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Effect of biofuel vulnerability on lungs in Chronic Obstructive Pulmonary disease patients.

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Abstract

Background: Incurable COPD is preventable and treatable. Airflow restriction, persistent lung inflammation, and respiratory tract symptoms lead to bronchiolitis and emphysema. It's caused by constant chemical and gas exposure. Comorbidities and exacerbations aggravate COPD, which is caused by complex biological processes. Globally, COPD will be the third greatest cause of death by 2030. Since 16th century, COPD, its diseases, and clinical presentation have been understood. Smoking, tobacco, industrial pollutants, interior pollution, outdoor air pollution, gender, and genetic inheritance affect worldwide incidence, morbidity, and mortality. Chemical exposure and population ageing will exacerbate COPD in the coming years. COVID-19 accelerates COPD and slows recovery.

Keywords: Copd,Airflow Restriction,Respiratory Inflammation,Environmental Factors,Covid-19 Synergies

Authors Contribution
AU. Concept & Design of Study ,IL,Drafting, FS.Data Analysis,ZT. Critically Review, FS,SR,Final Approval of version

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Introduction

COPD, a complicated disorder caused by gas and chemical exposure, is characterised by recurring respiratory symptoms, airflow restriction, and increased airway and lung inflammation. Several host characteristics affect it (Colarusso et al., 2017). Inhaling harmful gases and particles from biomass-based fuels and cigarette smoke causes emphysema and airway fibrosis, which damage parenchymal tissues and disrupt the body's defence and repair processes, increasing lung inflammation. Regardless of FEV1, smoking is strongly connected to disease development, emphysema, and poor prognosis. Never- smokers had a better COPD prognosis in Western nations (Mitra et al., 2022). With high mortality rates, COPD is the leading cause of worldwide deaths. It was the third greatest cause of mortality worldwide in 2010 and is expected to become the fourth and fifth top causes of COPD disease incidence by 2030. The most frequent COPD phenotype is partially caused by active smoking among other factors. Smokers do not always get COPD, indicating that intrinsic or extrinsic factors contribute to the disease. COPD patients also vary clinically. It is also well recognised that COPD patients' inception, early phases, and development vary greatly. Comorbidities include coronary artery disease, diabetes, lung cancer, and osteoporosis affect how COPD develops in older adults. Early COPD detection has been hampered by clinical delays, early pulmonary function loss, patient social and psychological variables, and early pulmonary function loss (Lange et al., 2021). Epidemiological studies on COPD are limited to certain locations. The goal of this project is to evaluate and assemble data on the epidemiological effect of COPD and its risk factors worldwide. This article also discusses COPD therapy advances (Hu et al., 2015).

Origin and history of COPD

In 16th-century literature, emphysema was described as having "voluminous lungs." Morgagni described 19 air-induced "turgid lungs" and Baille portrayed Samuel Johnson's emphysematous lungs in 1789 (Ayilya & Nazeer, 2023). Persistent bronchitis and COPD were

originally described by Badham in 1814. He labelled the main symptoms, a persistent cough with excessive mucus output, "catarrh" and bronchiolitis and chronic bronchitis "disabling disorders." William Briscoe may have coined "COPD" during the "9th Aspen Emphysema Conference" to start a conversation. Current COPD definition: progressively worsening health concerns (Bustos, 2022). The 1962 US Thoracic Society Commission on Diagnostic Standards and the Central Institute for Brackish Thoracic Diseases defined COPD and its components. Water Aquaculture (CIBA) Guest Symposium, 1959. In 1993, The Lung Section of the National Heart, Lung, and Blood Institute (NHLBI) created "The National Lung Health Education Programme (NLHEP)" to study COPD. The disease's pathophysiology became clearer (Wu et al., 2021). In 2001, WHO and NHLBI launched GOLD to increase awareness of the condition's severity and encourage early detection and treatment. In 2004, 'The European Respiratory Society (ERS)' and 'The American Thoracic Society (ATS)' recommended COPD. Charles Fletcher meticulously investigates the natural course of COPD by identifying smoking risk indicators and the abrupt reduction in FEV1 in susceptible smokers to correlate to debilitating symptoms. The scientific foundation for stopping smoking at different illness stages was established. When high slumpers had the worst prognosis, Burrows et al. named it "The Horse Racing Effect". This showed the need of early diagnosis and treatment. Spirometry can show early physiological changes due to complicated biochemical and cellular responses that are damaged with lose elastic recoil in the tiny airways and alveoli, lung expansion, and a rise in FVC. Clinical symptoms often emerge in severe and intermediate COPD (Ayilya & Nazeer, 2023).

Epidemiology of chronic obstructive pulmonary disease in LMICs (low- and middle-income countries)

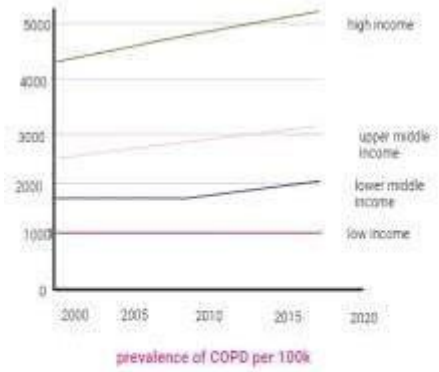
Most LMICs are in Eurasia, Latin America, and Africa. Since primary care institutions in LMICs don't collect data, prevalence surveys are our main source of information on COPD's aetiology. Asia has conducted most surveys on chronic respiratory disorders in LMICs, and the following methods are used to estimate COPD prevalence: GOLD standard definition (clinical symptoms with past dangers verified by spirometry) or

