

ISSN:
2181-3337



ScienceInnovation
INTERNATIONAL SCIENTIFIC JOURNAL

SCIENCE AND INNOVATION

International scientific journal

VOLUME 3 ISSUE 4

D : BIOLOGY
AGRICULTURE
MEDICINE
PHARMACETICS
VETERINARY

April 2024



International Scientific Journal
SCIENCE AND INNOVATION
Series D
Volume 3 Issue 4
April 2024

Tashkent 2024

ISSN: 2181-3337

International Scientific Journal SCIENCE AND INNOVATION. Series D volume 3 issue 4 – 457p.

The collection contains scientific articles accepted for issue 4 for 2024 of the international scientific journal "Science and Innovation".

In this scientific journal, in the form of scientific articles, the results of scientific research conducted by professors and teachers of the Republic of Uzbekistan and international higher educational institutions, independent researchers, doctoral students, undergraduates were published. In addition to higher educational institutions, the journal also includes scientific articles by employees working in other research institutes, production organizations and enterprises of our region and republic.

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This issue of the journal is indexed in the international scientific databases Index Copernicus, OpenAire, EuroPub, ZENODO, Cyberleninka and Google Scholar.

All articles were placed in the electronic scientific database of the journal (scientists.uz).

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EXACERBATIONS OF COPD AND THE IMPACT ON THE QUALITY OF LIFE OF PATIENTS

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<https://doi.org/10.5281/zenodo.10969516>

Abstract. *Chronic obstructive pulmonary disease (COPD) is characterized by persistent inflammation of the lower respiratory tract, impaired mucociliary activity, and emphysematous destruction of the lungs, resulting in irreversible airflow limitation. These clinical signs sharply limit the physical activity of patients and lead to a decrease in quality of life and disability.*

Keywords: *chronic obstructive pulmonary disease (COPD), exacerbations, physical activity*

Chronic obstructive pulmonary disease (COPD) ranks third in terms of mortality in the last decade[59]. Frequent exacerbations of COPD cause increased costs for COPD treatment [14].

The frequency of exacerbations of COPD remains high and, according to numerous long-term studies, in more than 50% of patients COPD remission does not occur for 3 or more years [22]. In addition, according to multicenter studies, 23% of patients with a spirometry-confirmed diagnosis of COPD experienced more than 2 moderate or severe exacerbations per year, and 14% of patients had more than 3 exacerbations per year [51,35]. In addition, frequent exacerbations are accompanied by severe hospitalization, which undoubtedly indicates that all measures in the treatment of COPD should be aimed at preventing exacerbations of COPD. This review will focus on the definition, triggers, reporting and impact of exacerbations of COPD.

Exacerbations of COPD vary in clinical course, and the symptoms of the disease vary [20]. According to the 2020 GOLD definition of exacerbation of chronic obstructive pulmonary disease, where the main symptom of the exacerbation is shortness of breath and acute worsening of respiratory symptoms requiring immediate treatment [14]. In addition, there may be other symptoms of respiratory inflammation such as purulent sputum, cough and wheezing [14]. Depending on the severity of an exacerbation of COPD, it is classified as mild, moderate or severe, depending on the condition of the patient. The degree of obstruction and the treatment required and the need for hospitalization [14]. Mild exacerbation of COPD is when clinical symptoms respond to treatment with short-acting bronchodilators [14,54]. Moderate exacerbations of COPD require treatment with antibiotics and/or oral corticosteroids [14]. Severe exacerbations of COPD require hospitalization or treatment in intensive care units, as patients may experience acute respiratory failure, which can be life-threatening [14]. Determining the severity of exacerbations of COPD is not necessary to determine the severity of COPD, which is classified from mild to very severe depending on the degree of obstruction [14]. The classification of the severity of exacerbations is a combination of the severity of the underlying disease, the severity and frequency of exacerbations and the presence of concomitant diseases.

The differential diagnosis of exacerbations of COPD includes pneumonia, pneumothorax, pleural effusion, pulmonary embolism, cardiac arrhythmias, and pulmonary edema due to cardiac pathologies [14]. Difficulties in the differential diagnosis of exacerbation of COPD and pneumonia, since the clinical symptoms are identical [14, 25], and very often exacerbation of COPD, the risk of developing pneumonia remains very high [34]. Pneumonia is often

underdiagnosed in patients hospitalized with exacerbation of COPD [25,44] or, conversely, there may be overdiagnosis. It is important to note that the treatment of patients with COPD and pneumonia differs from the treatment of exacerbations of COPD [25, 44].

