-10)	31 (31)
m-MRC grade of dyspnea	
0	10 (10)
1	49 (49)
2	32 (32)
3	9 (9)
4	0
GOLD stage	
1	3 (3)
2	32 (32)
3	39 (39)
4	26 (26)
FeNO (ppb) at 50 ml/s	
0-24	75 (75)
25-50	19 (19)
>50	6 (6)

BODE: Body mass index, airflow obstruction, dyspnea, and exercise, m-MRC: Modified Medical Research Council, GOLD: Global initiative for chronic obstructive lung disease, FeNO: Fraction of exhaled breath nitric oxide

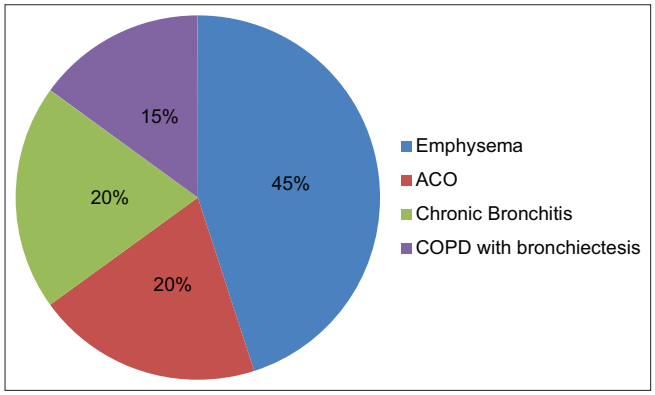

Figure 1: Distribution according to chronic obstructive pulmonary disease phenotype

Ninety patients were in smoker category followed by 19 patients having biofuel exposure. In smoker category, the most common phenotype was emphysema (50%) followed by chronic bronchitis (20%). The most common phenotype among biofuel exposure category was bronchiectasis phenotype (36.8%) followed by chronic bronchitis (31.6%) (P = 0.0383).

Patients having sputum expectoration for more than 3 months per year had chronic bronchitis (37%) followed by emphysema (29.6%). In emphysema phenotype, 91% patients had ≥1 exacerbation in the past 1 year followed by 85% patients of chronic bronchitis phenotype, 73.33% patients of COPD with bronchiectasis phenotype, and 70% patients of ACO phenotype had ≥1 exacerbation in the past 1 year (P = 0.132) [Table 2].

Among patients having chronic bronchitis, 40% had quartile-2 and quartile-4 each and 10% had quartile-1 and 3 BODE index. Similarly, in emphysema patients, 37.8% had quartile-3 and 4 each and 24.4% had quartile-2. In ACO, 35% had quartile-3 and 30% had quartile-1 and 2 each. In COPD with bronchiectasis, 33.3% had quartile-3 and 4 each while 26.6% had quartile-2 and 6.6% had quartile-1 BODE index (P = 0.01) [Figure 2][Table 3].

On assessment of dyspnea by mMRC among patients having chronic bronchitis, 20% had Grade-0, 16.3% had Grade-1, 25% had Grade-2, and 22.2% had Grade-3. Similarly, among emphysema patients, 30% had Grade-0, 42.8% had Grade-1, and 46.8% had Grade-2, and 66.7% had Grade-3. In ACO, 40% had Grade-0, 26.5% had Grade-1, 9.4% had Grade-2, and none had Grade-3. In COPD with bronchiectasis, 10% had Grade-0 and 14.2% had Grade-1 and 18.7% had Grade-2 and 11.1% had Grade-3 (P = 0.576) [Figure 3].

Patients having ACO phenotype had mean FVC% predicted of 77 followed by COPD with bronchiectasis – 66.8, chronic bronchitis – 61.5, and emphysema – 58.8 with significant P = 0.0003. Similarly, FEV1% predicted for ACO was 53.5 followed by 43.9 in chronic bronchitis, 42.6 in COPD with bronchiectasis, and 37.5 in emphysema phenotype with significant P = 0.0021. Similarly, bronchodilator reversibility% for ACO was

