

RISK FACTORS FOR COPD EXACERBATION A REVIEW ARTICLENashida A.¹, Smrithi Muraleedharan², Ajith A.³ and Soumya R. V.^{4*}^{1,2,3}Doctor of Pharmacy Students, Sree Krishna College of Pharmacy and Research Centre, Thiruvananthapuram, Kerala.⁴Assistant Professor, Department of Pharmacy Practice, Sree Krishna College of Pharmacy and Research Centre, Thiruvananthapuram, Kerala.***Corresponding Author: Soumya R. V.**

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ABSTRACT

Chronic obstructive pulmonary disease (COPD) has become a global health issue. As the global population ages, COPD burden increases which is considered as the leading cause for morbidity and mortality. One of the important event in COPD is an exacerbation which is characterised by increased baseline respiratory symptoms. The most common cause of disease is cigarette smoking. There is evidence supporting history of hospitalisation as strong predictor for identifying patients at risk for COPD exacerbation. Other riskfactors for exacerbation identified are comorbidities, disease severity, compliance with treatment, respiratory infections. Research works are going on to assess newer riskfactors for exacerbation of COPD. Identifying the potential risk factors may assist in reducing the economic burden of exacerbation and hospitalization. In this review we are attempted to brief the known riskfactors of COPD exacerbation.

KEYWORDS: COPD, COPD exacerbation, riskfactors.**INTRODUCTION**

COPD is defined as "a chronic slowly progressive disease characterised by airflow obstruction that does not change markedly over several months".^[1] COPD exacerbations are defined as events of acute onset, characterized by worsening in respiratory symptoms beyond the day-to-day variations and that may warrant a change in regular medication of the COPD patient.^[3] COPD is estimated to become the fifth-leading cause of years lost through early mortality by 2020, while according to World Health Organization estimates it is predicted to become the third-leading cause of global mortality by the year 2030.^[3] Increased dyspnea is the key symptom of an exacerbation. Other symptoms include increased sputum purulence and volume, together with increased cough and wheeze. Predictive factors of exacerbation are still not completely understood. The severity of airflow limitation, its impact on the patient's health status and the risk of future events (such as exacerbations, hospital admissions or death) are determined by COPD assesment. In the refined ABCD assessment scheme, patients should undergo spirometry to determine the severity of airflow limitation (i.e., spirometric grade). They should then undergo assessment of either dyspnea using mMRC or symptoms using CATTM. Finally, their history of exacerbations (including prior hospitalizations) should be recorded.^[7] Health education of patients, smoking cessation, pulmonary rehabilitation, good nutritional status, and early medical

intervention are all considered helpful in preventing exacerbations.^[5] Global Initiative for Obstructive Lung Disease (GOLD) recommends guidelines for the management of COPD and its exacerbation. Management of exacerbation of COPD include antibiotics, oxygen therapy, β 2-agonist, anticholinergics, Methylxanthines, and systemic steroids.

Factors Which Contribute To Increased Frequency of Exacerbation of Copd**Age**

Age is a factor associated with poor health status and poor quality of life. Older patients are at higher risk of acute exacerbation episodes, probably because pulmonary function decreases with time and because of the accumulative effect of risk factors such as smoking.^[4] Alexpoulos et al showed that patients with age ≥ 76 years had more exacerbations compared to patients aged 61-75.^[3] The study conducted by Uma et al and Sawant MP et al showed that majority of patients are in the age group of 61-70 years and mean age of 67.8 years.^[6,8]

Gender

The male sex is a risk factor of exacerbation due to the smoking habits. Most of the study reported a higher prevalence of COPD exacerbation in males than in females.^[3,4,5,8] However, some studies have reported a higher risk of exacerbation in females.^[4]

Smoking

Smoking is a major factor in COPD exacerbations. There is a high prevalence of COPD exacerbations requiring admission to a hospital unit in those patients who continue to smoke. Most smokers admitted for exacerbation of COPD include in severe COPD group^[9]. Passive exposure to cigarette smoke may also contribute to increased respiratory symptoms by increasing the lung's total burden of inhaled particles and gases.

Duration of COPD

Increased time since diagnosis of COPD increases the number of exacerbation.^[3] Increase in duration of COPD is associated with increase in age of patient which negatively impact the health status and quality of life. Older patients might have fewer exacerbations that however might be more severe due to the longer duration of COPD leading to more hospitalizations^[3]. The results from alexpoulos et al showed higher incidence –rate ratio in both the 6-10 and ≥ 11 years since COPD diagnosis groups compared to those with ≤ 5 years since diagnosis.^[3]

Disease severity

Assessment of disease severity, which is based on determining the severity of airflow limitation using spirometry, severity of symptoms or risk of exacerbation using Modified medical research council questionnaire (mMRC) or CATTM score^[7]. Increased severity of COPD as defined by GOLD staging based on severity of airflow limitation was associated with an increased number of exacerbations. Specifically, compared to patients with GOLD stage I, those with GOLD stage III and IV are at higher risk of exacerbations. Increased disease severity has been linked with an increased frequency of exacerbation and ICU admissions.^[3,7] This also increases the economic burden of disease.

Infections

Respiratory infection is assumed to be the main risk factor for the exacerbation of COPD.^[5] The role of respiratory viruses, especially rhinoviruses and respiratory syncytial virus have been found to be important in the etiology of COPD exacerbation. The common bacterial etio-pathogens involved in COPD exacerbations are *H. influenzae*, *S. pneumoniae* and *Moraxella catarrhalis*. As per uma et.al study, the most common microorganism isolated from sputum are *Candida albicans*, followed by *Pseudomonas aeruginosa*.^[8] This infectious agents in lungs results is associated with an intense airway inflammation and progression of the disease. Antibiotics are required for the management of infective exacerbation of COPD. Specific identification of causative agent allows adequate choice of effective antibiotic therapy for eradication of pathogen which will decrease the risk of recurrence and improve the prognosis of the disease. High percentage of prescribing antibiotics would contribute to increase in prevalence of resistant strains of pathogenic organisms.^[8] Influenza and Pneumococcal vaccination should be

recommended to reduce the further risk of respiratory infections.

