Risk factors of acute exacerbation of chronic obstructive pulmonary disease among Egyptian elderly patients. (A prospective study)

Thesis

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Ahmed Adel Abdelgaleel Mahomoud

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List of Abbreviations

1,25(OH) 2D2 : 1,25-Dihydroxy vitamin D2

1,25(OH) 2D3 : 1,25-Dihydroxy vitamin D2

25(OH)D : 25-hydroxy vitamin D

7-DHC : 7-dehydrocholesterol

AD : Alzheimer's disease

AECOPD : Acute exacerbation of COPD

BMD : Bone mineral density

BMI : Body mass index

COAD : Chronic obstructive airway disease

COPD : Chronic obstructive pulmonary disease

DRI : Dietary reference intakes

DRV : Dietary reference values

FEV1 : Forced expiratory volume in one second

FVC : Forced vital capacity

GOLD : Global Initiative for Chronic Obstructive Lung Disease

HRQL : Health-related quality of life

ICUs : Intensive care units

IOM : Institute of Medicine

LTOT : Long term oxygen therapy

MNA : Mini nutritional assessment

OA : Osteoarthritis

PEF : Peak expiratory flow

PH : Pulmonary hypertension

PTH : Parathyroid hormone

RDA : Recommended dietary allowance

sPAP : Systolic pulmonary artery pressure

TGF-β1 : Transforming growth factor β1

UK : United Kingdom

UV : Ultraviolet

UVB : Ultraviolet - B

VD2 : Vitamin D2

VD3 : Vitamin D3

VDR : Vitamin D receptors

WHO : World Health Organization

YLD : Years of living with disability

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Introduction

Chronic obstructive pulmonary disease (COPD) is the persistent obstruction of airways (bronchiolitis) associated with progressive destruction of lung parenchyma (emphysema) and this is associated with medical history of chronic inflammation, related to exposure to many pathogens as cigarette smoking. Clinically patient suffers from progressive shortness of breath, at first under stress and later at rest as cases become more severe ***(Lauretti et al., 2016).*** COPD patient suffers usually from progressive decrease of lung function, loss of exercise capacity, frequent exacerbations, and development of extra-pulmonary comorbidities like infection, osteoporosis, and cardiovascular disease ***(Barnes and Celli, 2009).***

The prevalence of COPD in elderly increases with age and may reach up to 15% in those over 65 years of age ***(Orvoen-Frija et al., 2010).*** COPD is considered the fourth leading cause of death worldwide ***(Zhu et al., 2016),*** and the second most common cause of emergency admissions in the United Kingdom, with 1 in 8 hospital emergency admissions is due to COPD, costing more than £800 million ($1.3 billion) ***(Wedzicha et al., 2014).***

Course of COPD is interrupted by episodes of respiratory symptom worsening, named exacerbations ***(Wedzicha et al., 2014).*** COPD exacerbation is important event in COPD and is major determinant of health status in COPD patients as it is associated with cardiovascular complications, especially myocardial infarction ***(McAllister et al., 2012)*** and considered as independent predictor of mortality in COPD with about 25% of the lung function reduction attributed to exacerbation ***(Donaldson et al., 2002).***

Multiple risk factors were investigated to play a major role in acute exacerbation of COPD (AECOPD) as sex, age at diagnosis, disease severity (based on Global Initiative for Chronic Obstructive Lung Disease (GOLD) category) ***(Vogelmeier et al., 2017a)***, body mass index (BMI), asthma, smoking status, other respiratory comorbidities (history of respiratory failure, pneumonia, cor-pulmonale), non-respiratory comorbidity (chronic kidney disease, cancer, liver disease, depression, dementia, heart failure, coronary heart disease, diabetes and stroke), and prior COPD admissions ***(Hunter et al., 2016).***

Many observational studies also showed that vitamin D deficiency has been associated with lung function reduction, emphysema, respiratory tract infection, ***(Moberg et al., 2014)***, impaired immunologic function and elevated airway inflammation ***(Lehouck et al., 2012).*** So, in this study

we also explore the correlation between serum vitamin D level and acute exacerbation in patients with COPD among Egyptian elderly.

