



Pulmonary Medicine

A SMALL STEP TOWARDS PRECISION MEDICINE IN PHENOTYPIC APPROACH TO COPD MANAGEMENT

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ABSTRACT **Background:** COPD phenotypes are useful to predict the response to a treatment and progression of the disease. This personalized approach allows identification of the right treatment for each COPD patient, it leads to improvement in the effectiveness of therapies, avoidance of treatments not indicated, and reduction in the onset of adverse effects. **Materials And Methods:** It is a prospective study Done among 100 patients who visited Department of Respiratory medicine in Narayana medical college and hospital over 1 Yr. (JULY 2021-JULY 2022) Diagnosis of COPD is done according to GOLD guidelines. Age, sex, Duration symptoms, number of exacerbation's per year, history of smoking, comorbidities, allergy, CAT score, BMI, spirometry, CT Radiological findings are taken into consideration. And they are characterized into specific COPD phenotype- Chronic Bronchitis, Emphysematous, Asthma-COPD-Overlap, Frequent exacerbator, Rare exacerbator, Pulmonary cachexia phenotype, Overlap COPD and bronchiectasis, Upper lobe-predominant emphysema phenotype, The fast decliner phenotype, The comorbidities phenotype, No smoking COPD. Treated precisely and followed up with PFT. **Results:** We took 100 COPD patients according to GOLD guidelines .63 patients had rare exacerbation's 37 are frequent exacerbation, mean age of 55 ±5yrs, Mean duration of symptoms -8 ±3days, male predominance (86%)>female 14%, age of onset of smoking -22yrs ±5yrs, Chronic bronchitis 32%, 66% emphysematous, 52% of co-morbidities (htn-15, dm-22, cad-8, cvs-4, ckd-3), 41% cachexic, 4% asthma COPD overlap, 17% had upper lobe emphysematous phenotype, 10% had overlap COPD bronchiectasis, 14% no smoking phenotype, 6% fast decliner phenotype (FEV1 MILD-62%, MOD-15%, SEVERE-16%, VERY SEVERE-7%, MIXED -10%), treated accordingly and cases are followed up. **Conclusion:** Most of the patients had overlap of phenotypes. Emphysematous, chronic bronchitis, comorbid phenotypes, cachexic phenotypes are top four most common phenotypes. Co- presence emphysematous, frequent exacerbation, pulmonary cachexia, comorbid phenotype had increased mortality. 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. We need to treat COPD from one size fit all approach to precise medicine approach by COPD phenotyping.

KEYWORDS : COPD, Phenotype, precision Medicine.

INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) is a common, preventable and treatable disease that is characterized by persistent respiratory symptoms and airflow limitation that is due to airway and/or alveolar abnormalities usually caused by significant exposure to noxious particles or gases⁽¹⁾. Chronic obstructive pulmonary disease (COPD) is third leading cause of deaths, causing 3.23 million deaths world wide in 2019. up to 90% of COPD deaths in those under 70 years of age occur in low and middle income countries⁽²⁾. Early diagnosis and treatment, including smoking cessation support, is the need to slow the progression of symptoms and reduce exacerbations⁽³⁾. "phenotype" refers to a set of observable characteristics with which individuals can be grouped⁽⁴⁾.

One of the classic phenotype is emphysema, which is a significant component of COPD and the extent increases with increasing the severity of airflow limitation, making that subgroup a very stable phenotype. The same concept can be stated with chronic bronchitis, which is been associated with excess forced expiratory volume in the first second (FEV1) and is observed predominantly in young adults. One clinical feature of the different types of phenotypes is the frequency and severity of exacerbations. Exacerbation has a great impact in the COPD prognosis because exacerbations are linked to a bad prognosis and an excess FEV1 decline. According to exacerbation, symptoms, rate of disease progression, response to therapy, mortality risk COPD phenotype can be defined as a single or combination of disease attributes that can describe different individuals with COPD⁽⁵⁾. COPD phenotypes are useful to predict the response to a treatment and progression of the disease. This personalized approach allows identification of the right treatment for each COPD patient, it leads to improvement in the effectiveness of therapies, avoidance of treatments not indicated, and reduction in the onset of adverse effects⁽⁵⁾. In this study we aimed to Exact identification of phenotype for more Personalization of the treatment of COPD and to increase the quality of life and to prevent mortality.

