

Chronic obstructive pulmonary disease

Introduction

Definition and overview

It is a chronic inflammatory lung disease that causes obstructed airflow from the lungs. It is the third leading cause of death worldwide, causing 3.23 M deaths in 2019. Specifically, it affects people under the 70^s in low- and middle-income countries. People's lungs who suffer from this disease can get damaged or clogged with phlegm (mucous). Smoking, air pollution, and gas breathing are the main factors of disease exposure. Sometimes, the severity of this one can be light which can be treated by oxygen and pulmonary rehabilitation.

Historical context

This disease isn't a modern one in contrast, it is dated be found since the 17th century known as "Catarrh", which was discovered for the first time by Willis and Richard Morton. In the 1970s, the Global Initiative for Chronic Obstructive Lung Disease (GOLD) was established to create standardized guidelines for diagnosing and preventing the disease. In the late 20th century, especially the beginning of the new Millennium COPD was recognized as a leading cause of morbidity and mortality worldwide. The development of pharmacological treatments improved the management of symptoms and exacerbation. Studying and investigating the devastating causes of this serious disease is one of the roles of "Epidemiology" which is a branch of the medical science that focuses on determining and analyzing the factors that contribute to the presence or absence of a specific disorder.

Epidemiology

Recently, scientists estimated that most of the factors that contribute to disease incidence some of them to be mentioned are (smoking, Environmental exposure, Genetics, and Demographic factors) Let's break down them one by one:

- Smoking: excessive smoking can lead to damaging air sacs in the lungs, this smoking includes direct and indirect smoking, additionally, indirect smoking has a higher percentage of contribution than direct smoking. Furthermore, smoking with its two kinds can block airways in the bronchus with mucus leading to heavy breathing and entry of a little amount of oxygen to the lungs leading to COPD.

- Environmental exposure: Air pollution and dust accumulation in air pathways, especially in polluted and industrial areas account for 10-20% of either respiratory or lung function symptoms.
- Genetics: one of the common factors to correlate the exposure of this disease to it, the most common genetic cases of this disease are caused by the deficiency of “**Alpha-1 Antitrypsin deficiency**” which is a protein that protects the lungs from inflammation as a result, individuals which deficiency of (AAD) are more likely exposed to this disease.
- Demographic factors: As we’ve mentioned before, age is one of the main reasons for disease exposure due to immune system deficiency.

Etiology

Cases and Risk factors

Recently, studies have demonstrated that smoking plays a major contribution to exposure to this disease, by which, 75% of all COPD cases occur in people with a history of smoking. As the smoker inhales the fumes of a cigarette, he inhales about 7000 chemicals, many of which are harmful. Consequently, the number of blood vessels number decreases with each cigarette as well as reducing the air space in his lungs, resulting in less oxygen to critical parts of the body. Additionally, smoking with its types motivates the cells in the lungs which are responsible for producing mucous to grow more than normal, so, the amount of mucous increases in his lungs, and his lungs are not strong enough to clean excessively thus, it stuck in the airways of air making breathing process is harder. One of the main risky sequences of mucous accumulation is raising the infection rate with the infectious disease which decreases the efficiency of both the respiratory and the immune systems. All these mentioned sequences of smoking result the certain exposure to COPD in the long term.

Genetic and environmental Influences

Genetic inheritance and mutations can contribute to this disease. Some people may have a genetic link to COPD, this genetic condition is called AAT (Alpha-1 antitrypsin). People with this deficiency are more likely to develop the disease even if they aren’t smokers, live in clean areas, and have no occupational risks. Studies have demonstrated that this deficiency is a result of mutations in SERPINA 1gene. The most common mutations in this gene are in alleles (PiZ) and (PiS). Individuals with 2 copies of allele

Z (Homozygous Z PiZZ) are at the highest risk for severe symptoms of COPD. These mutations can occur due to exposure to sunlight at mid-day, radiation chemical pollution, especially among residents who live near factories. Resulting in errors in DNA replication during cell division. Sometimes, Viral infections can lead to DNA mutations contributing to the (AAT) gene elevating the risk of COPD exposure.

Clinical features

Signs and symptoms

Symptoms may not be familiar to normal patients that are due to COPD, they are like the normal flu, so patients infected with these symptoms must visit doctors to check if they are infected with COPD or not. These symptoms of COPD may include:

- 1- Shortness of breath, especially during physical activities such as running or making any effort.
- 2- A chronic cough that may produce mucous with different colors (white, yellow, or greenish). The indicator of infection is a chronic cough for a long time because it is not normal for flu patients to cough chronically.
- 3- Swelling in ankles, feet, or legs which is known as (peripheral edema) the main reason behind this is enlargement and failure in the right side of the heart, caused by the low oxygen levels in the body due to COPD, this low oxygen level heart can't pump blood effectively causing fluid back to veins, leading to swelling in ankles.
- 4- Lack of energy frequently and Unintended weight loss are some of the common symptoms of COPD.