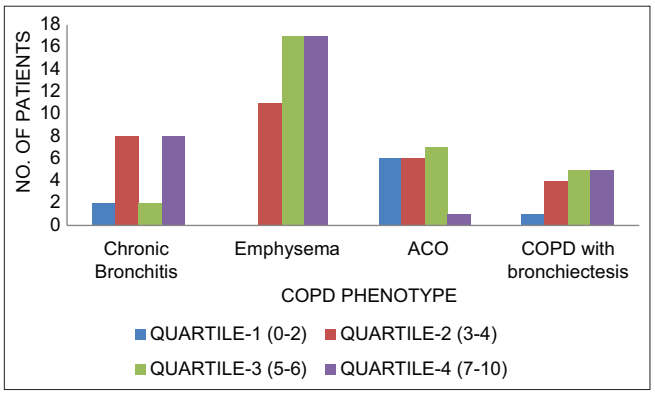

Figure 2: Distribution of chronic obstructive pulmonary disease phenotypes according to body mass index, airflow obstruction, dyspnea, and exercise index

Table 2: Clinical characteristics

Clinical parameter	ACO	Chronic bronchitis	Emphysema	COPD with bronchiectasis
Age distribution (years)				
35-45	5 (25)	2 (10)	1 (2.2)	1 (6.6)
46-55	6 (30)	2 (10)	6 (13.3)	2 (13.3)
56-65	8 (40)	9 (45)	23 (51.1)	8 (53.3)
>65	1 (5)	7 (35)	15 (33.3)	4 (26.6)
P			0.575	
Gender				
Male/female	18/2	18/2	44/1	10/5
P			0.0070	
BMI				
Underweight (<18.5)	3 (8.1)	7 (18.9)	18 (48.6)	9 (24.3)
Normal (18.5-<25)	16 (30.2)	10 (18.9)	23 (43.4)	4 (7.5)
Overweight (25-<30)	1 (10)	3 (30)	4 (7.5)	2 (20)
P			0.091	
Biofuel exposure	3 (15.8)	6 (31.6)	3 (15.7)	7 (36.8)
Smokers	16 (17.8)	18 (20)	45 (50)	11 (12.2)
P			0.0383	
Sputum expectoration (>3 months/year)	6 (11.1)	20 (37.0)	16 (29.6)	12 (22.2)
Exacerbation in the past 1 year	14 (70)	17 (85)	41 (91)	11 (73.3)
P			0.132	

P value calculated using Chi-square test. BMI: Body mass index, COPD: Chronic obstructive pulmonary disease, ACO: Asthma COPD overlap

Table 3: Distribution of chronic obstructive pulmonary disease phenotypes according to body mass index, airflow obstruction, dyspnea, and exercise index

	Chronic bronchitis, *n* (%)	Emphysema, *n* (%)	ACO, *n* (%)	COPD with bronchiectasis, *n* (%)
Quartile-1 (0-2)	2 (10)	0	6 (30)	1 (6.6)
Quartile-2 (3-4)	8 (40)	11 (24.4)	6 (30)	4 (26.6)
Quartile-3 (5-6)	2 (10)	17 (37.8)	7 (35)	5 (33.3)
Quartile-4 (7-10)	8 (40)	17 (37.8)	1 (5)	5 (33.3)
Total	20 (100)	45 (100)	21 (100)	15 (100)
P		0.010		

P value calculated using Chi-square test. COPD: Chronic obstructive pulmonary disease, ACO: Asthma COPD overlap

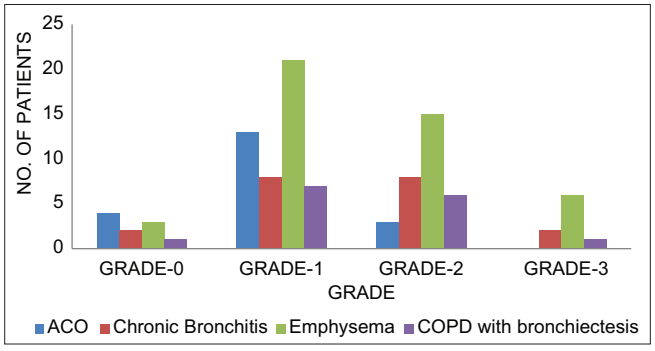

Figure 3: Distribution of chronic obstructive pulmonary disease phenotypes according to dyspnea by modified Medical Research Council grade

17.6 followed by 9.7 in emphysema, 7.9 in chronic bronchitis, and 6.8 in COPD with bronchiectasis with significant $P = 0.0002$. FEV predicted (25%–75%) for ACO was 25.6 followed by 17.7 in chronic bronchitis, 16.4 in COPD with bronchiectasis, and 16.0 in emphysema with significant $P = 0.023$. FEV1/FVC ratio for ACO was 0.57 followed by 0.56 in chronic bronchitis, 0.55 in COPD with bronchiectasis, and 0.52 in emphysema phenotype which is insignificant ($P = 0.3317$) [Table 4].