Data from multicenter studies and meta-analyses have shown that a quarter of patients hospitalized with suspected exacerbation of COPD have pulmonary embolism [38,30]. In addition, many patients with exacerbations of COPD experience cardiac arrhythmias [41], and the presence of heart failure due to the similarity of symptoms makes it difficult to diagnose this patient population [18,33, 42]. Thus, misdiagnosis of exacerbation of COPD represents a potential risk that can lead to inappropriate treatment.

Exacerbation of COPD is provoked by many factors, such as respiratory infections (bacteria, fungi and, most importantly, viruses), fluctuations in ambient temperature and air pollution [42]. Consequently, the frequency of exacerbations in patients varies depending on the season and other environmental factors [17]. According to data, the frequency of exacerbations in winter is approximately 2 times higher than in summer [26,58], which may be associated with a high increase in the prevalence of respiratory viral infections [26,10]. In addition, exacerbations that occur in winter, when respiratory viral infections are more common, tend to recover slowly [1]. According to researchers from the UK, the presence of inflammatory infiltrates during exacerbations of COPD was more common in winter than in summer, which is associated with increased systemic inflammation [57].

Additional independent risk factors for exacerbation in patients with COPD are female gender, degree of obstruction, increased shortness of breath, decreased lung function, as well as deterioration in quality of life and previous exacerbations, comorbidities such as cardiovascular disease, depression and gastroesophageal reflux. A persistent increase in the level of white blood cells, which signals a long-term infection [32,24]. In addition, a high blood eosinophil count is an independent risk factor for future exacerbations [60], and pulmonary hypertension is significantly associated with an increased risk of severe exacerbations of COPD [55]. Exacerbations of COPD are more common in patients with higher degrees of obstruction.

In clinical practice, the diagnosis of exacerbations is difficult due to underestimation of exacerbations by patients themselves, with almost three quarters of patients having difficulty understanding the term “exacerbation” [29], and more than 40% of patients during an exacerbation do not recognize the symptoms and do not consult a doctor; if necessary, they are not observed when increasing the dose of the drug or taking another drug, non-compliance with rest and sleep, or quitting smoking [6]. Factors influencing patients' seeking of care and recognition of exacerbations include access to care, distance from the clinic, availability of personal and public transportation, ability to get to the clinic, and limited financial resources that impede timely seeking and access to care. Treatment of patients with COPD It has been established that timely seeking medical help reduces the duration of symptoms and treatment time, and patients who do not seek help note a longer duration of symptoms and lengthen the treatment period. [27], and in patients diagnosed with COPD, exacerbations may not be detected; for example, in smokers receiving antibiotics or oral corticosteroids to treat bronchitis.

Even a single exacerbation of COPD can lead to a significant decrease in lung function [16] and an increased risk of further exacerbations [49]. Data from a randomized controlled trial showed that study patients who had more than one exacerbation of any severity since their last visit had significantly decreased quality of life compared with those who had no exacerbation [39].

Additionally, within 2–3 months after a severe exacerbation, patients were at greatest risk of developing a new exacerbation [49]. Each exacerbation further increases the risk of a new event; Compared with the first severe exacerbation, the risk of a subsequent severe exacerbation increased 3-fold after the second severe exacerbation and 24-fold after the tenth severe exacerbation [49]. The duration of exacerbations is also associated with an increased risk of further exacerbations and worsening health status in patients with exacerbations of COPD [8]. Exacerbations in which lung function does not recover are associated with symptoms of viral infection and accelerated decline in lung function [8]. Taken together, these results show that even a single exacerbation can have consequences for patients and highlight the importance of recognizing COPD exacerbations, as timely treatment can reduce symptoms that impair lung function. In this regard, the goal of managing patients with COPD is to minimize the frequency of exacerbations.

Many studies have reported the impact of COPD exacerbations on lung function. Exacerbations of COPD are associated with accelerated loss of lung function, especially in patients with moderate to severe obstruction and severe exacerbations [11]. In addition, patients who experience frequent exacerbations of COPD tend to be the most symptomatic and have the greatest decline in lung function [28,9]. Recovery of lung function after an exacerbation can be lengthy. Results show that in 25% of exacerbation cases, lung function does not return to pre-exacerbation levels, and in 7% of exacerbation cases, lung function does not return to pre-exacerbation levels even after 3 months [46]. Therefore, patients should be monitored until the COPD exacerbation completely goes into remission [46]. While prolonged duration of symptoms during a COPD exacerbation has been associated with an increased risk of further exacerbations [8], rapid recovery of lung function after treatment has been found to be significantly associated with a lower risk of COPD exacerbations [31].

