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Evaluation of Co-morbidities among Different Chronic Obstructive Pulmonary Disease Phenotypes

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Abstract

Background: Co-morbidities are associated with increasing risk of mortality, hospitalizations and costs of treatment in Chronic Obstructive Pulmonary Disease patients. Identification of Co- morbidities related to COPD phenotypes may guide individualized therapies and achieve better prognosis.

Methods: A prospective study of one hundred ten patients of confirmed COPD diagnosis were carried out and divided into five different phenotypes with related co-morbidities. History taking, clinical examination, Chest X-ray, Computed chest Tomography, laboratory investigations, arterial blood gas, Echocardiography and Electrocardiography were done for all patients. St. George's Respiratory Questionnaire, COPD assessment test (CAT score) and BODEx (BMI, FEV1, dyspnea and exacerbations) were used for assessment of disease impact on quality of life, severity, and exacerbation respectively.

Results: Emphysema group were 31% among all cases with mean age 61.8±9.1, frequent exacerbator group and Chronic bronchitis phenotype were 18% with mean age 64.4±11.3, and 48.8±9 respectively. COPD with bronchiectasis group were 19% with mean age 60.3±6 and Asthma COPD Overlap Syndrome (ACOS) were 12% with mean age 62.8±15.8. There was significant difference as regards age between different group of phenotypes P- value <0.001. There was significance difference in BODEx index and in (CAT) score among different COPD phenotypes P-value 0.020, 0.001 respectively. There was significant difference in all items of SGRQ among different COPD phenotypes P–value 0.001. Diabetes was commonly presented in 50 % ACOS cases, Ischemic heart disease was present more in Emphysema 22.9%, Osteoporosis was more in COPD with bronchiectasis 28.6%, Cor-pulmonale was more present in frequent excerbator 65%, and Anemia more common in COPD with bronchiectasis 23.8%. Depression was more common in frequent excerbator phenotype (45.0 %). Gastro-esophageal reflux was the most common co-morbidities (58 %) then cor-pulmonale 41.8%, systemic hypertension 40 % and pulmonary hypertension 28%.

Conclusion: The presence of significant co-morbidities is important modifying risk factors for severity in COPD. They contribute to the overall severity in individual patients, have a major impact on quality of life, and major causes of hospitalization. Co-morbidities can be associated with any clinical phenotype.

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Introduction

Chronic obstructive pulmonary disease (COPD) is a common disease that severely threatens human health. As World Health Organization (WHO) has predicted, social and economic burden of COPD will rise to the fifth and COPD will become the third leading cause of death worldwide by 2030.[1] COPD is a complex syndrome with pulmonary and extra-pulmonary manifestations. In the recent years, clinicians also proved that the heterogeneity of COPD is associated with different clinical outcomes including symptoms, exacerbations, responses to recommended therapy, decline of lung function and death.[2]

Generally, phenotype is any observed quality of an organism, like its morphology, development or behavior, as opposed to its genotype, which is the inherited instructions it carries, which may or may not be expressed.[3] However, only phenotypes associated with symptoms, prognosis, progression and response to therapy are relevant in clinical practice. So, the term clinical phenotype in the field of COPD is defined as "a single or combination of disease attributes that describe differences between individuals with COPD as they relate to clinically meaningful outcomes symptoms, exacerbations, response to treatment, speed of progression of the disease or death.[3]

Adding to lung involvement, a lot of "co-morbidities" may present in patients with COPD such as cardiovascular disease, metabolic dysfunctions, and depressive disorders are more commonly present. A number of potential mechanisms linking COPD and co-morbidities have been hypothesis: The pro-inflammatory cascade,[4,5,6] increased oxidative stress,[7] increased arterial stiffness,[8,9] catabolic state,[10] and sedentary lifestyle.[11] Patients with COPD are often "multi-system diseased patients," presenting with different clinical pictures, with a poorer quality of life and outcomes,[12] and a high disease-related burden.[13,14] Therefore, the phenotype should be able to classify the patients into subgroups with a prognostic value that allow for determining the best therapy in order to achieve better clinical results.