In ACO phenotype, 4 patients had FeNO level between 0 and 24 ppb and 10 and 6 patients in 25–50 ppb and >50 ppb level category, respectively. Similarly, in chronic bronchitis, 20 patients had FeNO level between 0 and 24 ppb, none in 25–50 ppb and >50 ppb, respectively. In COPD with bronchiectasis, 13 patients had FeNO level 0–24 ppb and 2 and 0 patients in 25–50 ppb and >50 ppb, respectively. In emphysema, 38 patients had level of 0–24 ppb and 7 and 0 patients in 25–50 ppb and >50 ppb, respectively [Table 5] ($P = 0.0001$).

Among ACO, emphysema, and COPD with bronchiectasis phenotypes, 1 patient each had positive response for OSA screening by BQ. The most common phenotype with pulmonary arterial hypertension (PAH) was emphysema (57.1%) followed by chronic bronchitis (21.4%), ACO (10.7%), and COPD with bronchiectasis (10.7%) [Table 6].

Table 4: Distribution of chronic obstructive pulmonary disease phenotypes according to spirometry values

	FVC% predicted (mean)	FEV1% predicted (mean)	FEV1/FVC ratio (mean)	Bronchodilator reversibility % (mean)	FEV (25%-75%) predicted (mean)
ACO	77±16.3	53.5±16.4	0.57±0.1	17.6±6.6	25.6±20.5
Chronic bronchitis	61.5±13.6	43.9±16.5	0.56±0.13	7.9±9.0	17.7±9.1
Emphysema	58.8±15.6	37.5±13.6	0.52±0.11	9.7±8.2	16.0±6.6
COPD with bronchiectasis	66.8±21.7	42.6±18.7	0.55±0.12	6.8±4.64	16.4±7.6
P	0.0003	0.0021	0.3317	0.0002	0.023

P value calculated using ANOVA test. FVC: Forced vital capacity, FEV1: Forced expiratory volume in 1, COPD: Chronic obstructive pulmonary disease, ACO: Asthma COPD overlap

Table 5: Distribution of chronic obstructive pulmonary disease phenotypes according to fraction of exhaled breath nitric oxide level at 50 ml/s

FeNO level	0-24 ppb, *n* (%)	25-50 ppb, *n* (%)	>50 ppb, *n* (%)
ACO	4 (5.3)	10 (52.6)	6 (100)
Chronic bronchitis	20 (26.7)	0	0
Emphysema	38 (50.7)	7 (36.8)	0
COPD with bronchiectasis	13 (17.3)	2 (10.5)	0
Total	75 (100)	19 (100)	6 (100)
P		0.0001	

P value calculated using Chi-square test. COPD: Chronic obstructive pulmonary disease, ACO: Asthma COPD overlap

Table 6: Distribution of chronic obstructive pulmonary disease phenotypes according to pulmonary arterial hypertension and obstructive sleep apnea screening by Berlin questionnaire

COPD phenotype	OSA screening by BQ, *n* (%)	PAH present, *n* (%)
ACO	1 (33.3)	3 (10.7)
Chronic bronchitis	0	6 (21.4)
Emphysema	1 (33.3)	16 (57.1)
COPD with bronchiectasis	1 (33.3)	3 (10.7)
Total	3 (100)	28 (100)

COPD: Chronic obstructive pulmonary disease, ACO: Asthma COPD overlap, PAH: Pulmonary arterial hypertension, BQ: Berlin questionnaire, OSA: Obstructive sleep apnea

On GOLD stage assessment, among patients having chronic bronchitis, none had Stage-1 and 25% in Stage-2 and 17.9% had Stage-3 and 19.2% in Stage-4. Similarly, in ACO patients, 66.7% had Stage-1 and 34.4% in Stage-2 and 12.8% had Stage-3 and 7.7% in Stage-4. In emphysema, none had Stage-1 and 28.1% in Stage-2 and 53.8% had Stage-3 and 57.6% in Stage-4. In COPD with bronchiectasis, 33.3% had Stage-1 and 12.5% in Stage-2 and 15.3% each had Stage-3 and Stage-4 [Figure 4].

