Research Article

Clinical Outcomes of Different Phenotypes of Chronic Obstructive Pulmonary Disease

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Abstracts
Introduction: Chronic obstructive pulmonary disease (COPD) is a critically important international health problem. **Aim of the study: The aim of this study was to:** Assess the effect of different COPD phenotypes on disease outcomes as regard disease severity, inflammatory burden, comorbidity and exacerbation. **Patients and Methods:** Design of work The clinical study was a prospective study included 100 patients with stable COPD who were presented as out-patients to chest clinic at Cardiothoracic Minia University hospital during the period between October 2018 to December 2019. **Results:** Distribution of different COPD phenotypes cases:- patients with chronic bronchitis were more than emphysema in both exacerbator and non exacerbator phenotypes.
Key Words: Chronic obstructive pulmonary disease,

Introduction
Chronic obstructive pulmonary disease (COPD) is a critically important international health problem. The World Health Organization predicted that COPD will become the third leading cause of death worldwide by 2030 (Mathers and Loncar, 2006).

COPD is now widely recognized as a complex heterogeneous disease with pulmonary and extra pulmonary features. In the assessment of patients with COPD, it is important to identify clinical traits or phenotypes that may have consequences for the choice of treatment (Han et al., 2010).

COPD phenotypes is essential to provide patients with precise and personalized therapy. Most phenotypes rely on clinical and physiological parameters and biological markers may complete them, clinicians should select the tools to be used according to the aim of phenotyping such as prognosis evaluation , treatmet response or research (Roche, 2016).

Some research studies have examined specific phenotype frequencies and features but limited ones are available to address the effect of these phenotypes on clinical outcome, purposing to intensify the lines of treatment available for those with the worst outcomes.

Aim of the study
The aim of this study was to:
Assess the effect of different COPD phenol-types on disease outcomes as regard disease severity, inflammatory burden, comorbidity and exacerbation.

Patients and Methods
Design of work:
The clinical study was a prospective study included 100 patients with stable COPD who were presented as out-patients to chest clinic at Cardiothoracic Minia University hospital during the period between October 2018 to December 2019.

Ethical considerations:
The nature of the present study was explained to all patients. The laboratory and radiological procedures represented standard care and pose no ethical conflicts. A verbal consent was obtained from all patients.

The study was approved by the research ethics committee of Minia faculty of medicine.

Inclusion criteria:
Previously or newly diagnosed patients with stable COPD.

Patients were diagnosed as COPD according to the Global Initiative for chronic obstructive lung disease (GOLD) definition in the form of (presence of risk factors like smoking ,biomass fuel exposure , occupational exposure in addition to presence of chronic cough , and or expectoration and dyspnea) with post-bronchodilator (FEV1/FVC <0.7)**.**

Stable COPD was defined by the lack of hospitalization, urgent care visits, antibiotic use or changes in medications within 4 weeks prior to study.

Exclusion criteria

1- Patients with acute exacerbation of COPD within 1 month prior to study.
2- Combined COPD and interstitial lung disease.
3- Patients with past history of tuberculosis.
4- Patients on long term oxygen therapy.

Methods

All patients had been subjected to the following

History taking:

- Included: age, sex, occupation (current and previous), smoking status, history of biomass fuel exposure.
- Assessment of chest symptoms like cough and or expectoration, dyspnea and its grade by mMRC, COPD Assessment Test Score (CAT score) and GOLD stages according to ABCD assessment tool.
- History of medication used to treat COPD.
- Assessment of the presence of some comorbidities as diabetes mellitus (DM), arterial hypertension, ischemic heart disease (IHD) and COPD index (COPD Comorbidity index) was calculated (Divo et al., 2012).
- Evaluation of anxiety and or depression using Hamilton Anxiety Rating scale (Shear et al., 2001) and Patient Health Questionnaire (PHQ-9) (Kroenke and Spitzer, 2002).

Results

- Table (1) shows the features of COPD phenoltypes, there was significant difference as regard age among COPD phenotypes, as patients were older in exacerbator and non exacerbator group than ACO group (p= 0.019).
- It was found that there was a significant difference as regard sex as females were significantly higher in ACO cases rather than other phenotypes while males were highly significantly in exacerbator and non-excerbator COPD (p=0.0001).
- It was found that there was a significant difference as regard occupation. Farmers were significantly higher in exacerbator and non exacerbator phenotype,while house-wives were significantly higher in ACO phenotype (p=.0001).
- It was found that nonsmokers were significantly higher in cases of ACO while smoking (current or ex-smoker) was significantly higher in other phenotypes (p=0.0001).
- Biomass fuel exposure was significantly higher in ACO group on the other hand smoking was higher in both exacerbator and non-exacerbator groups (p=0.0001).