Patients and Methods

This prospective study of phenotypes of chronic obstructive pulmonary disease and its co-morbidities was carried out on 110 patients (74 males and 36 females) with mean age (59.8±11.3), they were admitted to chest department of Qena university hospital from our outpatient clinic and emergency room during the period from January 2016 to December 2016.

Inclusion Criteria

1-Patients were diagnosed to have COPD after assessing the presence of chronic cough, sputum production, dyspnea or history of exposure to risk factors as smoking and fumes (post-bronchodilator ratio (FEV1/FVC<0.70).

2- Their age ≥ 40 years.

3-Patients presented with one or more co-morbidities diagnosed previously or on current medical therapy. Co-morbidity was confirmed by the physician through a detailed examination and investigations and medications or therapy specific to any disease. Self-reported diagnoses were not considered.

Exclusion Criteria

1-Patients presented with bronchial asthma with reversible airway obstruction or other lung diseases.

2-Young aged patients < 40 years.

All Patients in the Study Investigated Thorough

Medical History Including

- Age, sex, occupation, residence.
- Smoking history , type of smoking , smoking index.
- History of exposure to biomass fuel, and other special habits .
- History of chronic cough.
- History of exertional dyspnea using (mMRC) dyspnea scale (Modified Medical Research Council) Questionnaire for Assessing the Severity of breathlessness.
- History of other symptoms orthopnea, chest pain, fever, heamptosis, wheezes, palpation, epigastric pain, cyanosis, anorexia, loss of weight, muscle and bone pain.
- Family history.
- History of exacerbation, previous hospitalization and ICU admission and classification of exacerbation

severity according to the intensity of the medical intervention required to control the patient's symptoms :-

A. Mild (treated with short acting bronchodilators only, SABDs)
B. Moderate (treated with short acting bronchodilators plus antibiotics and/or corticosteroids).
C. Severe (patients require hospitalization or visit emergency room) may be also associated with acute respiratory failure .

- Quality of life determined using the St. George's Respiratory

Questionnaire for COPD patients (SGRQ).[15] Using simple Arabic version of SGRQ-C translated and validated by (Mohamed MA, 2008).[16] It is a standardized, self administered questionnaire for measuring impaired health and perceived quality of life in airways disease (COPD and asthma). It consists of 50 items divided into three domains: Symptoms, Activity and Impacts. A score is calculated for each domain and a total score, including all items, is also calculated. Low scores indicate a better quality of life.

- BODEx index (BMI, FEV1, dyspnea and exacerbations) for assessment the COPD severity and predicts mortality, hospitalization, and exacerbation frequency .
- CAT score (COPD assessment test also for assessment of COPD severity.

Thorough Clinical Examination Including

- General examination (pulse, Blood pressure, temperature, respirtratory rate, JVP, lower limb edema, lymph node)
- Chest examination (inspection, palpation, percussion and auscultation).

Investigations Including

- Chest x ray (postero-anterior) .
- Abdominal ultrasonography.
- Pulmonary Function Tests (PFT):- Using spirometer (Microlab)

Micro lab spirometer pre and post-bronchodilation were performed in all study subjects and forced expiratory volume in 1 second (FEV1), forced vital capacity (FVC), FEV1/FVC ratio, peak expiratory flow (PEF), forced expiratory flow (FEF) 25, 50 and 75 values were recorded. Post-bronchodilator values (15 minutes after the administration of 400 µg salbutamol) were used for diagnosis of COPD (post-bronchodilator test FEV1/ FVC<0.70). [17]

- Arterial blood gases (ABG):- is a test that measures the partial pressure of arterial oxygen (PaO2) and carbon dioxide (PaCO2), oxygen saturation (SO2) and acidity (PH) in arterial blood. (ABL800) .
- Electrocardiography (ECG), and Echocardiography.
- Laboratory investigations:- complete blood count (white blood cells ,red blood cells, hemoglobin, haematocrite and platelets), liver function tests alanine aminotransferase (ALT), aspartate aminotransferase (AST) and serum albumin), renal function tests (serum creatinine , urea), blood sugar, prothrombin time and concentration and serum electrolytes (potassium, sodium and calcium).
- Computerized tomography (CT) scan for chest.