Disease stages and Progression

Patients can visit doctors as the case gets worse or its severity doesn't decrease. People with asthma's cases can have worse symptoms than non-asthma cases.

COPD stages are classified based on their severity by the Global Initiative for Chronic Obstructive Lung Disease (GOLD) into three stages:

- The first stage is called "Mild": symptoms in this stage are often minimal with chronic cough and sputum production, and people in this stage are unaware they have COPD at this stage because it is similar to the normal flu cases. The impact of this stage is little to no impact on daily activities.

- The second stage is called “Moderate” In this stage, the severity of cough increases as well as sputum production. But this case is specialized with shortness of breath, especially on exertion. This case may be more noticeable than the previous one and visiting a doctor is a must.
- The third stage is called “Severe” There is a prediction of chronic respiratory failure with a severe cough at rest with frequent exacerbation. People in this stage face limitations in doing activities and the need for oxygen therapies and medical interventions.

Complications

Some cases can get worse than severe conditions such that people with low immunity protection in their bodies are more likely to be infected with respiratory infections such as pneumonia and bronchitis which can increase COPD symptoms and lead to further lung damage. In some other cases, COPD patients, particularly smokers have a higher risk of developing lung cancer. One of the dangerous results of COPD is “Osteoporosis” which is bone density loss which can reduce a patient’s activity.

Diagnosis of COPD includes Clinical symptoms and Patient history and we have talked about them previously. There are three other options Doctors take to decide whether this disease is COPD or not. **Firstly**, something called “Spirometry”. Spirometry is the gold standard for the diagnosis of COPD. It measures the amount of air a patient person can exhale and how quickly they can do so. **Secondly**, the additional test required by doctors to make certain results about the case. Some of the additional tests are (Chest X-ray) which helps to detect whether there is an incidence or not like pneumonia and other respiratory diseases. Additionally, other genetic tests like AAT (Alpha-1 Antitrypsin) and it’s recommended for patients who have a family history of COPD because this disease can be inherited as we have mentioned above. Thirdly, arterial blood gas analysis is the measure of oxygen and carbon dioxide in the vesicles of the lungs and the amount of gas exchange to determine whether it is normal or abnormal and indicate the presence of COPD.

Pathophysiology

Mechanisms of disease development

As we have explained before concerning the mechanism of disease and what it does in the respiratory system, there are some changes and incidences that may happen to some people more than normal ones due to extensive exposure to the factors causing the disease as inhaling harmful substances like cigarettes and smoke irritates lungs, this irritation triggers inflammation that is known as the body's trial to improve itself by which immune system cells within the lungs responds to the damage including macrophages, neutrophils, and T lymphocytes which release pro-inflammatory cytokines and chemokines. These pro-inflammatory cytokines perpetuate the inflammatory response and recruit more cells to lung tissues, Furthermore, lung tissues are thin naturally by the way they can be damaged with medium stress or force, finally, the repetitive inflammation of the immune system to this action results in damaging and destroying Alveoli.

Cellular and molecular changes

COPD patients suffer from molecular and cellular changes in their bodies. So, beginning with **cellular changes**:

- Epithelial cells: chronic irritation causes **hyperplasia** (increase in number) and **metaplasia** (change in type) of epithelial cells such that they may not be functional in their original position or may cause harm in other positions in the body they are unfunctional within thickening of the airway walls.
- Goblet cell hyperplasia: abnormal increase in goblet cell number leads to excessive mucous production and obstruction of air in airways causing heavy breath.
- Macrophages: elevation of macrophages in the lungs of COPD patients especially in alveoli and airways, these macrophages release inflammatory cytokines and reactive oxygen species (ROS) perpetuating inflammation and tissue damage.

