



Impact of Diabetes Mellitus on Pulmonary Functions in COPD Patients

Thesis

*Submitted for Partial Fulfillment
of Master Degree in **Chest Diseases***

By

Salma Ayman Afifi
(M.B.B.CH. Ain Shams University)

Supervised by

Prof. Mona Mansour Ahmed

*Professor of Chest Diseases
Faculty of Medicine – Ain Shams University*

Prof. Nevine Mohamed Mohamed Abd ElFattah

*Professor of Chest Diseases
Faculty of Medicine – Ain Shams University*

Assist. Prof. Alyaa Ahmed El-Sherbeny

*Assistant Professor of Endocrinology
Faculty of Medicine – Ain Shams University*

Faculty of Medicine - Ain Shams University

2019

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قَالَ

سُبْحَانَكَ لَا عِلْمَ لَنَا
إِلَّا مَا عَلَّمْتَنَا إِنَّكَ أَنْتَ
الْعَلِيمُ الْعَظِيمُ

صدق الله العظيم

سورة البقرة الآية: ٣٢

Acknowledgments

*First and foremost, I feel always indebted to **Allah** the Most Beneficent and Merciful.*

*I wish to express my deepest thanks, gratitude and appreciation to **Prof. Mona Mansour Ahmed**, Professor of Chest Diseases, Faculty of Medicine, Ain Shams University, for her meticulous supervision, kind guidance, valuable instructions and generous help.*

*Special thanks are due to **Prof. Mevine Mohamed Mohamed Abd El Fattah**, Professor of Chest Diseases, Faculty of Medicine, Ain Shams University, for her sincere efforts, fruitful encouragement.*

*I am deeply thankful to **Assist. Prof. Alyaa Ahmed El-Sherbeny**, Assistant Professor of Endocrinology, Faculty of Medicine, Ain Shams University, for her great help, outstanding support, active participation and guidance.*

I would like to express my hearty thanks to all my family for their support till this work was completed.

Salma Ayman Afifi

List of Contents

Title	Page No.
List of Tables	5
List of Figures	7
List of Abbreviations.....	9
Introduction.....	- 1 -
Aim of the Work	12
Review of Literature	
▪ Chronic Obstructive Pulmonary Disease.....	13
▪ Diabetes Mellitus.....	36
▪ Pulmonary Function Changes in Diabetic Lungs	43
Patients and Methods	55
Results	64
Discussion.....	85
Summary	99
References	102
Arabic Summary	

List of Tables

Table No.	Title	Page No.
Table (1):	Spirometric classification of the severity of chronic obstructive pulmonary disease	22
Table (2):	Modified medical research council dyspnea scale.....	23
Table (3):	Criteria for the diagnosis of diabetes mellitus.....	41
Table (4):	Complications of DM.....	42
Table (5):	Descriptive data of the three studied groups:	64
Table (6):	Descriptive data of the three studied groups:	65
Table (7):	Comparison between the three studied groups as regards the spirometric parameters	66
Table (8):	Comparison between the three studied groups as regards post bronchodilator spirometric parameters with negative reversibility test.	67
Table (9):	Comparison between the COPD group (group II) and the COPD diabetic group (group III) as regards post bronchodilator spirometric parameters with negative reversibility test.	69
Table (10):	Comparison between the three studied groups as regards the severity of air flow limitation according to GOLD 2018.	71
Table (11):	Comparison between the three studied groups	73

List of Tables cont...

Table No.	Title	Page No.
Table (12):	Correlation between post bronchodilator spirometric parameters (FVC, FEV1, FEV1/FVC and MMEF 50) and HBA1C, FBS, 2 hr PP and duration of diabetes in years in the diabetic group (group I).....	76
Table (13):	Correlation between post bronchodilator spirometric parameters.....	77
Table (14):	Comparison between severity of air flow limitation according to GOLD 2018 and smoking index in years and number of exacerbations in COPD group (group II).....	78
Table (15):	Comparison between severity of air flow limitation according to GOLD 2018 and HbA1c, FBS, 2 hr PP, duration of DM, smoking index in years and number of exacerbations in COPD diabetic group (group III).....	79