Statistical Analysis

Analysis of data was done by IBM computer using SPSS (statistical program for social science version 24.0) as follows:

- Description of quantitative variables as mean, SD and range.
- Description of qualitative variables as number and percentage. The Student's *t*-test was used to compare the mean of continuous variables among different subsets of patients. Significant $P<0.05$ and highly significant $P<0.01$.

Results

In our study 110 COPD patients (74 males and 36 females), with mean age 59.8±11.3 divided into 5 different COPD phenotypes; (ACOS) were 12%, (Chronic bronchitis) 18%, (COPD with bronchiectasis) 19%, (Emphysema) 31% and (Frequent exacerbator) phenotype 18%. There was significant difference in age and sex between different phenotypes. The frequent exacerbator and ACOS were older than other

phenotypes. Most of COPD phenotypes were prevalent in male but only (COPD with bronchiectasis) phenotype was prevalent more in female. There was significance difference in smoking status between COPD phenotypes. Current smokers were prevalent in Chronic bronchitis phenotype as shown in table 1.

As regards pulmonary function tests of different COPD phenotypes, there was significance difference in all values except in FEF 25-75. The lowest parameters were recorded in frequent exacerbator followed by COPD with Bronchiectasis phenotypes as shown in table 2.

There was significance difference in all items of St. George's Respiratory Questionnaire of different COPD phenotypes. Symptoms score it was highest in (ACOS) followed by (Frequent exacerbator). Activity score, impact and total scores were highest in (Frequent exacerbator) then (COPD with bronchiectasis) as shown in table 3.

There was significance difference in BODEx index (BMI, FEV1,dyspnea and exacerbations) and CAT score of different COPD phenotypes P-value 0.020 and <0.001 respectively. As shown in figure 1, 2

The most common co-morbidities in all studied subjects was gastritis 58.2% of studied subjects, followed by cor-pulmonale 41.8%, Systemic hypertension 40.0 %, depression 25.5%, pulmonary hypertension 28.2%, and Diabetes Mellitus 19.1% as shown in figure 3.

More cases developed exacerbation in the last years, sever form of excerbation and ICU admission was related to frequent exacerbator phenotype with significant difference between phenotypes as regards one or two previous hospitalization and sever excerbation as shown in table 4.

As regards evaluation of co-morbidities in different COPD phenotypes, there was significance difference in IHD (ischemic heart disease) it was more present in (Emphysema) 22.9 %, but less in other phenotypes. .Also there was significance difference in Cor-pulmonale, founded more in (Frequent exacerbator) 65.0 %, less in (ACOS) 4.3%. There was significance difference in diabeties mellitus, it was present in 50% of (ACOS), and 5.7 % in (Emphysema) cases.

There was significance difference in Osteoporosis co-morbidity, presented more in (Emphysema) 11.4 %, it was rare in (ACOS) and (Chronic bronchitis) There was significance difference in anemia, it was more in (COPD with Bronchiectasis) 23.8 %, and it was rare in (ACOS), (Chronic bronchitis) and (Frequent exacerbator). There was significance difference in depression co-morbidity, it was more in (Frequent exacerbator) 45.0%, less in both (Chronic bronchitis) and (ACOS). There was no significance difference in Arrhythmia, Pulmonary HTN, systemic hypertension, Obesity hypoventilation syndrome, Liver disease, Renal disease, pulmonary co-morbidities (Pneumonia, Pleural effusion, Pneumothorax, Pulmonary embolism, Lung cancer), Polythesthemia, Anxiety, Stroke and gastritis co-morbidities between phenotypes as shown in table 5.