Table (1): General characteristics among different phenotypes

Variable	Exacerbator N: 45	Non exacerbator N:37	ACO N:18	p value
Age **Range** **Mean ± SD**	 47-82 63.9 ± 8.2	 50-78 62.1 ± 7	 50-75 57.8 ± 7.3	**0.019***
Sex: **Male** **Female**	 40 (88.8%) 5 (11.1%)	 34 (91.8%) 3 (8.1%)	 6 (33.3%) 12 (66.7%)	**0.0001***
Occupation: **Farmer** **Clerical** **Manual worker** **Housewife**	 32 (71.1%) 5 (11.4%) 4 (9.1%) 4 (9.1%)	 26(70.2%) 2 (5.3%) 5 (13.2%) 4 (10.2%)	 4 (22.2%) 4 (22.2%) 0 10 (55.6%)	**0.0001***
Smoking: **Non smoker** **Current smoker** **Ex smoker**	 8 (18.2%) 14 (31.8%) 23 (51.1%)	 4 (10.5%) 16 (43.2%) 17 (44.7%)	 12 (66.7%) 3 (16.7%) 3 (16.7%)	**0.0001***
Pack/year score **Mean ± SD**	 29.9 ± 23.6	 27.5 ± 15.3	 25.2 ± 27.4	**0.31**
Biomass fuel	2 (4.5%)	2 (5.3%)	6 (33.3%)	**0.0001***

Data are presented as number and %

Discussion

COPD is a leading cause of morbidity and mortality in countries of different income level. COPD is the third leading cause of death world-wide ,accounts for more than 3 million death per year (Soriano et al., 2017). Over 300 million people worldwide suffer from COPD, most of whom reside in low income countries (WHO, 2018).

There is substantial heterogencity of COPD regarding symptoms, disease progression ,functional outcomes and response to therapies (Spurzem and Rennard., 2005).

Some studies have shown that COPD patients with different phenotypes have variable disease characteristics as regard age, sex, smoking, severity of symptoms and numbers of compli-cations (Kania et al., 2018).

However the fate of these phenotypes on mobidity and mortality is still elusive.

Many of the national guidelines prefer tailored treatment recommendations on the basis of such patient phenotypes. Although this approach introduces complexiety into the treatment algorithm and departs from (the one size fits all), treatment based on the level of FEV1 alone, it is likely to improve the clinical outcomes of most patients with COPD (Lange et al., 2016).

We performed this study to asses the impact of different COPD phenotypes on disease outcome.

The outcome parameters that were used include:

COPD severity, systemic biomarkers, comor-bidities, frequency and severity of exacerbation.

COPD severity indices that were measured in our study were (CAT score, GOLD categories and BODE index).

- CAT score:

CAT is a rapid test for assessment of COPD symptoms a higher score indicates a worse impact of COPD on health related quality of life (Pinto et al., 2014).

- In this study, exacerbator and non exacer-bator groups had higher CAT score than

ACO group (14.7±1.5, 14.4±1.4vs 13.7±1.7 respectively p=0.04).

- In study done by (Cosio et al., 2016). The exacerbator phenotype mainly exacerbator chronic bronchitis had the highest CAT score (17.1±8.2, p<0.05 compared to the other phenotypes).
- Another study by Chai et al., 2018 found that patients with exacerbator chronic bronchitis had a significant higher CAT index than patients with other clinical phenotypes (Chai et al., 2018).
- Meta-analysis study found that in ten studies that included 4568 patients, the frequent exacerbator of chronic bronchitis phenotype was associated with a high CAT score than in the ACO phenotype (Han et al., 2020).

GOLD categories:

- Regarding COPD categories using A B C D assessment, we found that all exacerbators were in category class (C) and (D) (42.4% and 59% respectively) which represented the most severe categories, Non-exacerbators and ACO patients had a lower degree of disease severity as more than 50% of the involved patients were in category (B) (57.8% and 50% respectively.

Conclusion and Recommendations

This study demonstrated that:

- Exacerbator group is the most common phenotype followed by non exacerbator group then ACO group.
- The three types of COPD studied had a nearby clinical manifestation and systemic biomarker level.
- The exacerbator group has the lowest spirometric parameters.
- A higher CAT score and GOLD categories are found more in exacerbator phenotype.
- Exacerbetor phenotype has amore comorbidities as represented by a higher COTE index than other phenotypes.
- Regarding the frequency of exacerbation ,we found that frequent exacerbators have the higher frequency of exacerbation and a higher rate of hospital admission for these exacerbation than other phenotypes.

So we recommend:

- ✓ Phenotypes classification should be done early in all COPD patients from the time of diagnosis as exacerbator phenotypes has worse prognosis than other**.**
- ✓ Longitudinal studies are required to better define the long term outcome of different phenotypes of COPD**,** especially all-cause mortality.
- ✓ Other outcome measures are needed to asses the clinical benefits of therapeutic agents in different phenotypes.
- ✓ Future attention of comorbidities of COPD should be addressed to alleviate their impact on phenotypes outcomes.
- ✓ More follow up visits to outpatients clinics and treatment options need to be available for most affected phenotype.

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