List of Figures

Fig. No.	Title	Page No.
Figure (1):	The refined ABCD assessment tool.....	23
Figure (2):	Spirometry shape	57
Figure (3):	Displays the different post bronchodilator spirometric parameters with negative reversibility test among the three studied groups	68
Figure (4):	Displays the different post bronchodilator spirometric parameters with negative reversibility test among the COPD and the COPD diabetic groups.....	70
Figure (5):	Displays the severity of air flow limitation between the three studied groups.	72
Figure (6):	Displays the mean values of HbA1c between the three studied groups.	74
Figure (7):	Displays the mean values of fasting blood sugar (FBS) and 2 hour postprandial blood sugar (2 hr PP) between the three studied groups.	74
Figure (8):	Displays the mean value of the duration of diabetes in years between the diabetic group and the COPD diabetic group.	75
Figure (9):	Displays the mean value of the number of exacerbations between the COPD and the COPD diabetic group.	75
Figure (10):	ROC curve between Mild and Moderate restrictive affection regarding duration of DM in DM patients (group I).....	80
Figure (11):	ROC curve between Moderate and severe air flow limitation regarding duration of DM in COPD diabetic patients (group III).....	81

List of Figures *cont...*

Fig. No.	Title	Page No.
Figure (12):	ROC curve between Severe and Very severe air flow limitation regarding duration of DM in COPD diabetic patients (group III)	82
Figure (13):	ROC curve between Moderate and Severe air flow limitation regarding HbA1C in COPD diabetic patients (group III)	83
Figure (14):	ROC curve between Severe and Very severe Spirometry regarding HbA1C% in DM & COPD patients	84

List of Abbreviations

Abb.	Full term
<i>2 hr PP</i>	<i>Two hour postprandial</i>
<i>ACEIs</i>	<i>Angiotensin converting enzyme inhibitors</i>
<i>AECOPD</i>	<i>Acute exacerbations of COPD</i>
<i>AGEs</i>	<i>Advanced glycosylation end products</i>
<i>ARBs</i>	<i>Angiotensin II receptor blockers</i>
<i>BMI</i>	<i>Body mass index</i>
<i>CAP</i>	<i>Community-acquired pneumonia</i>
<i>COPD</i>	<i>Chronic obstructive pulmonary disease</i>
<i>DKA</i>	<i>Diabetic ketoacidosis</i>
<i>DLCO</i>	<i>Diffusing capacity of the lung for carbon monoxide</i>
<i>DM</i>	<i>Diabetes mellitus</i>
<i>EGFR</i>	<i>Epidermal growth factor receptor</i>
<i>FBS</i>	<i>Fasting blood sugar</i>
<i>FEV1</i>	<i>Forced expiratory volume 1</i>
<i>FVC</i>	<i>Forced vital capacity</i>
<i>GOLD</i>	<i>Global initiative for chronic obstructive lung disease</i>
<i>HbA1C</i>	<i>Glycated hemoglobin</i>
<i>ICS</i>	<i>Inhaled corticosteroids</i>
<i>LABA</i>	<i>Long-acting beta 2-agonists</i>
<i>LAMAs</i>	<i>Long-acting muscarinic antagonists</i>
<i>MMEF50</i>	<i>Maximal midexpiratory flow at 50%</i>
<i>mMRC</i>	<i>Modified British Medical Research Council</i>
<i>NGSP</i>	<i>National glycohemoglobin standardization</i>
<i>NHANES</i>	<i>National Health and Nutrition Examination Survey</i>
<i>no.</i>	<i>Number</i>

List of Abbreviations cont...

Abb.	Full term
<i>OGTT</i>	<i>Oral glucose tolerance test</i>
<i>PCV</i>	<i>Pneumococcal conjugate vaccine</i>
<i>PDE4</i>	<i>Phosphodiesterase-4 inhibitors</i>
<i>PH</i>	<i>Pulmonary hypertension</i>
<i>POST BD</i>	<i>Postbronchodilator</i>
<i>PPSV</i>	<i>Pneumococcal polysaccharide vaccine</i>
<i>PRE BD</i>	<i>Prebronchodilator</i>
<i>PVD</i>	<i>Peripheral vascular disease</i>
<i>SABA</i>	<i>Short-acting B2 agonist</i>
<i>SAMAs</i>	<i>Short-acting muscarinic antagonists</i>
<i>TLC</i>	<i>Total lung capacity</i>

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a disease state characterized by progressive airflow limitation and is associated with an abnormal inflammatory response of the lungs to noxious particles or gases, primarily caused by cigarette smoking (*Gold, 2018*).