As regards discharge from hospital with domcilliary oxygen was more in frequent excerbator phenotype and four cases died in emphysema phenotypes denoting the more severe form of phenotypes and more responsive phenotypes related to ACOS and chronic bronchitis as shown in table 6.

Discussion

COPD is a major cause of chronic morbidity and mortality throughout the world; many people suffer from this disease for years, and die prematurely from it or its complications. Globally, the COPD burden is projected to increase in coming decades because of continued exposure to COPD risk factors and aging of the population.[18] The classical COPD classification has been based on Forced Expiratory Volume in the first second (FEV1), but this alone is no longer accepted as a single parameter to define severity or to guide treatment (GOLD 2015) The updated Global Initiative for Chronic Obstructive Lung Disease (GOLD) recommendations proposed treatment approach based on two additional parameters symptoms and exacerbations.[1] So it is important to identify specific attributes in order to group the heterogeneous COPD into different phenotypes and guide treatment a patient therapeutic approach.

Several phenotypes have already been proposed but the understanding of which attributes define which groups of patient's remains challenges.[19]

Table 1. Demographic data of different COPD phenotypes

-	Phenotypes										P. value
	ACOS		Chronic bronchitis		COPD with bronchiectasis		Emphysema		Frequent exacerbator		
	No.	%	No.	%	No.	%	No.	%	No.	%	
No. of cases	14		20		21		35		20		
Age											
Mean ±SD	62.8±15.8		48.8±9		60.3±6		61.8±9.1		64.4±11.3		<0.001**
Male	12	85.7	18	90.0	5	23.8	28	80.0	11	55.0	<0.001**
Female	2	14.3	2	10.0	16	76.2	7	20.0	9	45.0	
Smoking status											
Current smoker	7	50.0	17	85.0	3	14.3	17	48.6	9	45.0	<0.001**
Ex-smoker	5	35.7	1	5.0	0	0.0	11	31.4	6	30.0	
Passive smoker	2	14.3	0	0.0	12	57.1	5	14.3	4	20.0	
Nonsmoker	0	0.0	2	10.0	6	28.6	2	5.7	1	5.0	
Special habits											
Biomass fuel exposure	1	7.1	0	0.0	11	52.4	4	11.4	5	25.0	
Bird reader	1	7.1	0	0.0	0	0.0	0	0.0	0	0.0	
Car fuels exposure	0	0.0	2	10.0	0	0.0	0	0.0	0	0.0	
Drinker	1	7.1	0	0.0	0	0.0	0	0.0	0	0.0	
Dust, fumes exposure	0	0.0	0	0.0	1	4.8	0	0.0	1	5.0	
Hashish smoker	0	0.0	0	0.0	0	0.0	0	0.0	1	5.0	
Drugs	0	0.0	0	0.0	0	0.0	1	2.9	0	0.0	
No	11	78.6	18	90.0	9	42.9	30	85.7	13	65.0	

Table 2. Spirometry in different COPD phenotypes

	Phenotype					P. value
	ACOS	**Chronic bronchitis**	**COPD with bronchiectasis**	**Emphysema**	**Frequent exacerbator**	
	Mean ±SD	(Mean ±SD)	(Mean ±SD)	Mean ±SD	(Mean ±SD)	
FEV1	43.1±16.4	91.5±25.3	38.7±17.1	41.8±14.8	38.1±11.8	<0.001**
FVC	59.8±20.8	87.2±34.4	48.6±21.6	55.4±17	49±17.1	<0.001**
PEF	30.6±10.6	55.2±26	26.3±13.4	29±11.8	27.6±10.3	<0.001**
FEVI/FVC	58±5.6	79.5±12.5	58.9±9.9	59.6±11.5	59±7	<0.001**
FEF25	1.7±0.8	3.8±2.6	1.4±0.9	1.7±0.9	1.7±0.8	<0.001**
FEF50	1±0.6	3±2.2	0.9±0.5	1.2±0.7	1±0.5	<0.001**
FEF75	0.6±0.5	1.6±1.3	0.7±0.4	0.7±0.4	0.6±0.4	<0.001**
FEF25-75	0.9±0.5	2.4±2	2.2±6.2	1±0.6	1±0.5	0.248
MVV	57.6±19.1	101.4±65.9	43.8±24.7	59.3±24.6	49.9±17.6	<0.001**