Impact on quality of life and physical activity

Exacerbations of COPD affect many different factors that affect the quality of life of patients. As expected, patients who experienced frequent exacerbations of more than 3 per year experienced a significant decrease in quality of life compared to patients who experienced fewer than 3 exacerbations per year [45]. In addition, the severity of COPD exacerbations correlates with quality of life. According to the researchers, patients who had a recent severe exacerbation of COPD had higher levels of activity impairment and decreased quality of life, compared with those who had a recent moderate exacerbation of COPD [47]. However, even mild exacerbation of COPD can negatively affect the quality of life of patients. [43]

A global survey of patients with COPD found that the majority of patients with COPD responded that exacerbations prevented them from making plans for the future and affected daily activities and sleep [9]. In accordance with this, it has been found that during an exacerbation there is daytime sleepiness, a decrease in total sleep time, as well as a decrease in sleep efficiency and an increase in fatigue [53,5]. Hospitalization for an exacerbation of COPD has been shown to result in physical and functional impairment in patients that worsens after hospital discharge and continues for more than 1 month after the exacerbation [52]. Exercise capacity and muscle strength have been found to decline even after experiencing a mild exacerbation of COPD [2], and decreased physical activity levels are a risk factor for further exacerbations and mortality [13]. In addition, patients with COPD experience poor coordination resulting from increased shortness of breath and decreased muscle strength, which contributes to the high incidence of falls experienced

by these patients after hospitalization [36]. Therefore, decreased levels of physical activity following a COPD exacerbation may result in decreased muscle strength, leading to further deterioration of health.

Exacerbations of COPD have a major impact on mortality [49,21]. Mortality rates following a severe exacerbation have been found to peak in the first week after hospitalization [49]. Moreover, a meta-analysis of studies of mortality due to exacerbation of COPD showed that for at least 1.5 years after hospitalization, the predicted mortality rate was as high as 16% [23], and among newly hospitalized patients, one in five died during an exacerbation. within a year of discharge [21] and approximately 50% of patients died within 3.6 years [49]. Moderate and severe exacerbations were associated with an increased risk of mortality, which increased with the frequency of exacerbations [48,40].

Exacerbations of COPD are associated with many different comorbidities, and the presence and number of comorbidities are significantly associated with the duration and cost of treatment [50]. In patients with COPD, the most common diseases are arterial hypertension, diabetes mellitus, chronic heart failure, coronary heart disease, anemia and dyslipidemia [4]. Exacerbations of COPD have been found to increase the risk of cardiovascular disease, including myocardial infarction and stroke [7,30,15]. In addition, heart failure, visual impairment, lung cancer, depression, prostate disease, asthma, osteoporosis, diabetes mellitus, gastroesophageal reflux, and peripheral vascular disease are significantly associated with frequent (≥ 2 per year) exacerbations [56].

In conclusion, it is important to note that exacerbations of COPD are an important clinical problem, leading to impairment of lung function and quality of life, as well as comorbidities that increase the risk of death. In addition, patients may need several weeks to recover from exacerbations of COPD. Increasing awareness of the impact of COPD exacerbations is key to minimizing the impact. Patient education programs are needed to increase awareness and knowledge of the symptoms of exacerbations of COPD so that they can be quickly identified and treated. The occurrence of an exacerbation of COPD increases the risk of further exacerbations and can lead to a progressive cycle of deterioration in patients. Therefore, understanding the predictors of increased risk of exacerbation and preventing exacerbations of COPD should be a key focus of COPD clinical research. Although treatment options for the prevention and treatment of exacerbations of COPD are outlined in the GOLD 2020 report [14], further research is needed into approaches to better predict and therefore prevent exacerbations of COPD.

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**International Scientific Journal
Science and Innovation Series D
Volume 3 Issue 4**

ISSN: 2181-3337

Published: 30.04.2024. Font: "Times New Roman".

LLC “Science and innovation”
License Mass Media №:1597 27.04.2022
License Publisher №:038864 15.09.2022
Address: 100155, Uzbekistan, Tashkent city, Sergeli district, Quruvchi, 22/43.
www.scientists.uz, info@scientists.uz, +998901259654