COPD phenotype	Definition
Chronic Bronchitis	The presence of productive cough more than 3 months per year in two or more consecutive years
Upper lobe Emphysematous	Presence of all emphysema confirmed on imaging
Asthma-COPD-Overlap	Persistent airflow limitation with several features usually associated with asthma and several features usually associated with COPD (post bronchodilator FEV1 change >14% and 400ml)
Frequent exacerbator	Presence of frequent exacerbations (two or more per year)
Rare exacerbator	Presence of rare exacerbations (no or just one exacerbation)
Pulmonary cachexia phenotype	Body Mass index lower than 21 kg/m ²
Overlap COPD and bronchiectasis	HRCT confirmation of bronchiectasis and definite COPD diagnosis
The fast decliner phenotype	Rapid decline of lung function
The comorbidities or systemic phenotype	High comorbidities burden, predominantly cardiovascular and metabolic
No smoking COPD	Induced by biomass exposure

METHODS AND MATERIALS

This Study was conducted in the Department of Narayana medical college and general Hospital, Nellore from July 2021-july 2022 with a Sample Size of 100 patients. It is a prospective study Done among 100 patients who visited Department of Respiratory medicine in Narayana medical college and hospital over 1 Yr. (JULY 2021-JULY 2022). Diagnosis of COPD is done according to GOLD guidelines. We included study population More than 18yrs Both male, female Patients

willing for participating in the study With ratio of post bronchodilator FEV1/FVC<0.7.We excluded from study population More than 18yrs Both male, female Patients willing for participating in the study With ratio of post bronchodilator FEV1/FVC<0.7.Thorough history was taken including smoking history,type of smoking,pack year and biomass exposure in those patients.BMI was noted in every visit. Variables like Age, sex, Duration symptoms, number of exacerbations per year, history of smoking, comorbs, allergy, CAT score, BMI, spirometry, CT Radiological findings are taken into consideration.And they are characterized into specific COPD phenotype- Chronic Bronchitis, Emphysematous ,Asthma-COPD-Overlap, Frequent exacerbator, Rare exacerbator, Pulmonary cachexia phenotype, Overlap COPD and bronchiectasis, Upper lobe-predominant emphysema phenotype, The fast decliner phenotype, The comorbidities phenotype, No smoking COPD.

Statistics

Data has been entered into MS -EXCEL and statistical analysis done by using IBM.SPSS.VERSION 25.0. The Data values for categorical variation were expressed as number and percentages.

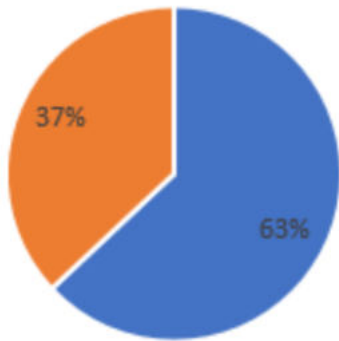
RESULTS

We took 100 COPD patients according to GOLD guidelines .63 patients had rare exacerbations 37 are frequent exacerbation, mean age of 55 ±5yrs,Mean duration of symptoms -8 ±3days,male predominance (86%)>females 14%,age of onset of smoking -22yrs ±5yrs,Chronic bronchitis 32%, 66%emphysematous ,52%of comorbidities(htn-15,dm-22,cad-8,cvs-4,ckd-3) ,41% cachexic ,4%asthma COPD overlap ,17% had upper lobe emphysematous phenotype,10% had overlap COPD bronchiectasis,14%no smoking phenotype,6%fast decliner phenotype(FEV1 MILD-62%,MOD-15%,SEVERE-16%,VERY SEVERE-7%,MIXED -10%) ,treated accordingly and cases are followed up

DISCUSSION

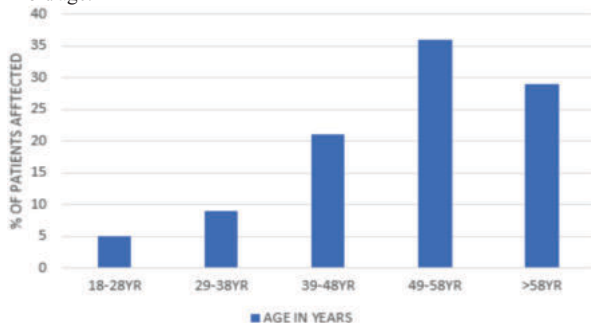
Among 100 copd patients. rare exacerbations (66%) more compare to frequent exacerbations (33%)

Chart Title

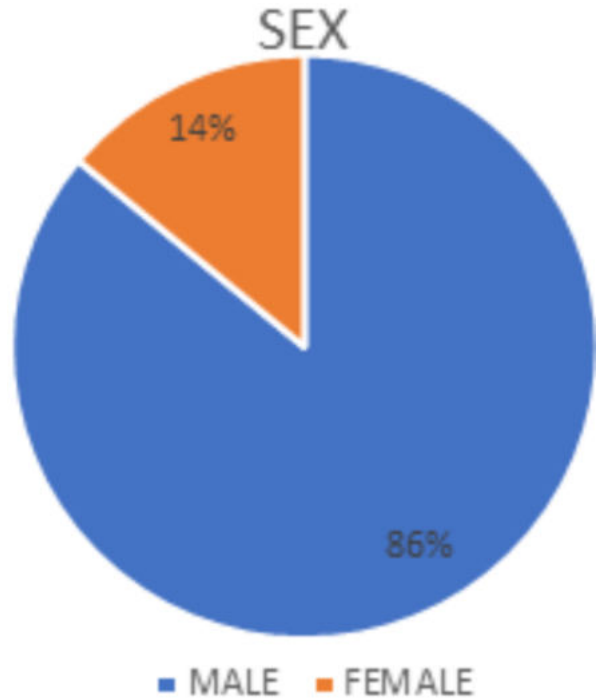


■ Rare exacerbation ■ Frequent exacerbation

COPD most common in older age groups of 55 ±5yrs. Because it's a progressive disease and manifest symptoms in late life and also Due to increase smoking index, associated co-morbs makes it more common in old age.