Table 3. St. George's Respiratory Questionnaire of different COPD phenotypes

	ACOS	**Chronic bronchitis**	**COPD with bronchiectasis**	**Emphysema**	**Frequent exacerbator**	**P. value**
Symptoms Score	81.43±10.51	53.5±8.65	68.77±10.07	62.2±15	72.59±7.32	<0.001**
Activity score	51.53±5.22	0±0	89.59±10.67	78.2±17.89	93.98±8.63	<0.001**
Impacts score	60.4±6.52	10.72±5.25	63.09±17.24	52.44±22.4	75.36±19.95	<0.001**
Total score	60.78±4.04	14.57±3.23	71.99±11.77	61.7±17.47	80.88±13.17	<0.001**

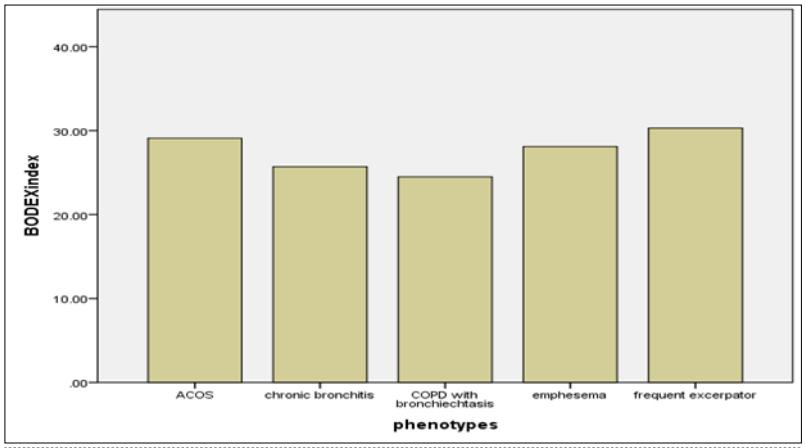

Figure 1. BODEX index of different COPD phenotypes

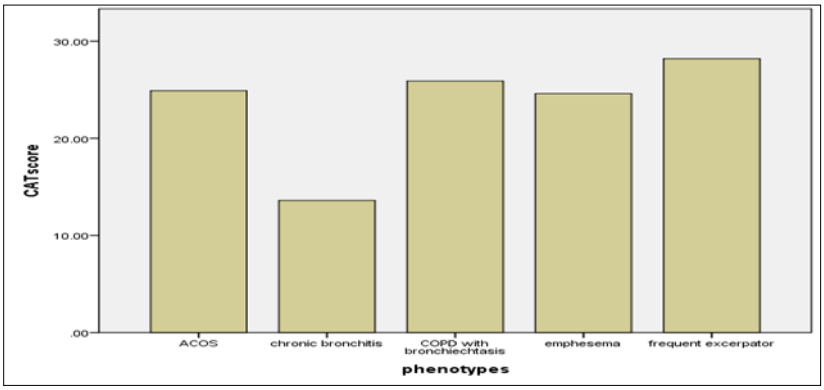

Figure 2. CAT score of different COPD phenotypes

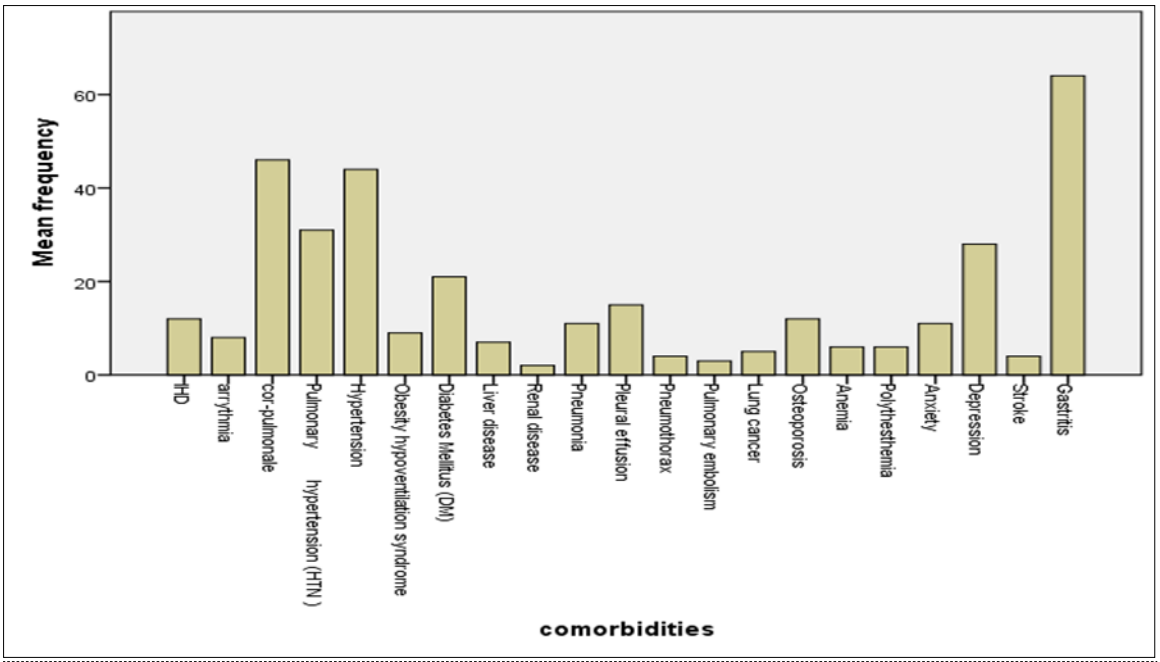

Figure 3. Co morbidities of all studied cases

Table 4. Exacerbation frequency and previous hospitalization in last year of different COPD phenotypes

	Phenotype										P. value