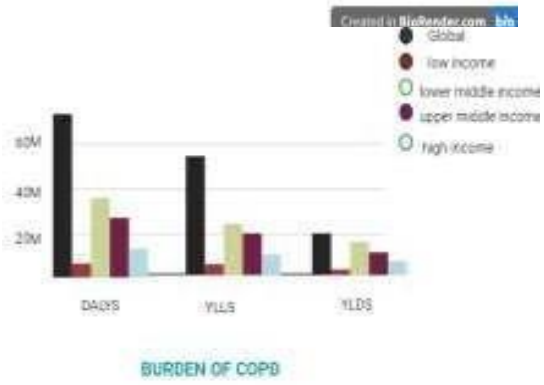
FEV1/FVC ratio, where applicable (Pollard et al., 2023). India, China, and Indonesia are three middle-income Asian countries where half the world smokes. Asia produces most tobacco. Also, Bangladesh has significant smoking rates. Based on specific risk variables and epidemiological connections, Hong Kong and Singapore have 3.5%, Vietnam 6.7%, Malaysia

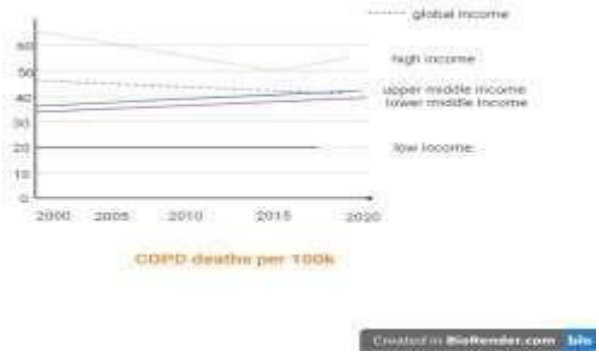
4.7%, Thailand 5%, Indonesia 5.6%, the Philippines 6.3%, Taiwan 5.4%, South Korea 5.9%, and Japan 6.1% (Islami et al., 2015). East and South-East Asian COPD prevalence data is sparse. Using standardised spirometry, the 2014 BOLD study in India found overall COPD prevalence rates of 5.7% to 17.3% for men and 6.8% for females in Pune, Mumbai, and Srinagar. Hand-held spirometers were utilised to assess Bangladesh's 10.3% COPD incidence using GOLD defining criteria and LLL standards. Males showed a higher COPD incidence than females, and over half of all cases were stage II (or "moderate") (Ho et al., 2019). The hidden COPD epidemic in Africa is a major public health concern. Africans had 26.3 million COPD cases in 2010, up 31.5% over a decade, especially among the elderly.A systematic review of nine cross-sectional and spirometry-based studies (including 3673 people from South Africa, Nigeria, Malawi, and Cape Verde) found that COPD prevalence ranges from 4% to 25%, depending on diagnostic criteria (Rossaki et al., 2021). The risk of COPD in Africa south of the Sahara has gotten little attention. Statistics from spirometry generally reveal a higher prevalence. Spirometry data showed that the average incidence of COPD in those under 40 was 13.4%, compared to 4.0% for those using questionnaires to assess exposures, demographics, and symptoms (Bai et al., 2022). Ho et al. also discovered that chronic airflow obstruction prevalence varies by country and demographic.The high smoking rate (30%) in South and Central America increases respiratory problems in the US. The PLATINO and PREPOCOL population-based investigations estimated the prevalence of COPD in people under 40 in several major urban centres to be between 6.2% and 19.6%, with up to 89% underdiagnosis and excessive diagnosis due to the lack of spirometric confirmation.A recent study of studies evaluating COPD incidence using portable spirometry and questionnaires in a few of Latin American locations reported a range of 7.8% to 19.7%. Larger and more

representative studies of numerous communities globally, especially in rural areas, have not been done.

COPD seems to be growing worldwide. Although HICs have the highest formal prevalence and incidence, LMICs' official data, which show far lower rates, are thought to misrepresent reality. In 2019, 5.4% of HICs had COPD, compared to 1.1% of LMICs. Unawareness, underdiagnosis, and underreporting of COPD in LMICs reduce its prevalence (Pleasants et al., 2016). Due to their reliance on forecasts rather than epidemiological data and risk factor exposure, most estimates of LMIC COPD incidence were inaccurate. Thus, lawmakers lack the data to create meaningful illness cost-cutting programmes. Due to expanding life expectancy, reducing infant mortality, and improved COPD awareness, LMIC occurrences are expected to rise (Prince et al., 2015).







Differences between distribution of tobacco and biofuel vulnerability

Both COPD and tobacco exposure are biomass products, but the social context distinguishes them epidemiologically. Tobacco smoke is intensively processed and industrialised and includes several inorganic harmful compounds. Most COPD knowledge originates from industrialised cigarette smoke, which is derived from unprocessed organic components (Ramírez-Venegas et al., 2021). From 1913 until 1920, tobacco industry breakthroughs caused the tobacco pandemic. The tobacco industry flourished unfettered locally and worldwide in the 1960s, killing millions (Celli & Agustí, 2018). Since humans began utilising organic fuels for heating and cooking, billions of women and children have been exposed to biomass without knowing the health risks. Because poverty limited electricity, rural women had to fire biomass, cook, and heat their houses (Bouza et al., 2020). The tobacco industry pushed recreational smoking to create a nicotine demand. Tobacco use, formerly associated with wealth and social status, is now connected to BE-COPD, which affects low- and middle-income people. Unfortunately, biomass smoke has long been linked to poverty and underdevelopment (Bouza et al., 2020).Approximately 1,100 billion people have been exposed to tobacco. These figures are far lower than those of almost half the world's population. In rural and impoverished countries, this proportion is higher (Alkan & Abar, 2020).