Secondly, **Molecular changes**:

- **Pro-inflammatory Cytokines:** Increased levels of tumor necrosis factor-alpha (TNF- α), interleukin-1 beta (IL-1 β), interleukin-6 (IL-6), and interleukin-8 (IL-8) are observed, promoting inflammation and recruiting more inflammatory cells.
- **Chemokines:** Elevated levels of chemokines like CCL2 (MCP-1) and CXCL1 (GRO- α) attract neutrophils, macrophages, and lymphocytes to the lungs.
- **Elastases and MMPs:** Proteases such as neutrophil elastase, MMP-9, and MMP-12 are elevated, leading to the degradation of elastin and other extracellular matrix components, contributing to alveolar destruction (emphysema).
- **Reactive Oxygen Species (ROS):** Increased production of ROS from inflammatory cells and exposure to cigarette smoke causes oxidative damage to lipids, proteins, and DNA.
- **Antioxidant Deficiency:** A relative deficiency of antioxidants exacerbates oxidative stress and lung damage.

Impact on body systems

COPD has an obvious impact on the body's systems excluding the respiratory system because it is the location of infection and we have talked in detail about it.

First, the Cardiovascular system: one of the main dangers sequenced from COPD in the Cardiovascular system is "Pulmonary hypertension" caused by increasing pressure in pulmonary arteries due to the destruction of pulmonary capillaries which leads to Pulmonary hypertension. Additionally, Cor pulmonale is one of the damages that result from COPD in the cardiovascular system. This damage affects the right side of the heart causing its failure due to pulmonary hypertension and the pressure on the right ventricle.

Second, the musculoskeletal system: is another affected system by COPD, some of the harms represented in this system are:

- **Muscle wasting and weakness:** physical inactivity and chronic inflammation are the leading reasons behind feeling weak and being ill while doing any of the activities.

- Osteoporosis: it is one of the most dangerous sequences of muscular system infection, it is the bone density loss so, it makes the patient more exposed to fractures and breaks in his body parts even if he hits something lightly.

Third, the Renal system:

- Kidney dysfunction: hypoxemia, systematic inflammation, and cardiovascular complications can impair kidney function as disorders in urination and filtration of impurities in kidneys leading to chronic problems in kidneys.
- Also, the blood filtration cycle in the kidneys becomes inefficient due to weakness of the kidneys in this case which affects blood circulation around the body systems and vice versa.

Management and treatment

Medical and surgical treatments

Beginning with surgical treatments, it includes particular cases only severe ones, that don't respond to medical therapies. There are some options based on the case and severity:

- Lung volume reduction: This operation includes the removal of diseased, emphysematous lung tissue from the upper lobes which allows the change healthy lung to expand and function more and more. There is a medium percentage of risk in this operation due to the probability of infection and lengthy recovery period.
- Bronchoscopic lung volume reduction: this is an alternative way of lung volume reduction that uses endoscopic techniques to place devices such as endobronchial valves, coils, or thermal vapor ablation to reduce lung volume and improve airflow rather than operation interference.
- Lung transplantation: this is the final stage of the severity of COPD In this condition lung becomes damaged at 90% which makes it impossible to live with this lung, as a result, doctors are forced to transplant another lung instead of the damaged one from a healthy donor. This operation isn't successful 100% all the time, some sequences may face specific people represented in immune system rejection to the new transplanted organ.

Pharmacological therapies

Secondly, Pharmacological therapies:

- One of the common pharmacological therapies for COPD is “short-acting Bronchodilator inhaling”. This therapy is composed of relaxers, their function, and widening and relaxing airway walls in the patient’s lungs including beta-2 agonist inhalers such as “Salbutamol”. Short-acting bronchodilators are called with this name because they only continue for four hours.
- Long-acting Bronchodilator: In contrast, this Bronchodilator is called this name because the effect lasts at least twelve hours, while they have the same effect on the respiratory system which is relaxing muscles and walls pathways allowing the entrance of more air in the lungs, and preventing heavy breath. One of the best long-term Bronchodilators is salmeterol.
- Mucolytics: they’re used to thin mucous layers in the lungs which are accumulated more than normal and facilitate their clearance providing a good way for inhaling air normally once again. One example of mucolytics is “N-acetylcysteine”.

Lifestyle and dietary modifications

Avoiding and reducing symptoms of this disease can be done by following some healthy tips suggested by doctors:

- Smoking cessation: as we have mentioned before smokers represent about 75% of COPD patients so taking off smoking for smokers represents more than half of the healing process whether by direct or indirect smoking.
- Physical activity is required for medium and early infections of COPD due to its role in the renewal of blood circulation in the body frequently, also, it avoids patients' muscle weakness and fatigue and maintaining a healthy weight.
- Living in places far away from factories, dust and smoke of cars can be effective in these conditions, recommendations fall on living beside green areas and trees due to oxygen excessive presence.