	ACOS		Chronic bronchitis		COPD with bronchiectasis		Emphysema		Frequent exacerbator		
	No.	%	No.	%	No.	%	No.	%	No.	%	
No. of exacerbation in last year	11	78.6	18	90.0	15	71.4	32	91.4	20	100.0	0.054
Mild to moderate	7	50.0	8	40.0	9	42.9	16	45.7	2	10.0	0.071
Severe	4	28.6	3	15.0	4	19.0	14	40.0	17	85.0	<0.001**
No of previous hospitalization											
1	7	50.0	8	40.0	9	42.9	16	45.7	2	10.0	0.002**
2 or more	4	28.6	3	15.0	4	19.0	14	40.0	17	85.0	

** Statistically significant difference (p<0.01)

Table 6. Discharge status of different COPD phenotypes

	Phenotype										P. value
	ACOS		Chronic bronchitis		COPD with bronchiectasis		Emphysema		Frequent exacerbator		
	No.	%	No.	%	No.	%	No.	%	No.	%	
Discharge status											
Died	0	0.0	0	0.0	0	0.0	4	11.4	2	10.0	0.006**
Discharge with domiciliary O2	1	7.1	0	0.0	4	19.0	2	5.7	7	35.0	
Discharge without O2	13	92.9	20	100.0	17	81.0	29	82.9	11	55.0	