Use of biogas fuel causes COPD in rural women

In most countries, rural women lead their homes and study and cook when men are away for different reasons. Home pollution is the most common source of pollutants for women, particularly in developing countries. Due to biomass-based fuel's low burning efficiency, carbon monoxide, hydrocarbons, and chlorinated organics are produced, which are harmful to respiratory health and the main cause of BE-COPD (Jindal & Jindal, 2021). High indoor smoking exposure, especially in poorer countries, doubles COPD risk. COPD was the third biggest cause of death worldwide in 2019, accounting for 6% of fatalities. WHO reports COPD as the fourth biggest cause of mortality in lower-middle income countries, causing over

one million deaths in 2019 (Ramírez-Venegas et al., 2018).Data linking biomass exposure to COPD is considerable. Women who cook with indoor smoke are more likely to have chronic bronchitis than those who use electricity or gas. Actually, the sickness is more common in men than women, hence it may be considered a disorder that only affects women. Its exclusive impact on women and rising global female illness rates make it a potential public health issue (Ramírez-Venegas et al., 2019).

The Beginning Lung Damage due to Biomass Exposure

Rural women spend long hours cooking, frequently inside in unventilated rooms. This cooking method emits air pollution. Biomass burnt in unvented open fires causes milligrammes per cubic metre pollution in homes (Lange et al., 2021). Most women and girls' cumulative exposures occur over time. On average, they spend four to eight hours a day in the cramped, poorly ventilated kitchen. They stay awake for almost half the day in a tiny, poorly ventilated kitchen. They may have been exposed for 40 years (Assad et al., 2016). They breathe almost 25 million litres of smoke-containing particles for over 60,000 hours. This sustained, high-level exposure increases the risk of airway wall inflammation, which may take years to show. Continuous biomass exposure in infancy may cause recurrent respiratory tract infections that modify airway walls or predispose (Sana et al., 2018).

Risk factors

Behavioral risk factors: tobacco smoking

The most significant contributing factor to COPD is generally believed to be tobacco use. More than 80% of the 1.3 billion smokers in the world reside in LMICs. In 2015, smoking alone was the cause of about 1.5 million Cardiovascular Obstructive Pulmonart Disease-related deaths. However, LMICs are home to the large majority of non-parties (Keto et al., 2016). Quitting smoking lowers family danger from secondhand smoke and one's own chance of acquiring COPD. It shouldn't, however, solely be seen as a preventative step. The only COPD intervention that has been shown to reduce COPD development is quitting smoking. This is also known as Article 14 of the FCTC. A great number of smokers in many nations have access to

primary care for help quitting (Soneji et al., 2017).

Environmental risk factors: air pollution

Air pollution was blamed for almost 1.8 million COPD-related fatalities in 2015. Additionally, exposure to air pollution at work (such as particulate matter, fumes, as well as gases) was linked to 354,000 COPD-related fatalities. Household (interior) as well as ambient (outdoor) pollution are 2 different types of air pollution (To et al., 2016).

The use of fuels made from biomass (such as wood, agricultural waste, or animal dung) for heat and cook purposes is the main cause of indoor air pollution. Other instances include lighting kerosene lights, lighting incense at places of worship, and lighting mosquito coils. Solid fuels are used by three billion people globally, or 40% of homes, and 90% of rural LMIC families rely on them. Consumption of solid fuel is centered in LMICs, particularly in Africa. Air pollution in the home poses a major risk to one's health. An exposure-related 41% increase in the risk of COPD was found in an up-to-date investigation that focused on residential air pollution in Thirteen LMICs. Women who live in rural locations are more at risk for acquiring COPD as a result of biomass exposure, probably because of the prolonged time spent indoors (de Miguel-Díez et al., 2019). It's interesting to note that the phenotype of COPD may vary depending on the disease's etiology. For instance, COPD caused by biomass more frequently seen in younger individuals . The exposure of ambient air pollution from sources for example forest fires, storms of dust, and vehicle and industrial exhausts is highest in developing nations. In locations with low- and low-middle sociodemographic indices during the past ten years, there has been a marked rise in DALYs attributable to ambient air pollution. As a result, air pollution continues to be an important risk indicator for DALYs in LMICs, particularly in South Asia and eastern sub-Saharan Africa (Li et al., 2016). The Sustainable Development Goals' seventh strategic recommendation is to convert to more accessible, greener energy. There are schemes in place for the switch to greener fuels in Indonesia and India. In the interim, if switching is not an option, using better cookstoves or enhancing ventilation are workable intermediate measures.However, various programs to provide better cookstoves

haven't shown sustained results. Notably, research and discussion on the link between COPD and biomass exposure are ongoing. Contradictory and erratic relationships between airflow restriction and indoor pollution have been shown in a number of research, including the BOLD (Hu et al., 2015). The evidence supporting the involvement of environmental pollutants in the genesis of COPD is also suggestive but not definitive. Exposure to environmental pollutants is major reason of COPD in low-income countries, according to the Global Burden of Illness research. However, chronic contact with polluted indoor air is challenging to assess and may also be linked to other risk factors, such as poverty and a lower socioeconomic level, which can lead to poorer eating habits and reduced fetal lung development (Santos et al., 2021).

Genetic and physiological risk factors: host characteristics

The relationship between genetic predisposition to COPD and early-life risk factors, beginning with conception, is a relatively recent issue that has drawn interest. The development and trajectory of embryonic lung formation or lung function are influenced by maternal, health and lifestyle factors (such as asthma, smoking, and diet). Lung function is strongly influenced by early age difficulties such low birth weight, preterm, starvation, childhood respiratory illnesses, and allergy disorders (Agustí et al., 2022). Similarly, prolonged exposure to air pollution slows down the development of full lung capacity in children, hastens the aging process. It has becoming crucial since the development of COPD seems to be influenced by the lung-function. Similarly, having a low body weight, which is typically the result of malnutrition, increases your likelihood of developing COPD, has a worse prognosis, and affects your ability to breathe (Agustí et al., 2020). In terms of diseases, Human immunodeficiency virus and TB are both quite common in numerous LMICs, have devastating impacts on the lungs, or are thus COPD risk factors. A risk factor of COPD may also include non-infectious disorders. For instance, asthma is linked to COPD as a result of reduced lung function. Despite the reality that asthma is thought to be poorly diagnosed and poorly understood in LMICs, the frequency of the condition is rising there and its considerable

severity has been recorded there. It is clear that clinical tools are required for correct diagnosis, and also incentives for systems that allow for routine evaluations to assure disease control (Lange et al., 2021).