Discussion

In the present study, 45% patients had emphysema phenotype followed by 20% having ACO type and chronic bronchitis type of phenotype each, and 15% had COPD with bronchiectasis.

A study by Marsh *et al*.[5] found that among the subjects with COPD, the most common phenotype was asthma (53/96, 55.2%), and Izquierdo-Alonso *et al*.[6] found that 44.7% (148/331) patients were chronic bronchitis. Cosío *et al*.[7] also found that 63.5% of patients were chronic bronchitis phenotype. The result of present study and other studies suggest that COPD had different phenotypes. Relative difference in the proportion of various phenotypes in these studies might be due to number of study patients, difference in selection criteria, geographic and racial variations among study participants.

In the present study, the mean age of patients was 54 ± 9.8 years in chronic bronchitis patients, 61.8 ± 9.5 years in emphysema patients, 63.2 ± 6.8 years in ACO, and 61.4 ± 10.7 years in COPD with bronchiectasis group. A study conducted by Izquierdo-Alonso *et al*.[6] observed mean age for emphysema group of 66 years and for bronchitis group was of 60 years. A similar study by Badawy *et al*.[8] on 110 COPD patients found a mean age of 59.8 ± 11.3 among 5 different COPD phenotypes, i.e. 14 patients ACOS phenotype with mean age 62.8 years, 20 patients chronic bronchitis phenotype with mean age 48.4 years, 21 patients COPD with bronchiectasis phenotype with mean age 60.3 years, 35 patients emphysema phenotype with mean age 61.8 years, and 20 patients frequent exacerbator with mean age of 64.4 years. Boschetto *et al*.[9] found that mean age of emphysema patients was 68 ± 2 years. These data suggest that all COPD phenotypes do not differ much among age groups.

In this study, there were 90% male and 10% female with male–female ratio of 9:1. All COPD phenotypes were more common in male as compared to females. In a study by Badawy *et al*.[8] among 110 COPD patients, there were 74 males and 36 females. A similar study conducted by Cosío *et al*.[7] also found that patients in different phenotypes were predominantly male. There were 85% males and 15% females in ACO phenotype, 94.4% males and 4.6% females in emphysema, and 87.1% males and 11.9% females in chronic bronchitis. Male predominance among various phenotypes in the present study and all other studies reflect high incidence of smoking among males.

In the present study, 53% patients were normal in weight followed by 37% in underweight and 10% patients in overweight category as per their BMI. In the present study, the distribution of underweight patients was 48.6% in emphysema,

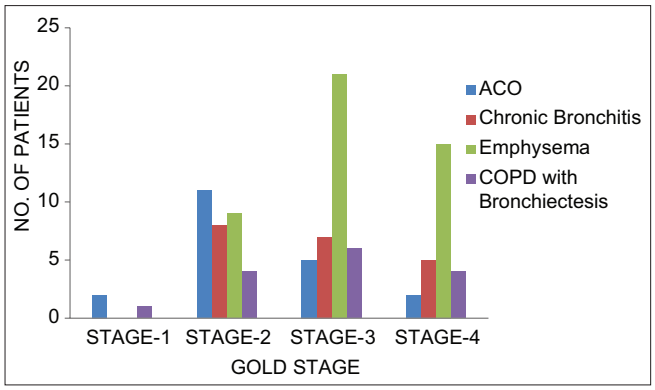

Figure 4: Distribution of chronic obstructive pulmonary disease phenotypes according to global initiative for chronic obstructive lung disease stages

24.3% in COPD with bronchiectasis, 18.9% in chronic bronchitis, and 8.1% in ACO phenotype. Guerra *et al*.[10] observed that patients with emphysema were more likely to be underweight, whereas patients with chronic bronchitis more likely to be obese. Emphysema patients can progressively lose weight due to several mechanisms like oxygen cost of breathing are increased in these patients, and the caloric intake is reduced since large meals can induce shortness of breath. Weight loss is an important determinant of symptoms, disability, and quality of life. Furthermore, low BMI is an independent risk factor for mortality and a profound decline in FEV1 over time in subjects with COPD.[11]