Rehabilitation and supportive care

All these lifestyle tips are mainly supportive care instructions given to any patient with COPD, as well as pharmacological and medical therapies to shorten the symptoms of this disease. Repeating that the most effective factor that can make a high transformation in any case of COPD is smoking cessation as it contributes to the highest percentage of the cases, and avoiding it increases healing chances.

Prevention and Control

Primary, secondary, and tertiary prevention strategies

Primary prevention strategies are some tips and lifestyles that should be followed to decrease the severity of this disease in its early stages some of them to be mentioned are:

Smoking cessation: This is one of the leading steps to resist the heavy symptoms of COPD, especially for infected smokers because they become more exposed to multiple.

Reducing the existence of polluted and industrial areas as well as avoiding inhaling pollutants including chemicals dust and fumes, specifically people who suffer from allergies to specific fumes reduce their dealing with these fumes

Secondary protection: maybe it isn't familiar for some people to do this stage of prevention because most of them think that this is a normal flu or seasonal allergy similar to (spring allergy) in contrast, this stage must be taken into consideration also not to have multiples by early checking ups and visiting doctors as soon as the patient begins to suffer from the early symptoms. Additionally, vaccination is one of the pioneer stages of prevention if the case requires this, especially early stages of fighting the disease.

Public Health interventions

Public health services have varied to cope with modern and chronic diseases, avoid their spreading, and prevent them from becoming a pandemic. These services are demonstrated in some points including:

- Making campaigns to induce young residents and people by launching the initiative "Stop the Lies" in November 2023 to encourage young smokers to stop smoking and warn others from trying this killing habit for other people.
- Making supportive initiatives induces people to plant trees in industrial areas due to their effectiveness in combatting oxygen deficiency in these

places. This step has already been done by WHO as well which is called “One Million Trees” which aims to plant 170,000 trees by 2030 in industrial places.

Prognosis

Disease outcomes and survival rates

Survival rates of COPD disease vary from one country to another depending on several factors including the medical level and economics as well as the climate and the common industrial activities in these. The mentioned estimations and statistics are abstracted from academic articles concerning COPD:

The 5,10 and 15-year survival of COPD following clinical exacerbations was 43.75 %, 19.9% and 7.3% respectively

While in the general population, survival has reached 76.9%, 57.2%, and 40.6%.

Current Research and Future Directions

Recent advancements in the understanding and management of Chronic Obstructive Pulmonary Disease (COPD) have focused on improving diagnosis, treatment options, and overall patient care. Here are some of the notable discoveries and developments:

- **Genetic Research:** Advances in genetic research have identified specific genes and genetic variations associated with COPD. This knowledge helps in understanding individual susceptibility to COPD and tailoring personalized treatment plans.
- **Biomarkers:** The discovery of biomarkers for COPD can aid in early diagnosis, monitoring disease progression, and predicting response to treatments.
- **Biological Therapies:** Development of biologic drugs targeting specific inflammatory pathways involved in COPD. For example, monoclonal antibodies that inhibit proteins such as interleukin-5 (IL-5) are being investigated for their potential to reduce inflammation and exacerbations.

- **Stem Cell Therapy:** Investigating the potential of stem cell therapies to repair or regenerate damaged lung tissue and improve lung function in COPD patients.

Case studies

Example cases

COPD Case Study Example

Patient: Sarah Jones, a 65-year-old woman

Symptoms:

Increasing shortness of breath, especially during exertion

Frequent cough with mucus production

Tightness in the chest

Fatigue

Medical History:

- Smoked cigarettes for 40 years (quit 2 years ago)
- No prior lung diagnoses

Diagnosis:

- Spirometry test shows airflow limitation, consistent with COPD

Real-Life Application:

Based on Sarah's symptoms and medical history, her doctor suspects COPD. Spirometry confirms the diagnosis.

Here's how this case translates to real life:

- **Smoking cessation:** Since Sarah is a recent quitter, her doctor will strongly advise her to avoid smoking triggers and provide support to stay smoke-free.
- **Medication:** The doctor may prescribe medications like bronchodilators to relax airways and inhaled corticosteroids to reduce inflammation.

- Pulmonary rehabilitation: A personalized exercise program can help Sarah improve her breathing and maintain daily activities.
- Vaccination: The doctor might recommend a yearly flu shot and pneumonia vaccine to prevent respiratory infections that can worsen COPD.
- Education: Sarah's doctor will educate her about COPD management, including proper inhaler technique and recognizing signs of worsening symptoms.

This example highlights how doctors diagnose and manage COPD, aiming to improve a patient's quality of life.