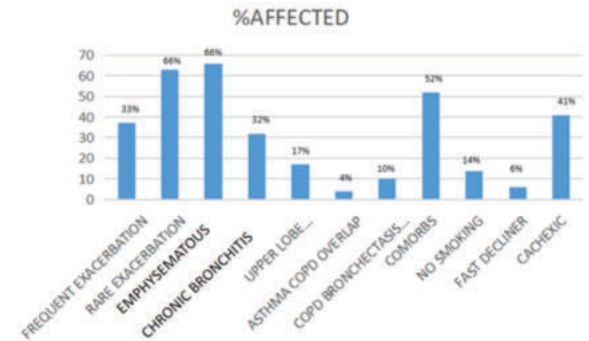
Male COPD (86%) predominant than females COPD (14%). Male COPD is most commonly due to history of smoking. Female COPD patients had more exposure of biomass fuel. Most of the male patients were emphysematous phenotype. Female patients had chronic bronchitis phenotype, No smoking phenotype.



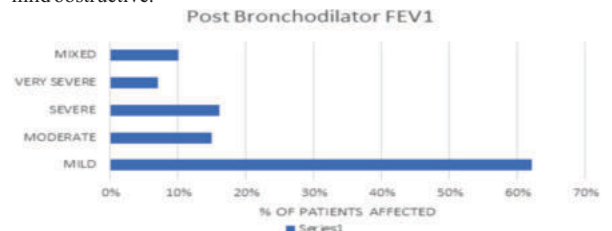
Chronic bronchitis (32%) -treated with inhaled bronchodilators

Emphysematous phenotype (66%)-treated with inhaler bronchodilator, pulmonary rehabilitation Upper lobe emphysematous (17%)-with Severe air flow obstruction referred to lung volume reduction surgery Asthma copd overlap (4%)-treated with inhaled bronchodilator and steroids Bronchiectasis copd overlap (10%)-added postural drainage and mucolytics Co-morbs phenotype (52%)-treated underline co-morb.Targeting aggressive disease management of comorbidities may help improve symptoms and health outcomes.Frequent exacerbators (66%)-added macrolides, Triple combination of inhalersFast decliner phenotype (6%)- had co presence emphysematous, frequent exacerbation, pulmonary cachexia, comorbid phenotype had increased mortality

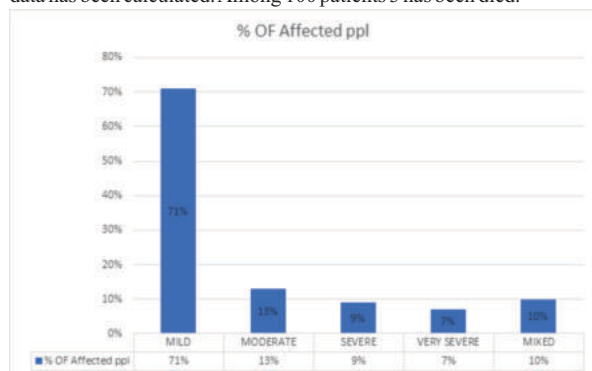
Cachexic phenotype (41%)-targeted on nutritious food



All the patients have been underwent spirometry and post bronchodilator FEV1 noted .Among them Most of the patients showed mild obstructive.



55 patients have been followed up with spirometry every 4 months and data has been calculated. Among 100 patients 3 has been died.



According to study done in ajmer Rajasthan in 2021. they have taken 5 phenotypes -45%-emphysematous,15% copd bronchiectasis, 20% asthma copd ,20%chronic bronchitis ,48%under weight ⁽⁶⁾ A study was done in China in 2021. among 9134 copd patients ,90.3% non-exacerbators, 2.9% frequent exacerbators without chronic bronchitis ,2% frequent exacerbators with chronic bronchitis,4.8 %asthma copd overlap⁽⁷⁾

CONCLUSION:

Certain patients had over lap of phenotypes. Emphysematous, chronic bronchitis, comorbid phenotypes, cachexic phenotypes are top four most common phenotypes.Co- presence emphysematous, frequent exacerbation, pulmonary cachexia, comorbid phenotype had increased mortality.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.We need to treat COPD from one size fit all approach to precise medicine approach by COPD phenotyping.

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