In the present study, only 19% patients had a history of biofuel exposure. The most common phenotype among biofuel exposure category was bronchiectasis phenotype (36%) followed by chronic bronchitis (31%). A study by Badawy *et al*.[8] found similar result that maximum patients of COPD with bronchiectasis phenotype were exposed to biofuel. Biomass smoke exposure predominantly affects women in rural areas who use these fuels for cooking. With the increasing understanding of the risk of developing COPD conferred by biomass smoke, it is apparent that it also increases the risk for developing chronic bronchitis and bronchiectasis. Compared to COPD due to tobacco smoking, those with COPD related to biomass smoke exposure have more cough, phlegm symptoms, and air trapping on CT scan.[12]

Patients having sputum expectoration for more than 3 months per year in the present study were seen in chronic bronchitis (37%) followed by emphysema (29.6%), COPD with bronchiectasis (22%), and ACO (11.1%). Out of 45 patients of emphysema, 21 (46.7%) patients were severe breathless (mMRC Grade-2 and Grade-3). Out of 20 patients of chronic bronchitis, 10 (50%) patients were severe breathless (mMRC Grade-2 and Grade-3). These data show chronic bronchitis and emphysema phenotype had more severe phenotype of COPD as per symptoms. A study conducted by Elgazzar[13] concluded that among the clinical phenotypes, emphysema phenotype was more prevalent among the bad outcome group patients than in the good outcome group (52.7% vs. 22.8%, $P < 0.05$), while the other clinical phenotypes were more prevalent in the good outcome group.

In the present study, there was a significant difference of exacerbation in the past 1 year ($P = 0.132$) in different phenotypes. Seventy percent of ACO phenotype, 85% of chronic bronchitis phenotype, 91% of emphysema phenotype, and 73.33% of COPD with bronchiectasis phenotype patients had exacerbation or need hospital visit in the past 1 year. This was in agreement with Badawy *et al*.[8] and Izquierdo-Alonso *et al*.[6] According to their study, no significant differences were observed in the percentage of patients who had at least one exacerbation in the past year, in the number of exacerbations, in the number of visits to emergency room (total and due to COPD), or in the number of hospital admissions.

In the present study, 49% patients had mMRC Grade-1 followed by 32% had mMRC Garde-2, 10% had mMRC Grade-0, and 9% had mMRC Garde-3. Patients who have Grade-0 of mMRC of dyspnea and ACO phenotype were most common followed by emphysema. In Grade-1 patients, emphysema was most common. In Grades-2 and 3 patients, emphysema was again most common followed by COPD with bronchiectasis. A similar study conducted by Badawy *et al*.[8] concluded that there was significant difference in dyspnea (mMRC score) between different COPD phenotypes, most ACOS phenotype patients had Grade-3 and Grade-4 (50.0%), most chronic bronchitis phenotype patients had Grade-2 (50.0%), most COPD with bronchiectasis phenotype patients had Grade-4 (47.6%), most emphysema phenotype patients had Grade-3 (48.6%), most Frequent exacerbator phenotype patients had Grade-4 (75%), and their results were consistent with Izquierdo-Alonso *et al*.,[6] where significant difference in dyspnea (mMRC score) was observed among different phenotypes with most phenotypes having Grade-2 (emphysema phenotype 37.8%, chronic bronchitis 48%, and ACOS phenotype 47.5%).

In the present study, patients having chronic bronchitis, the most common GOLD stage was 2 followed by 4 and 3. Similarly, in ACO patients, the most common GOLD stage was 1 followed by 2. In COPD with bronchiectasis, the most common GOLD stage was 1 followed by 2. Cosío *et al*.[7] found that in ACO type of phenotype, majority (55.2%) had GOLD-2 stage followed by 20% had GOLD-3; in emphysema phenotype, 55.3% had GOLD-3 and 26.3% had GOLD-2 stage; in bronchitis patients, 39.4% had GOLD-2 and 29.3% had GOLD-3 stage.

