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REVIEW ON CLINICAL ETIOLOGY OF COPD AND CO-MORBIDITIES

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ABSTRACT

Chronic Obstructive Pulmonary Disease (COPD) is a common chronic and progressive disease which is characterized by persistent respiratory symptoms and airflow limitation that is due to alveolar abnormalities which is not fully reversible. In the past 2 decades there was a substantial increase in prevalence and mortality of COPD. Mortality rate is six times higher in males when compared to females, however the prevalence among females also increasing in smoking. Environmental exposures to multiple toxins result in increased risk of COPD. The complex interaction between the genes and environmental factors which may result in COPD. The progression of COPD can vary from different factors which depends on the development of systemic complications as well as the different phenotypes and comorbidities. some people may not expose to any environmental noxious dust particles but still they develop COPD. COPD co- exists with the other chronic medical conditions such as coronary artery disease, corpulmonale, Diabetes mellitus, Osteoporosis, Depression, Anxiety, pulmonary embolism and muscle wasting are common in COPD, but their prevalence varies among the various studies. Co-morbidities increase the risk of exacerbations, reduce the quality of life and may increase the risk of mortality. Cardiovascular disease is the common comorbidity associated with the COPD.

KEYWORDS: Chronic Obstructive Pulmonary Disease, Smoking, Environmental exposures, Co-morbidities, Cardiovascular disease, Exacerbations.

INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) is a chronic and progressive disease which

is characterized by persistent respiratory symptoms and airflow limitation that is due to alveolar abnormalities which is not fully reversible.[1] COPD includes an anatomical condition emphysema, a condition characterized by destruction of alveoli with enlargement of air space, chronic bronchitis a clinical condition with chronic cough with sputum and small airway disease in which small bronchioles are reduced in number.[1]

In the past 2 decades there was a substantial increase in prevalence and mortality of COPD.[2] Mortality rate is six times higher in males when compared to females, however the prevalence among females also increasing in smoking.[2] About 85 to 90% of cases are reported due to smoking.[2] Cigarette smoking is the one of the major risk factors for COPD, yet in this only about 50% will COPD during their lifetime.[2] Through passive smoking or second hand smoking, the children and spouses of smokers are at increased risk of developing significant pulmonary dysfunction.[2]

Environmental exposures to multiple toxins result in increased risk of COPD (2). COPD is a common, preventable and treatable disease and may cause extrapulmonary effects which results in disease severity.[2,3] The hereditary deficiency of α1-antitrypsin (AAT) is a best documented genetic risk factor for the development of COPD.[2,3] The deficiency α1-antitrypsin (AAT) accounts for not more than 1% of COPD cases.[2,3] The complex interaction between the genes and environmental which may result in COPD.[3] The most characteristic symptom of COPD is the chronic and progressive dyspnea.[3]

The characteristic feature of COPD is chronic airflow limitation caused by airway disease which results in structural changes, destruction of lung parenchyma and narrowing of airways that leads to limitation of airflow and dysfunction in mucociliary clearance.[3] Annually three million deaths were reported in worldwide.[3] With the increased smoking among the population, the prevalence of COPD expected to rise over next 30 years and by 2030 there may be over 4.5 million deaths annually.[3] Currently, COPD is the fourth leading cause of death among worldwide but it projected to be third leading cause of death by 2020.[4]

The progression of COPD can vary from different factors which depends on the development of systemic complications as well as the different phenotypes and comorbidities.[4] The hospitalization of elder people with COPD have been increasing due to various comorbid conditions which include Cor-pulmonale, coronary artery disease, diabetes mellitus, osteoporosis, muscle weakness.[5]

ETIOLOGY

The major environmental risk factors the development of COPD is cigarette smoking accounts for about 85 to 90%, whereas the development of obstruction of airways is highly variable in smokers and non-smokers.[1,2] Smoking cigarettes of packs per year is the most significant predictor of FEV1.[1] α1-antitrypsin (α1AT) deficiency is a proven genetic risk factor for COPD.[1-3] Along with the cigarette smoking, COPD is considered to be a combination of risk factors which results in tissue destruction and lung injury.[1-3] Age and sex may also influence COPD which increases with age.[3]