Role of climatic factors and air pollution in spreading COPD

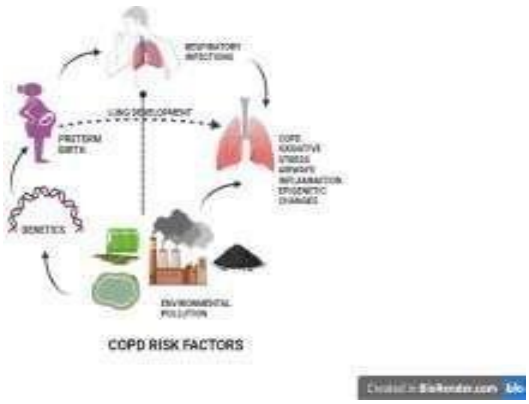
Climate variables including the pressure of the air, humidity, and air temperature all have an effect on how harmful air pollutants affect COPD. The relationship between air temperature and the pathogenic impact of contaminants on COPD is complex, however there is debate concerning the distinctions between the influence of hot and cold temperatures. Lower temperature significantly exacerbated the impact of PM2.5, PM10, and the level of SO2 affecting the COPD hospitalization rate, proved by a research by Qiu et al., (Hansel et al., 2016). Several studies from China found the possibility that the admissions to the hospital for COPD “are more associated with SO2, NO2, and O3 in the colder seasons than in summertime” and “the association between air pollution and the hospitalization rate for COPD is stronger in autumn than in winter” . These results can be explained by the fact that higher temperatures make a “substantially greater proportion of O3, as well as other pollutants, penetrates into the atmosphere” . More recent investigations in these countries have shown that “the days when the temperature is very high with a large variation in barometric pressure were significant in increasing the hospitalization rate of COPD in downtown elderly patients . The investigators postulated that fluctuating pressure may aggravate the symptoms of COPD. Moreover, increased atmospheric pollution on hot days could also play a role in worsening COPD.Gao et al.'s study showed that air contamination was more influential in summer months (August to October) for those suffering from COPD than the winter period (November to March).Admission for COPD may also be influenced by relative humidity. In one study the likelihood of COPD hospitalizations increased by 1.070 (95% CI: 1.054-1.086) for every 1% increase in relative humidity. Furthermore, temperature and humidity had a significant interactive impact (Alahmari et al., 2015)It is still unclear what exact impact air pollution has on the pathophysiology of people with COPD. However, current research focuses on factors such as oxidative stress and inflammatory damage, as well as DNA damage.

Oxidative stress damage

The pathophysiology of COPD is significantly influenced by free radicals generated by oxidative stress, particularly oxygen free radicals. Reactive oxygen species, also known as ROS, can be produced in huge quantities by cells when free radicals of oxygen, which are produced by PM, are inhaled. Additionally, the huge concentrations of metal and organic debris carried by PM might cause the creation of ROS in cells. The fundamental source of harm brought on by PM exposure may be such oxidative breakdown of lung cells caused by ROS (Kruk et al., 2019).

Genetic damage

Within a particular concentration range, contact to air contamination can result in genotoxicity, which damages chromosomes in living organisms. In addition to harming lung epithelial cells with alveolar macrophages, exposure to PM2.5 can increase the formation of ROS brought on by oxidative stresses, which results in DNA damage and alterations in gene expression. Without any changes to the DNA sequence, epigenetic alterations to DNA, such as DNA methylation, histone modifications, and non-coding RNA modifications, can affect how genes are expressed. The development of COPD may potentially be influenced by air pollution through changes to epigenetic alterations (Boas et al., 2018). Nitric oxide (FeNO) exhaled while breathing is regarded as a sensitive indicator of airway inflammation and can provide insight into the severity of airway infection in COPD patients. A Shanghai panel research that looked at the connection between PM2.5 hence DNA methylation in COPD discovered that PM2.5 may control the generation of FeNO by altering the methylation of biomarkers in the NOS2A promoter zone and escalating airway inflammation (Song et al.) discovered that PM2.5 may enhance the expression of IKK- and maintain NF-B activation in human airway epithelium cells by inhibiting miR-331 by disrupting the ROS/PI3K/AKT pathway (Heffler



Protective measures

Policy intervention

Improvements in air pollution levels are mostly due to government regulation. For instance, there was historically significant air pollution in the United States. As a result, the American government created a number of policies to prevent and reduce air pollution, including the amendments made to the Clean Air Act in 1990 along with the NOx State Strategy Plans Call in the year 2002. In the United States, PM2.5 and O3 concentrations drastically dropped after 1990 (Zhang & Samet, 2015). The burden of COPD mortality has dramatically lowered as a result of air quality improvements. China saw the worst pollution occurrences in the previous ten years, a period of tremendous industrial expansion and urbanization.To reduce air pollution in China, the government has enacted a number of effective preventative and control measures. The Air Pollution Strategy Control and Prevention Plan (2013-2017) was created by the state council in 2013. The Three-Year Action Strategy Towards Winning the Blue Sky Defense Conflict, published by the state council in 2018, served as a roadmap for the subsequent phase of air pollution management and prevention (Zhang et al., 2016). The Beijing City Strategic Plan (2016- 2035) is one of the comparable policies that the provincial and municipal administrations have also released (Duan et al., 2020). Since 2013, PM2.5, PM-10, and SO2 levels have dramatically dropped and the majority of Chinese cities have improved in terms of air quality. Emission regulations decreased PM2.5 mortality by 88.7%, and these measures also had some positive health effects. According to Liang et al., the levels of SO2 and PM2.5 were 68 percent and 33% lower in 2017 than they were in 2013. The number of advanced acute COPD exacerbations caused by PM2.5 exposure also showed a trend toward decline (Hooftman et al., 2018). Despite a decline in air pollution, the WHO requirements for air quality have not yet

been met. The levels of O3 has drastically increased, the NO2 concentration is unchanged, and the PM quantities are still high. Therefore, to limit emissions from industrial pollution sources and achieve a general improvement in air quality, the government should develop effective air prevention and control measures (Maloney & McCormick, 2017).