In the present study, 28% COPD subjects have PAH on echocardiography. Among COPD phenotype, 10.7% of ACO subject, 21.4% of chronic bronchitis subject, 57.1% of emphysema subject, and 10.7% of COPD with bronchiectasis subject have PAH. In a recent study performed on 120 patients with severe emphysema, Scharf *et al*.[14] reported that a very high incidence of 91% of the patients had pulmonary hypertension. The actual incidence

of pulmonary hypertension in COPD is not known, because it has not been screened systematically using reliable diagnostic tools (right heart catheterization) in the wide clinical spectrum of COPD.

Conclusion

The overall conclusions of our study are that there is a wide heterogeneity among COPD patients. All COPD cases are not the same, i.e., they differ in various clinical, functional, radiological, and inflammatory parameters among them; therefore, we cannot treat all COPD patient with the same treatment irrespective without knowing the underlying phenotype. All patients have different pathological process of disease that makes them a specific phenotype. COPD patients with high sputum eosinophil count need inhaled corticosteroids while those with bronchiectasis need additional in their treatment, i.e., frequent antibiotics, mucolytic, compulsory vaccination, and physiotherapy. Having knowledge of different phenotypes and their correct identification will definitely improve the management strategies, treatment outcome, and survival among COPD patients that are increasing at an alarming speed all over.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Miravitlles M, Soler-Cataluña JJ, Calle M, Soriano JB. Treatment of COPD by clinical phenotypes: Putting old evidence into clinical practice. Eur Respir J 2013;41:1252-6.
2. Han MK, Agusti A, Calverley PM, Celli BR, Criner G, Curtis JL, *et al.* Chronic obstructive pulmonary disease phenotypes: The future of COPD. Am J Respir Crit Care Med 2010;182:598-604.
3. Netzer NC, Stoohs RA, Netzer CM, Clark K, Strohl KP. Using the berlin questionnaire to identify patients at risk for the sleep apnea syndrome. Ann Intern Med 1999;131:485-91.
4. Miniati M, Monti S, Stolk J, Mirarchi G, Falaschi F, Rabinovich R, *et al.* Value of chest radiography in phenotyping chronic obstructive pulmonary disease. Eur Respir J 2008;31:509-15.
5. Marsh SE, Travers J, Weatherall M, Williams MV, Aldington S, Shirtcliffe PM, *et al.* Proportional classifications of COPD phenotypes. Thora×2008;63:761-7.
6. Izquierdo-Alonso JL, Rodriguez-Gonzálezmoro JM, de Lucas-Ramos P, Unzueta I, Ribera X, Antón E, *et al.* Prevalence and characteristics of three clinical phenotypes of chronic obstructive pulmonary disease (COPD). Respir Med 2013;107:724-31.
7. Cosío BG, Dacal D, Pérez de Llano L. Asthma-COPD overlap: Identification and optimal treatment. Ther Adv Respir Dis 2018;12:1753466618805662.
8. Badawy MS, Rashad AM, Elhabashy MM, Qasem RM. Evaluation of co-morbidities among different chronic obstructive pulmonary disease phenotypes. Thora×2018;1:8-13.
9. Boschetto P, Miniati M, Miotto D, Braccioni F, De Rosa E, Bononi I, *et al.* Predominant emphysema phenotype in chronic obstructive pulmonary. Eur Respir J 2003;21:450-4.
10. Guerra S, Sherrill DL, Bobadilla A, Martinez FD, Barbee RA. The relation of body mass index to asthma, chronic bronchitis, and emphysema. Chest 2002;122:1256-63.
11. Sun Y, Milne S, Jaw JE, Yang CX, Xu F, Li X, *et al.* BMI is associated with FEV_1 decline in chronic obstructive pulmonary disease: A meta-analysis of clinical trials. Respir Res 2019;20:236.
12. Kim V, Han MK, Vance GB, Make BJ, Newell JD, Hokanson JE, *et al.* COPD Gene investigators. The chronic bronchitic phenotype of COPD: An analysis of the COPD Gene Study. Chest 2011;140:626-33.
13. Elgazzar AE. Clinical phenotype as a predictor of outcome in mechanically ventilated chronic obstructive pulmonary disease patients. Egypt J Bronchol 2018;12:180-6.
14. Scharf SM, Iqbal M, Keller C, Criner G, Lee S, Fessler HE, *et al.* Hemodynamic characterization of patients with severe emphysema. Am J Respir Crit Care Med 2002;166:314-22.