Comorbidities

Comorbidities are common in patients with acute exacerbation of COPD. The most common comorbidities includes diabetes, hypertension, hypothyroidism, ischemic heart disease, heart failure. Therefore proper treatment for comorbidities is also important along with the respiratory management in patients. The Charlson index has been shown to be a specific indicator of mortality in patients with COPD. Patients with one, two, three, and four or more comorbidities may increase the number of exacerbations compared to those without comorbidities.^[3] High incidence of comorbidities increases the number of medications for patients. Prescribing multiple drugs to the patient should be closely monitored to avoid negative consequences of polypharmacy such as higher health care cost, adverse drug effects, drug interactions, medication non adherence and should be kept to minimum required drugs.^[6]

Medication omission

Patient adherence in chronic diseases remains a task, resulting in poor health outcomes and increased health care expenditures.^[11] Patients who omit their medication to have an increased frequency of both exacerbations and hospitalizations. Adherence in COPD is commonly influenced by such factors as patient age, cost of the drug, comorbidities and dosing frequency.^[3] Respiratory maintenance therapy is recommended for most of the patients along with medications for comorbid conditions. Patients' acceptance of the disease process and recommended treatment, knowledge about and faith in the treatment, effective patient-clinician interaction, and routinization of drug therapy are critical for optimal medication adherence in patients with COPD.^[12] Therefore counselling or educating the patients regarding their condition, pathology, warning signs and symptoms and adherence to medications can help reduce exacerbations.

History of hospitalization

A history of exacerbation is the best predictive factor for exacerbation, followed by an age over 68.^[4] The study by Hurst et al. also concluded that a history of exacerbation during the previous year was the best predictive factor of acute exacerbation. The exacerbator phenotype could be identified based on history of previous hospitalisation for COPD exacerbation. Once identified, personalised preventive and pharmacological measures could be put in place to avoid acute exacerbation in patients at higher risk.^[4]

CONCLUSION

So, our review mainly tries to explore the major risk factors that are associated with COPD exacerbation. In terms of age and gender, older individuals and males are at a higher risk for COPD exacerbation. This may be due to decrease in pulmonary function due to ageing and

prevalence of smoking habits more in the male population. Studies have also highlighted the impact of duration and severity of COPD, in the development of exacerbation. Studies associated with GOLD standard scale have clearly outlined the severity of COPD and its progression to exacerbation. COPD exacerbation has also been associated with infections caused by pathogens such as H. influenzae, S. pneumoniae. Their progression and recurrence depends on the right choice and effectiveness of the antibiotic therapy. Patients poor medication adherence or medication omission is yet another factor associated with COPD exacerbation. Poor medication adherence may be due cost of the drugs, age or co morbidities. Thus, our review summarises the major factors which are associated with COPD exacerbation. Due to lack of information in the current literature, further studies needs to be done to obtain more information about these risk factors. Identifying these potential factors and implementation of specific interventions can reduce the number and severity of exacerbations.

REFERENCE

1. S.Burge et al. COPD exacerbations: definitions and classifications. *European respiratory Journal*, 2003; 21: 46s-53s.
2. J.C Fernandez de cordova-Aguirre et.al.Riskfactors for chronic obstructive pulmonary disease:result of FARIECE study. *Med Hosp Gen Mex*, 2015; 78(4):162-8.
3. Evangelos p alexopoulos et al. Frequency and risk factors of COPD exacerbations and hospitalizations: a nationwide study in Greece (Greek Obstructive Lung Disease Epidemiology and health ecoNomics: GOLDEN study). *International Journal of COPD*, 2015; 10: 2665–2674.
4. Monstrate capdevila et al. Riskfactors for exacerbation in chronic obstructive pulmonary disease : a prospective study. *INT J TUBERC LUNG DIS*. Oct, 2015; 20(3): 389-95.
5. Gracia aymerich et al. Patients hospitalized for COPD have a high prevalence of modifiable risk factors for exacerbation (EFRAM study). *Eur Respir J*, 2000; 16: 1037-1042.
6. Mahadeo.P.Sawant et al. Study of drug prescription pattern among COPD patients admitted to medicine inpatient department of tertiary care hospital. *International journal of Basic and clinical pharmacology*, 2017; 6(9): 22-28
7. Rabe KF, Hurd S, Anzueto A, Barnes PJ, Buist SA, Calverley P, et al; Global Initiative for Chronic Obstructive Lung Disease. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: GOLD executive summary. *Am J Resp Crit Care Med*, 2017; 176: 7-8.
8. Uma et al. Drug utilization pattern in chronic obstructive pulmonary disease inpatients at a tertiary care hospital. *International journal of pharmacy and pharmaceutical sciences* oct, 2015; 7(11): 389-91.
9. Elena Badaran et al. smoking and COPD exacerbations. *European respiratory journal* sep 2012;40(suppl 50):1055
10. Bahadori et al. Riskfactors of hospitalization and readmission of patients with COPD exacerbation- a systemic review .*International journal of COPD*, 2007; 2(3): 241-51.
11. Maryam Mahmoodan et.al .Drug utilization evaluation in chronic obstructive pulmonary disease patient. *Der pharmacia Lettre*, 2017; 9(6):142-151
12. Johnson George et al. Factors Associated With Medication Nonadherence in Patients With COPD. *chest journal*. nov, 2005; 128(5): 3198-3204.