Group intervention

Burning solid biomass for cooking is the major cause of indoor air pollution, which is linked to a number of respiratory conditions. Around a third of the worldwide population, particularly in rural LMICs, utilizes biofuels like charcoal and wood for heating or cooking. Numerous studies have found a connection between exposure to biofuels and a higher risk of COPD. In order to investigate the relationship between solid fuel consumption and the chances of developing both acute and persistent respiratory illnesses, a cohort research was carried out in China, which included 277,838 Chinese people who never used tobacco and had not had significant persistent illnesses in the previous nine years (Balmes, 2019). According to the findings, solid

fuel consumers had an increased hazard ratio for COPD of 1.10, which is (95% CI: 1.03-1.18) when compared to clean fuel users. The danger of respiratory infections can be decreased by using clean fuel with ventilation equipment. Additionally, using ventilation kitchenware or clean fuel can significantly lower the danger of respiratory illnesses (Assad et al.).

A non-randomized intervention was carried out by Zhou et al. to evaluate the long-term effects of better kitchen ventilation and alternative biomass fuel consumption on lung function in COPD patients. The use of biogas in place of biomass for cooking and better kitchen ventilation were shown to be associated with a lower chance of having a poor FEV1 and COPD, according to the findings. Additionally, a dose- response connection was seen: the longer enhanced kitchen ventilation and cooking fuel utilization lasted, the more of an influence it had on slowing the loss of lung function (Duan et al., 2020). The use of upgraded cookstoves also helped to lower the risk of COPD, the frequency of respiratory symptoms including coughing, expectoration, and wheezing, as well as the pollution caused by biofuels. To lower the incidence of COPD, better cookstoves, vented

cookware, better kitchen ventilation, and pure fuel must be utilized.

Individual intervention

When smog concentrations are high, it is best to limit the amount of time and intensity spent outside, and to wear masks that are good at trapping PM2.5 particles to lessen exposure. Wearing personal protection equipment, like the N95 mask or a comparable product, may help reduce your exposure to ambient air pollutants' detrimental effects. The majority of studies on the preventive effects of masks to far have been conducted on healthy individuals or those in certain vocations, and there have been very few studies done on sensitive persons like COPD sufferers (Laumbach et al., 2015). A research by Sundblad et al. involved 36 healthy individuals. The participants using masks had a lower concentration of systemic inflammatory markers and relatively greater lung function indicators as compared to the group not wearing masks, according to the results. The study proved that wearing a mask might help to protect your respiratory system. Indoor purifiers for air can lower the amount of PM2.5 in the air and help

with indoor air pollution. Uncertainty persists on whether this will actually enhance cardiopulmonary function (Jiang et al., 2016). In order to assess the real preventive impact of air purification systems and masks in people with chronic pulmonary disease (COPD), a more efficient experimental investigation is required.

Medical intervention

In addition to the aforementioned activities, various pharmacological interventions, such nebulization therapy, may aid in encouraging the removal of PM in the lower respiratory system in COPD patients and reducing the adverse impacts of air pollution. However, there are currently no suggested limits for lowering air pollution linked to atomizer inhalers (Laumbach et al., 2015).

ADVANCES IN DRUG DEVELOPMENT FORCOPD

Chronic obstructive pulmonary disease, also known as COPD maintenance therapy, which may include a variety of pharmacological treatments, concentrate on symptom relief and lowering the risk of disease progress, exacerbation, and death. Due to the variability

of COPD, pharmaceutical therapies can cause

people to respond differently. Over time, therapy choices for COPD have changed, moving from accuracy in pharmacologic strategy to optimizing treatments based on data from integrating clinical and biomarker. The best available evidence supports the use of combination therapy at varying levels, according to studies undertaken by several researchers (Barnes et al., 2015). The GOLD team strongly advised the urgent need for pharmacological therapies for exacerbations and dyspnea, as well as symptom-specific therapeutic approaches to reduce risks, reduce symptoms and their frequency, and improve health and exercise tolerance. On the contrary hand, there is currently no effective clinical data to support any COPD treatment that can enhance lung function over the long term. Using biomarkers, pharmacological treatment may be customized for people with different pathophysiological causes. Vaccinations are effective early prevention methods (Doryab et al., 2016). Based on the degree of lung damage and symptoms including cough, production of sputum, dyspnea, as well as exacerbation levels, pharmacological treatment is prescribed. The class of drugs that includes anticholinergics, asthmatics, inhaled corticosteroids (ICS), beta2-agonists, antimuscarinic medications, methylxanthines, phosphodiesterase-4 inhibiting agents, antiinflammatory agents, and mucolytic agents includes about 37 generic drugs, which are widely used worldwide. Although most medications work to relieve symptoms, some have unpleasant side effects. This emphasizes the need for additional naturally occurring bioactive substances with relatively less negative effects (Diebold et al., 2015).