COPD is usually progressive, chronic and not fully reversible with treatment. It is often associated with various comorbidities like diabetes, hypertension, coronary artery disease, malnutrition, endocrine disorders or anxiety. COPD is considered a disease that goes beyond the lung involvement giving it an expression of a multisystemic inflammatory disease (*Gläser et al., 2015*).

DM affects 1.6 to 16% of subjects with COPD. Metabolic syndrome, insulin resistance and systemic inflammation constitute risk factors for decreased lung function in healthy nonsmoking subjects which suggest that even in the absence of smoking DM can lead to similar effects on pulmonary function (*Yadav et al., 2013*).

Reduced lung function and DM has been described for many years suggesting that the lung is a target organ in DM and that glycemic exposure is a strong determinant of reduced pulmonary function in diabetic patients (*Martinez-cheron et al., 2012*).

AIM OF THE WORK

Assessment of the pulmonary functions in chronic Obstructive Pulmonary Disease patients with normoglycemia, Chronic Obstructive Pulmonary Disease with diabetes mellitus and diabetes mellitus patients.

Chapter 1

CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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 (*GOLD, 2018*).

However, in many patients, the disease is associated with several systemic manifestations that can effectively result in impaired functional capacity, reduced health related quality of life, worsening dyspnea and increased mortality (*Rabe et al., 2007*).

Co-morbidities such as congestive heart failure, pulmonary hypertension, depression, muscle wasting, weight loss, lung cancer and osteoporosis can be frequently found in patients with COPD and are considered to be part of the commonly non pulmonary sequelae of the disease (*Barnes et al., 2009; Chatila et al., 2008*).

The chronic airflow limitation characteristic of COPD is caused by a mixture of small airways disease (obstructive bronchitis) and parenchymal destruction (emphysema), the relative contributions of which vary from person to person.

Chronic inflammation causes structural changes and narrowing of the small airways. Destruction of the lung parenchyma, also by inflammatory processes, leads to the loss of alveolar attachments to the small airways and decreases lung elastic recoil; in turn, these changes diminish the ability of the airways to remain open during expiration (*Vestbo et al., 2013*).

Epidemiology:

COPD is a leading cause of morbidity and mortality worldwide. In 2001 the global burden of disease project of the world health organization (WHO) identified COPD as the sixth leading cause of mortality in countries of middle or low income, accounting for 4.9% of total deaths (*Buist et al., 2007*). In 2011, it ranked as the fourth leading cause of death (*Lozano et al., 2012*).

Statistical analysis of COPD prevalence in Egypt showed that 3 million from the Egyptian population have COPD. In different studies prevalence were from 3.3% up to 10%. Prevalence rate in men was ~6.7% while it was ~1.5% in women (*Khattab et al., 2011*).

A study published in 2014 showed that the prevalence of COPD among high-risk Egyptians by global initiative for chronic obstructive lung disease “GOLD” criteria was 9.6% (*Said et al., 2014*).

Risk Factors

Exposures to

- I- Tobacco smoke:** Smoking has been established through several major international reports (*Jindal et al., 2006*). Cigarette smoking is by far the most important risk factor for COPD either active or passive exposure to smoke (*Holt, 1987*).

- II- Occupational dusts and chemicals:** Studies of coal miners have shown an increased mortality due to bronchitis and emphysema especially centrilobular emphysema, A relationship between dust exposure and degree of emphysema has been found in studies of coal and hard-rock miners. (*Bergdahl et al., 2004*).

- III- Outdoor and indoor air pollution:** Exposure to high levels of outdoor air pollutants is associated with increased mortality and morbidity due to COPD and related cardiorespiratory diseases (*Liu et al., 2008*).

- IV- Infections:** whooping cough, bronchiolitis or pneumonia in the first year of life were associated with a significant reduction in forced expiratory volume in one second “FEV1” measured in the first decade (*Tager et al., 1988*).