In some studies it shows that the smoking is the major risk factor for the development of COPD, but the burden of COPD is also increases among the Non-smokers may be due to genetic factors or long term exposure to environmental tobacco smoke (passive smoking/second-hand smoking), outdoor air pollution from traffic, burning of biomass fuels, occupational, pulmonary tuberculosis, low socioeconomic status and infections.[4,5] Whereas some people may not expose to any environmental noxious dust particles but still they develop COPD.[5]

Risk Factors Which Influence the Dvelopment and Progression of COPD

Although, tobacco smoke is the most cause for COPD, there are many risk factors which influence the development and Progression of COPD which includes the noxious dust particles and hereditary factors.[5]

The risk factors which influence the development and progression of COPD includes:

Smoking Tobacco

Tobacco smoke which includes the pipe, cigarettes, cigar, water-pipe and other type of smoking and environmental tobacco smoke/passive smoke.[5]

Indoor and Outdoor Pollutants

The females are most commonly affected to the indoor air pollutants which results from biomass fuel used for cooking and heated in poor ventilated places, whereas outdoor pollution have relatively small effect on developing COPD but also contributes to burden of inhaled dust particles from traffic and industries.[6]

Occupational Exposures

Which includes inorganic and organic dust particles, chemicals and fuels which released from

the industries.[6]

INFECTIONS

Recurrent exposure to respiratory tract infections during childhood which reduces the pulmonary functions in adults and may suspectable to various infections which results in increased respiratory symptoms.[7] These infections are also responsible for the development of exacerbations.[7]

Co-Morbidities of COPD

Often, COPD co-exists with the other chronic medical conditions called as co-morbidities, which has a significant impact on the course of disease.[8] The other chronic medical conditions which includes the coronary artery disease, corpulmonale, Diabetes mellitus, Osteoporosis, Depression, Anxiety, pulmonary embolism and muscle wasting are common in COPD, but their prevalence varies among the various studies.[8]

These co-morbidities increase the risk of exacerbations, reduce the quality of life and may increase the risk of mortality.[9] Whereas some co-morbidities have been associated with specific treatments of COPD by the use of inhaled corticosteroids they may develop Oropharyngeal candidiasis, or with frequent systemic use of steroids Cushingoid effects.[10]

Cardiovascular disease is the common comorbidity associated with the COPD.[11] COPD with Gastroesophageal reflux increases the exacerbations and reduce the quality of life of patients which results in poor health outcome.[11]

Co-morbidities of COPD and Respiratory System

COPD found to be coexisted with other several respiratory condition which includes Asthma, Lung cancer, Pneumonia, Obstructive Sleep Apnea, Pulmonary embolism, Bronchiectasis and pulmonary fibrosis that results in the complication in the course of disease of patients.[11,12]

Pneumonia

Pneumonia may be responsible for the exacerbations of COPD; However, some studies shows that both pneumonia and COPD have sudden onset of symptoms, severity in illness, longer duration of hospital stays, more number of hospital admission and leading cause of death.[12]

Asthma

COPD and Asthma both are the chronic obstructive disease which found to be coexisted with each other especially in elder patients and their outcome will be worse than diseases alone.[11,12] The patient who often diagnosed with coexisting asthma with COPD will have a higher obstruction on a spirometry and higher risk of mortality during follow-up.[12]

In some cases, it may be difficult to diagnose between the Asthma and COPD who develop fixed limitation of airway flow and chronic obstruction of respiratory symptoms.[13] The co-existence of Asthma with COPD overlap syndrome associated with the increase in the greater number of frequent and severe exacerbation and reduced the quality of life when compared to only COPD patients.[13]

Pulmonary Fibrosis

Pulmonary interstitial fibrosis and COPD when exist together presented with characteristic pulmonary function tests, with relatively normal lung volumes and normal spirometry but impaired gas exchange by thickening of alveolar membrane and reduction of vascular surface.[12,13]