Anti-COPD compounds from natural sources

In cultured airway human epithelial cells, nine bioactive substances screened from underwater brown algae (Ecklonia cava, Ishige foliacea, Ishige okamura, and Hizikia fusiformis) and Apo9 1 fucoxanthinone obtained from Undariopsis peteseniana show superior protection against the cytotoxicity induced by cigarette smoke by preventing cigarette smoke- induced apoptosis, DNA damage, and mitochondria- According to research, astaxanthin and a xanthophyll carotenoids with a naturally occurring reddish-orange color that is abundant in marine species including algae,

crab, shrimp and krill, and salmon, has the strongest antioxidant effects of all the carotenoid and vitamin E (Rahman et al., 2022). By raising the expression of Nrf2 and HO-1 in the lung, it prevents mice from developing emphysema brought on by cigarette smoke. While the astaxanthin content in the mice's blood and its bioavailability were not established, and the ideal concentration of astaxanthin has not yet been tested for efficacy, the molecule was effective in vitro and in a mouse model of COPD. Brevenal, a marine dinoflagellate called Karenia brevis, has been suggested as a viable anti-inflammatory medication for mucociliary clearance since it lowers pre-inflammatory mediators while maintaining anti-inflammatory release from the cells on various cell lines. However, a vivo investigation would be important for demonstrating the compound's physiological benefit without affecting the immune system's ability to mend (Yang et al., 2020). Two polyphenols from Jaboticaba, 3,3′- dimethyellagic acid-4-O-sulfate and jaboticabin, showed anti-inflammatory effects in cell lines and may be used to treat COPD; however,

animal studies are still needed to corroborate these results. Naringenin, an organic flavanone derived from dormant Prunus persica flower petals, was hypothesized to have potential pharmacological effects against various phases of COPD. It is ingested by humans, abundant in citrus veggies and fruit, and has a wide range of bioactivity (Inada et al., 2021). Although the biological effect of this flavanone has been thoroughly investigated both in vitro and in vivo, additional clinical research is required to support its effects on humans, which are constrained by its poor bioavailability and solubility in aqueous solutions, and need an efficient drug delivery mechanism. The majority of the potentially effective anti-COPD compounds investigated were from plant sources, with very few coming from marine algae. These compounds tended to be more phenolic and flavonoid-based, with less bioavailability hence heavier for stomach absorption, and thus needed stronger supporting data based on in vivo investigations (Ayilya & Nazeer, 2023).

Burden of COPD

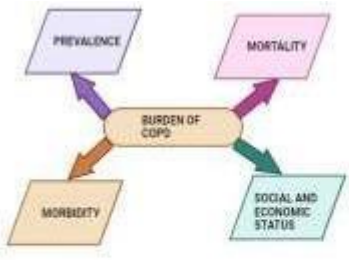
One of the main causes of illness and mortality worldwide is COPD, according to experts. Depending on the environmental factors that

various people are exposed to, the incidence, mortality, and morbidity of COPD may differ around the world. The most common cause of COPD is tobacco use, while other variables, including as occupational exposure and air pollution from both indoors and outdoors, also play a substantial role in many nations (López- Campos et al., 2016). The prevalence and incidence of COPD are predicted to significantly increase over the next several decades when taking into account ongoing exposure to hazardous chemicals and the aging of the global population (Zhu et al., 2018).

Prevalence

Between 1990 and 2015, the prevalence of COPD grew by approximately 44.2% worldwide. 'The World's Burden of Disease Study' projected that 251 million people worldwide had COPD in 2016. Over the years, a number of meta- analyses and systematic reviews have been carried out, and the combined prevalence of COPD from 37 studies was found to be 7.6%, and the prevalence from 26 approximated spirometrics to be 8.9%. Similar to this, a research done in over 28 nations between 1990 and 2004 indicated that smokers and ex-smokers over the age of 40 had a higher prevalence of COPD than non-smokers (Lee & Rhee, 2021). Additionally, it was discovered to be somewhat higher in men than in women.The Burden of Obstructed Lung Disease (BOLD) program examines the prevalence and risk of COPD among the global population over 40 years of age across 38 countries, nine of which are still being studied, using standardized pre- and post-questionnaires and data retrieved from various spirometric studies. According to BOLD, the prevalence of grade 2 or above was 10.1% overall, 11.8% among men and 8.5% among women, with a frequency of 3-11% amongst non-smokers. 9.2% of people in low- and middle-income nations have COPD (Machado-Duque et al., 2023). Over 90% of COPD-related fatalities, as reported by WHO (2021), are attributable to them. Additionally, estimations from meta-analyses indicated a prevalence of version 10.6 in LMICs among those over the age of 30. From 28.1 million cases recorded in 1990 to a startling 55.3 million cases reported in 2016 in India, COPD prevalence increased from 3.3 percent to 4.2%. Additionally, in less developed lower Epidemiologic Transitional Levels (ETL) states of Uttar Pradesh as well as Rajasthan in

India, the DALY rates and age-standardized COPD prevalence were highest in 2016 (Selçuk, 2020).



Morbidity and mortality

Morbidity includes illnesses that require medical attention, ER visits, and hospital stays. Studies show that COPD morbidity rises with age and people with COPD develop complications at a relatively young age since the information gathered from these variables is less trustworthy and not as easily accessible as that from the mortality data. The morbidity among COPD patients is also influenced by other chronic disorders, such as cardiovascular disease, diabetes mellitus, etc. COPD was ranked as the third leading cause of mortality in America in 2011 (May & Li). With over 90% of deaths occurring in low- and middle-income countries, COPD is a progressive respiratory disease that caused 3 million deaths in 2012, 5.7% of all deaths globally, 3.2 million deaths in 2017, and 3.23 million deaths out of 55.4 million worldwide in 2019. The WHO had predicted that COPD will be the third most common cause of death by 2030, however the condition was instead rated as the second-highest rate of death in 2017. In the next 40 years, the prevalence of COPD will rise due to rising rates of smoking in a number of developing countries and an aging population in high-income nations (Ko et al., 2016). By 2060, it is anticipated that there will be 5.4 million per year related to COPD along with its associated conditions. Additionally, the growing smoking epidemic, lower mortality rates from other diseases like heart attacks and strokes, the aging of individuals in high-income nations, and relatively lax measures to prevent illness in developing nations can all be linked to the significant rise in deaths from COPD (Criner & Han, 2018).