Table 5. Comorbidity in different COPD phenotypes

	Phenotype										P. value
	ACOS		Chronic bronchitis		COPD with bronchiectasis		Emphysema		Frequent exacerbator		
	No.	%	No.	%	No.	%	No.	%	No.	%	
IHD (Ischemic heart disease)	0	0.0	1	5.0	0	0.0	8	22.9	3	15.0	0.033*
Arrhythmia	0	0.0	0	0.0	1	4.8	5	14.3	2	10.0	0.228
Corpulmonale	2	14.3	4	20.0	11	52.4	16	45.7	13	65.0	0.008**
Pulmonary HTN	2	14.3	3	15.0	7	33.3	10	28.6	9	45.0	0.190
systemic Hypertension	6	42.9	7	35.0	9	42.9	14	40.0	8	40.0	0.988
Obesity hypoventilation syndrome	1	7.1	3	15.0	2	9.5	0	0.0	3	15.0	0.226
DM (diabeties mellitus)	7	50.0	4	20.0	3	14.3	2	5.7	5	25.0	0.009**
Liver disease	1	7.1	1	5.0	0	0.0	3	8.6	2	10.0	0.693
Renal disease	0	0.0	0	0.0	1	4.8	0	0.0	1	5.0	0.488
Pneumonia	2	14.3	2	10.0	2	9.5	4	11.4	1	5.0	0.921
Pleural effusion	0	0.0	3	15.0	0	0.0	8	22.9	4	20.0	0.067
Pneumothorax	0	0.0	2	10.0	1	4.8	1	2.9	0	0.0	0.444
Pulmonary embolism	0	0.0	1	5.0	0	0.0	2	5.7	0	0.0	0.540
Lung cancer	0	0.0	2	10.0	0	0.0	3	8.6	0	0.0	0.245
Osteoporosis	0	0.0	0	0.0	6	28.6	4	11.4	2	10.0	0.030*
Anemia	0	0.0	0	0.0	5	23.8	1	2.9	0	0.0	0.002**
Polythesthemia	1	7.1	2	10.0	0	0.0	3	8.6	0	0.0	0.404
Anxiety	0	0.0	0	0.0	4	19.0	4	11.4	3	15.0	0.187
Depression	1	7.1	2	10.0	8	38.1	8	22.9	9	45.0	0.032*
Stroke	0	0.0	0	0.0	0	0.0	2	5.7	2	10.0	0.315
Gastritis	9	64.3	9	45.0	15	71.4	17	48.6	14	70.0	0.275

Our study included 110 COPD patients (74 males and 36 females), with mean age 59.8±11.3 divided into 5 different COPD phenotypes 14 patients (ACOS) phenotype, 20 patients (Chronic bronchitis) phenotype, 21 patients (COPD with bronchiectasis) phenotype, 35 patients (Emphysema) phenotype and 20 patients (Frequent excerbator), it was compared with the study of (Jose´Luis et al.,)[20] the authors studied 331 patients with mean age 66.3± 2.5 and were divided into 3 different COPD phenotypes only, 143 patients (Emphysema), 148 (Chronic bronchitis), 40 patients (ACOS).

In our study there was significant difference in sex between different COPD phenotypes with more prevalent in males except (COPD with bronchiectasis) phenotype was more prevalent in female this was in agreement with (Jose´ Luis et al.,)[20] stated that all phenotypes more prevalent in male. Also there was significance difference in smoking status between different COPD phenotypes. current smokers were more prevalent in (Chronic bronchitis) and (ACOS) phenotype, less prevalent in (COPD with bronchiectasis) phenotype compared with same study there was no significance difference in smoking status among three different phenotypes this may be due to different study groups and numbers.

In our study there was significant difference in dypsnea (MMRC score) between different COPD phenotypes, most (ACOS) phenotype had Grade3 and Grade 4 50.0% , most (Chronic bronchitis) phenotype had Grade2 50.0%, most (COPD with bronchiectasis) phenotype had Grade4 47.6 % , most (Emphysema) phenotype had Grade3 48.6%, most (Frequent excerbator) phenotype had Grade4 75% and this is consistent with (Jose´ Luis et al.,) study who stated that there was significance difference in dypsnea (MMRC score), most phenotypes had Grade 2, (Emphysema) phenotype 37.8%,(Chronic bronchitis) phenotype 48% and (ACOS) phenotype 47.5% .