Lung Cancer

The main cause of mortality and frequently encountered comorbidity in COPD is Lung cancer and reported with poorer outcomes.[13] The existence of lung cancer in COPD patients will have severe impairment in pulmonary function.[13] The incidence of occurrence of lung cancer in COPD is four times higher in COPD when compared to general population.[13]

Around 40-70% of population are found to have lung cancer with COPD.[13] Lung cancer along with other co-morbidities like Cardiovascular diseases, are the leading cause of death in COPD patients with mild to moderate disease, Airway obstruction due to respiratory failure becomes predominant in advanced COPD.[13]

Bronchiectasis

Co-existence of COPD with Bronchiectasis may exacerbate the severity of the disease which is characterized by the destruction of bronchial airways along with inflammation and chronic bacterial infection.[14] Both COPD and Bronchiectasis share a common pathophysiologic approach and clinical manifestations.[14]

Obstructive Sleep Apnea

Obstructive sleep apnea is a condition which is characterized by increased resistance of upper airway associated with an intermittent decrease or absence of inspiratory air flow, often causes sleep awakenings during night.[15] When compared to healthy individuals, the quality of sleep is decreased or may worsen in population with COPD.[15]

Co-morbidities of COPD and Metabolic Syndrome

The existence of metabolic syndromes like Type 2 Diabetes mellitus, Obesity with COPD is found to be more common when compared to the general population.[16] In both COPD and Diabetes mellitus associated with a systemic inflammation marker like IL-6, TNF-α and CRP are elevated, which is an important factor.[16]

Co-Morbidity of Osteoposrosis with COPD

Among the systemic comorbidities Osteoporosis is the major comorbidity in COPD, the relationship between both remains unclear, but recent studies suggest that prevalence is more in patients with COPD.[17] Osteoporosis is associated with low body mass index, emphysema, reduced bone mineral density and fractures which are common in COPD.[17]

Co-Morbidities of COPD in Cardiovascular Diseases

Cardiovascular disease (CVD) remains the significant and frequent co-morbidity with COPD. Ischemic Heart disease, Arrythmias, Heart failure, Peripheral vascular disease and Hypertension are considered to be common comorbidities of CVD.[18]

Hypertension is most commonly encountered comorbidity in COPD which is associated with increased systemic inflammation, reduced physical activity, high dyspnea scores and airflow obstruction but not associated with increased mortality.[19]

Congestive heart failure and COPD both may have similar risk factors, which includes smoking, and common pathophysiological mechanisms and frequently co-exist with each other may worsen their prognosis and increased number of hospital admissions.[20]

COPD and ischemic heart disease (IHD) are both have common risk factors, such as exposure to cigarette smoke, older age. Ischemic heart disease is more prevalent among the COPD patients.[21]

Atrial fibrillation often co-exists with COPD, the severity of COPD is associated with

increased risk for atrial fibrillation/ atrial flutter and ventricular tachycardia.[22]

OTHER CO-MORBIDITIES

Anxiety and Depression in COPD

Anxiety and depression often common and more prevalent among COPD patients and associated with a poor prognosis.[23]

Anemia in COPD

Anemia of chronic disease (ACD) often co-existed with the COPD which is associated with the major symptoms of anemia include fatigue, dyspnea and these can be related with reduced oxygen capacity of blood to tissues.[24]

Gastroesophageal Reflux Disease (GERD) in COPD

Among COPD patients, the prevalence of Gastroesophageal reflux disease is significantly higher and one of the potential risk factors for the exacerbation of COPD. The possible mechanism which responsible for the exacerbations are not fully understood.[25]

CONCLUSION

Chronic Obstructive Pulmonary Disease (COPD) is a heterogenous and complex disease, whereas the more number of patients associated with the pulmonary and extra-pulmonary comorbidities. Among these comorbidities some are related with the mortality. These comorbidities may not be explained with their risk factors.

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CONFLICT OF INTEREST

We declare that we have no conflict of interest.

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