Social and economic burden

In 2016, India was responsible for 32 percent of all DALYs worldwide caused by chronic respiratory disorders, with COPD accounting for 75.6% of all DALYs in that country. This very high illness burden and enormous health loss in India, especially in the states with low epidemiological transition levels, highlight the need for more converging policy actions to look into the country's large disease burden. In 2016, India's DALYs per case of COPD were 1.7 times

higher than the global average, and even most

of the states in the nation had higher DALY rates than most other regions with comparable Socio-demographic Index globally (Kalkana et al., 2016; ur Rehman et al., 2020). Around 6% of the total annual health budget in the European Union, or 38.6 billion euros, is estimated to be set aside for respiratory diseases, of which COPD accounts for 56%. In the United States, the cost of COPD is predicted to be $32 billion or $20 billion, respectively. Previous research indicates that the impact on the Indian economic growth in terms of direct and indirect medical expenditure was indicated to be considerably high (direct medical cost: roughly Rs. 29,885 11,995.33, or US$300-500; direct nonmedical cost: roughly Rs. 7,441.25 2,228.90, or US$90-

155) and is also related to lack of daily wages for an essential amount of time (Zafari et al., 2021).

Conclusion

There is a lot of data to back up the claim that respiratory illnesses like COPD are linked to air pollution. The relationship between pollution in the air and COPD has been proven by epidemiological and clinical investigations. Air

pollution has a detrimental influence on the onset and development of COPD, both over short and extended periods of time. It is crucial to pay greater attention to air pollution because it is one of the main risk factors for COPD and may be modified. In the future, extensive clinical research and in-depth study of fundamental mechanisms will be required, which can not only improve patient treatment but also encourage policymakers to support health care initiatives to eradicate air pollution internationally.

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References:

1. Agustí, A., Melén, E., DeMeo, D.L., Breyer-Kohansal, R., Faner, R. 2022. Pathogenesis of chronic obstructive pulmonary disease: understanding the contributions of gene–environment interactions across the lifespan. The Lancet Respiratory Medicine, **10**(5), 512-524.

2. Agustí, A., Vogelmeier, C., Faner, R. 2020. COPD 2020: changes and challenges, Vol. 319, American Physiological Society Bethesda, MD,pp. L879-L883.

3. Alahmari, A.D., Mackay, A.J., Patel, A.R.C., Kowlessar, B.S., Singh, R., Brill, S.E.,

   Current opinion in pulmonary medicine, **22**(2), 150-157.

4. Alkan, Ö., Abar, H. 2020. Determination of factors influencing tobacco consumption in Turkey using categorical data analyses1. Archives of environmental & occupational health, **75**(1), 27-35.

5. Assad, N.A., Balmes, J., Mehta, S., Cheema, U., Sood, A. Chronic obstructive pulmonary disease secondary to household air pollution. 2015. Thieme Medical Publishers. pp. 408-421.

6. Assad, N.A., Kapoor, V., Sood, A. 2016. Biomass smoke exposure and chronic lung disease.

   improve its taxonomy? ERJ open research, **4**(1). Colarusso, C., Terlizzi, M., Molino, A., Pinto, A., Sorrentino, R. 2017. Role of the inflammasome in chronic obstructive pulmonary disease (COPD). Oncotarget, **8**(47), 81813.

7. Ayilya, B.L., Nazeer, R.A. 2023. Epidemiological burden, risk factors, and recent therapeutic advances in chronic obstructive pulmonary disease. J. Adv. Biotechnol. Exp. Ther., **6**, 109. Bai, J., Zhao, Y., Yang, D., Ma, Y., Yu, C. 2022.

8. Barnes, P.J., Bonini, S., Seeger, W., Belvisi, M.G., Ward, B., Holmes, A. 2015. Barriers to new drug development in respiratory disease, Vol. 45, Eur Respiratory Soc, pp. 1197-1207.

9. Boas, D.S.V., Matsuda, M., Toffoletto, O., Garcia, M.L.B., Saldiva, P.H.N., Marquezini, M.V. 2018. Workers of São Paulo city, Brazil, exposed to air pollution: Assessment of genotoxicity. Mutation Research/Genetic Toxicology and Environmental Mutagenesis, **834**, 18-24.

10. Bouza, E., Alvar, A., Almagro, P., Alonso, T., Ancochea, J., Barbe, F., Corbella, J., Gracia, D., Mascarós, E., Melis, J. 2020. Chronic obstructive pulmonary disease (COPD) in Spain and the different aspects of its social impact: a multidisciplinary opinion document. Revista Española de Quimioterapia, **33**(1), 49.

11. Celli, B.R., Agustí, A. 2018. COPD: time to

12. de Miguel-Díez, J., Hernández-Vázquez, J., López-de-Andrés, A., Álvaro-Meca, A., Hernández-Barrera, V., Jiménez-García, R. 2019. Analysis of environmental risk factors for chronic obstructive pulmonary disease exacerbation: A case-crossover study (2004-2013). PLoS One, **14**(5), e0217143.

13. De Ramón Fernández, A., Ruiz Fernández, D., Marcos-Jorquera, D., Gilart Iglesias, V. 2020. Support system for early diagnosis of chronic obstructive pulmonary disease based on the service-oriented architecture paradigm and business process management strategy: development and usability survey among patients and health care providers. Journal of Medical Internet Research, **22**(3), e17161.

14. Diebold, B.A., Smith, S.M.E., Li, Y., Lambeth, J.D. 2015. NOX2 as a target for drug development: indications, possible complications, and progress. Antioxidants & redox signaling, **23**(5), 375-405.

15. Duan, R.-R., Hao, K., Yang, T. 2020. Air pollution and chronic obstructive pulmonary disease. Chronic diseases and translational medicine, **6**(4), 260-269.