The most common co-morbidity present in our studied cases was gastritis followed by cor-pulmonale and hypertension and this is inconsistent with (Gianna et al.,).[21] In our study there was no significance difference in number of exacerbation in last year of different COPD phenotypes, this was in agreement with (Jose´ Luis et al.,) [20]

In our study there was significance difference between number of hospitalization in last year between different COPD phenotypes compared with (Jose´Luis et al.,) study there was no significance difference between number of hospitalization in last year. In our study there was no significance difference in number of ICU admission between phenotype, this was agreed with Beeh, Glaab et al., 2013)[22] and (Jose´Luis et al.,)[20].

In our study there was significance difference in FEV1, FVC, FEV1\FVC ratio, FEV1, FVC values showed the lower value in (Frequent excerbator), and (COPD with Bronchiectasis) phenotype, FEVI/FVC ratio values showed the lower value in (COPD with Bronchiectasis), then (ACOS) phenotype. This in agreement with (Jose´Luis et al.,) study there was significance difference in FEV1 values, the (Emphysema) phenotype showed lower FEV1 values, in (Chronic bronchitis) and in (ACOS) phenotype. There was also significance difference in FEVI/FVC ratio, in (Emphysema) phenotype showed lower FEVI/FVC ratio value, in (Chronic bronchitis) phenotype, in (ACOS) phenotype, there was no significance difference in FVC.

In our study there was no significance difference in systemic hypertension between different COPD phenotypes. But there was significance difference in (Jose´Luis et al.,), it was more prevalent in (chronic bronchitis) phenotype 60.8%. In our study there was significance difference in diabeties mellitus, it was more common in (ACOS) phenotype. This was in agreement with (Jose´Luis et al.,) study there was also significance difference but it was more common in (chronic bronchitis). In our study there was significance difference in IHD (ischemic heart disease) co-morbidity between different COPD phenotypes, it was more common in (Emphysema) phenotype, Also there was significance difference in Cor-pulmonale co-morbidity, it was more common in (Frequent excerbator) phenotype 65.0 %. But in (Jose´Luis et al.,) study there was no significance difference, and it was more common in (ACOS) phenotype.

In our study there was no significance difference in (Obesity hypoventilation syndrome) co-morbidity between different COPD phenotypes. This was inconsistent with (Jose´Luis et al.,), as it was more present in (chronic bronchitis) phenotype. Our study and (Jose´Luis et al.,) study was consistent as regards no

significance difference in arrhythmia and cerebrovascular disorder.

Osteoporosis was founded more in COPD with bronchiactasis, Emphysema and Frequent excerbator phenotypes with significant difference and this was in agreement with Gianna et al. [21]

Our results showed that the highest association of co-morbidities is seen mostly in patients with severe COPD phenotypes. These findings were in agreement with Mahboub et al.,[23] and Dal Negro et al.,[24] who reported an association between the prevalence of comorbidity and COPD severity measured by a COPD assessment test score >10 or by Global Initiative on Obstructive Lung Disease stages, respectively, and disagreement with with findings of Watz et al.[25]

The co-morbidity related to heart dysfunction in frequent excerbator and emphysema phenotypes are particularly important predictors of increased risk of death in patients with COPD and indicate the importance of cardiovascular disease as a factor contributing to COPD mortality and this was consistent with Zielinski et al.,[26]

Conclusion

The presence of significant co-morbidities is one of the most important modifying risk factors for severity in COPD. They contribute to the overall severity in individual patients, have a major impact on quality of life, increase the risk of certain causes of mortality and of all-cause mortality and are major causes of hospitalization , Co-morbidities can be associated with any clinical phenotype. But we found that distribution of Co morbidities not much different between these phenotypes, gastritis was the most frequent co-morbidity in all phenotypes, then systemic hypertension and cor-pulmonale. But diabetes mellitus was more common in ACOS phenotypes, depression was more common in frequent excerbator phenotype.

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