Vitamin D deficiency is very common across many populations and also among patients with several skeletal and non-skeletal conditions including diabetes, autoimmune diseases and pulmonary diseases as COPD ***(Monadi et al., 2012).***

Vitamin D is well known for its roles in bone health and both calcium and phosphorus homeostasis ***(Reid et al., 2014),*** but now vitamin D is increasingly studied for its potential immunomodulatory role ***(Rafiq et al., 2015).*** Vitamin D is not just a vitamin as it is recognized as a pleiotropic prohormone that has receptors (vitamin D receptors [VDR]) ***(Hollis and Wagner, 2013)*** which are significantly low in lung tissues of patients with COPD ***(Sanjari et al., 2015).***

Aim of the Work

This prospective study is designed to assess the risk factors of acute exacerbation among elderly patients with COPD.

Chronic Obstructive Pulmonary Disease in Elderly

COPD is a common, preventable disease characterized by persistent respiratory symptoms and airflow limitation that occurs due to airway and/or alveolar abnormalities caused by significant exposure to noxious gases or particles ***(Vogelmeier et al., 2017a).***

The chronic airflow limitation is characteristic of COPD and is caused by a mixture of small airways disease (obstructive bronchiolitis) and parenchymal destruction (emphysema), the relative contributions of these both elements vary from patient to another. Chronic inflammation causes structural changes and small airways narrowing. Lung parenchyma destruction, also by inflammatory processes, leads to the loss of alveolar attachments to the small airways and lung elastic recoil reduction; in turn, these changes decrease the ability of the airways to remain open during expiration ***(Vestbo et al., 2013).***

A meta-analysis and systemic review carried out in 28 countries between 1990 and 2004 provided evidence that COPD prevalence is significantly higher among smokers and ex-smokers than non-smokers, in those over 40 than those under 40 and in males than females ***(Halbert et al., 2006).***

The estimated prevalence of COPD among high-risk Egyptians by GOLD criteria was 9.6%, with a higher prevalence of grade 2 (69%) and grade 3 (17%) and lower prevalence of grade 1 (3%) ***(Said et al., 2015).***

The most important risk factor for COPD universally is Cigarette smoking. Other factors, such as exposure to many outdoor and indoor air pollution, infections and occupational hazards are also very important ***(Mannino and Buist, 2007).***

I-Burden of COPD:

COPD is a leading cause of death all over the world. In addition to causing high healthcare costs, COPD imposes a significant burden in terms of impaired quality of life and disability ***(Halbert et al., 2006).*** Burden of COPD is suspected to increase in the coming decades due to the continued exposure to COPD risk factors and aging of the world's population ***(Vestbo et al., 2013).***

Morbidity data extremely underestimate the total burden of COPD as the disease is usually not diagnosed until it becomes clinically apparent and moderately advanced ***(Pauwels et al., 2001).***

Another way to estimate the morbidity burden of a disease is to calculate years of living with disability (YLD). The Global Burden of Disease Study estimates that COPD results in 1.68 YLD per 1,000 populations, representing 1.8% of all YLDs, with a greater burden in males than in females (1.93% vs. 1.42%) ***(Lopez et al., 2006).***

In the next 20 years, it is anticipated that COPD will be the fifth cause of disability worldwide ***(Faulkner et al., 2006).***

Also Mortality data underestimate COPD as a cause of death because the disease is more likely to be considered as a contributory than as a direct cause of death, or may not be cited at all ***(Pauwels et al., 2001).*** However**,** statistics in the United States ranked COPD to be the third most common cause of death in the US***(Bang, 2015),*** as in 2004, 120,000 persons in the US died of COPD, an increase of 67% from 1980, and more than twice the number of deaths due to congestive heart failure ***(Barr et al., 2009).*** Globally, COPD is suspected to rise from the sixth most common cause of death in 1990 to the third most common cause of death in 2020 ***(McGarvey et al., 2007).***

World Health Organization (WHO) estimated deaths and disability-adjusted life years attributable to COPD in Egypt. Age adjusted deaths of COPD in Egypt was found to