16. T. 2019. Socioeconomic status (SES) and 30-day hospital readmissions for chronic obstructive pulmonary (COPD) disease: a population-based cohort study. PLoS One, **14**(5), e0216741. Grigsby, M., Siddharthan, T., Chowdhury, M.A.H., Siddiquee, A., Rubinstein, A., Sobrino, E., Miranda, J.J., Bernabe-Ortiz, A., Alam, D., Checkley, W. 2016. Socioeconomic status and COPD among low-and middle-income countries. International journal of chronic obstructive pulmonary disease, 2497-2507.

17. Hansel, N.N., McCormack, M.C., Kim, V. 2016. The effects of air pollution and temperature on COPD. COPD: Journal of Chronic Obstructive Pulmonary Disease, **13**(3), 372-379.

18. Heffler, E., Carpagnano, G.E., Favero, E., Guida, G., Maniscalco, M., Motta, A., Paoletti, G., Rolla, G., Baraldi, E., Pezzella, V. 2020. Fractional Exhaled Nitric Oxide (FENO) in the management of asthma: a position paper of the Italian Respiratory Society (SIP/IRS) and Italian Society of Allergy, Asthma and Clinical Immunology (SIAAIC). Multidisciplinary respiratory medicine, **15**(1).

19. Ho, T., Cusack, R.P., Chaudhary, N., Satia, I., Kurmi, O.P. 2019. Under-and over-diagnosis of COPD: a global perspective. Breathe, **15**(1), 24- 35.

20. Hooftman, N., Messagie, M., Van Mierlo, J., Coosemans, T. 2018. A review of the European passenger car regulations–Real driving emissions vs local air quality. Renewable and Sustainable Energy Reviews, **86**, 1-21.

21. Hu, G., Zhong, N., Ran, P. 2015. Air pollution and COPD in China. Journal of thoracic disease, **7**(1), 59.

22. Inada, K.O.P., Leite, I.B., Martins, A.B.N., Fialho, E., Tomás-Barberán, F.A., Perrone, D., Monteiro,

23. M. 2021. Jaboticaba berry: A comprehensive review on its polyphenol composition, health effects, metabolism, and the development of food products. Food Research International, **147**, 110518.

24. Islami, F., Stoklosa, M., Drope, J., Jemal, A. 2015. Global and regional patterns of tobacco smoking and tobacco control policies. European urology focus, **1**(1), 3-16.

25. Jindal, S., Jindal, A. 2021. COPD in Biomass exposed nonsmokers: a different phenotype. Expert Review of Respiratory Medicine, **15**(1), 51-58.

26. Keswani, A., Akselrod, H., Anenberg, S.C. 2022. Health and clinical impacts of air pollution and linkages with climate change. NEJM Evidence, **1**(7), EVIDra2200068.

27. Keto, J., Ventola, H., Jokelainen, J., Linden, K., Keinänen-Kiukaanniemi, S., Timonen, M., Ylisaukko-Oja, T., Auvinen, J. 2016. Cardiovascular disease risk factors in relation to smoking behaviour and history: a population- based cohort study. Open Heart, **3**(2), e000358. Ko, F.W., Chan, K.P., Hui, D.S., Goddard, J.R.,

28. J.E. 2019. Oxidative stress in biological systems and its relation with pathophysiological functions: the effect of physical activity on cellular redox homeostasis. Free radical research, **53**(5), 497-521.

29. Lange, P., Ahmed, E., Lahmar, Z.M., Martinez, F.J., Bourdin, A. 2021. Natural history andAsna Umer, Iqra Lodhi, Faiza Sultan-Ext Al mechanisms of COPD. Respirology, **26**(4), 298-321.

30. Laumbach, R., Meng, Q., Kipen, H. 2015. What can individuals do to reduce personal health risks from air pollution? Journal of thoracic disease, **7**(1), 96.

31. Lee, E.G., Rhee, C.K. 2021. Epidemiology, burden, and policy of chronic obstructive pulmonary disease in South Korea: a narrative review. Journal of Thoracic Disease, **13**(6), 3888.

32. Li, J., Sun, S., Tang, R., Qiu, H., Huang, Q., Mason, T.G., Tian, L. 2016. Major air pollutants and risk of COPD exacerbations: a

systematic review and meta-analysis. International journal of chronic obstructive pulmonary disease, 3079- 3091.

33. Machado-Duque, M.E., Gaviria-Mendoza, A., Valladales-Restrepo, L.F., González-Rangel, A., Laucho-Contreras, M.E., Machado-Alba, J.E. 2023. Patterns and Trends in the Use of Medications for COPD Control in a Cohort of 9476 Colombian Patients, 2017–2019. International Journal of Chronic Obstructive Pulmonary Disease, 1601-1610.

34. Maloney, M.T., McCormick, R.E. 2017. A positive theory of environmental quality regulation. in: Distributional Effects of Environmental and Energy Policy, Routledge, pp. 185-209.

35. Prince, M.J., Wu, F., Guo, Y., Robledo, L.M.G., O'Donnell, M., Sullivan, R., Yusuf, S. 2015. The burden of disease in older people and implications for health policy and practice. The Lancet, **385**(9967), 549-562.

36. Rahman, M.M., Bibi, S., Rahaman, M.S.

37. Rahman, F., Islam, F., Khan, M.S., Hasan, M.M., Parvez, A., Hossain, M.A., Maeesa, S.K. 2022. Natural therapeutics and nutraceuticals for lung diseases: traditional significance, phytochemistry, and pharmacology. Biomedicine & Pharmacotherapy, **150**, 113041.

38. Ramírez-Venegas, A., Montiel-Lopez, F., Falfan- Valencia, R., Pérez-Rubio, G., Sansores, R.H. 2021. The “slow horse racing effect” on lung function in adult life in chronic obstructive pulmonary disease associated to biomass exposure. Frontiers in Medicine, **8**, 700836.