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The Impact of COPD and Smoking History on the Severity of COVID-19

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ABSTRACT

Patients with chronic obstructive pulmonary disease (COPD) are particularly vulnerable to respiratory tract infections causing respiratory exacerbations. There is no enough evidence to say either it are at higher risk of COVID infection or its complications like severe pneumonia or death. The study's purpose is to examine if COPD is linked to bad outcomes of COVID19 like hospitalization, or death due to COVID19. COVID-19 development and prognosis are both exacerbated by chronic obstructive pulmonary disease and a history of smoking. Many who smoke are so much more susceptible to respiratory infections. Smoking can enhance the activity of ACE-2 receptor, which would be recognized as site for both the SARS-CoV2 and NL638 which are two human respiratory coronaviruses. This is also true for latest electronic devices used for smoking that "heat instead of burn, "such as electronic cigarettes and IQOS devices.

Virus -causing Covid-19 adheres to ACE2 receptor. On all the cases of Covid-19 that have been detected, Smoking status data should be gathered. Transmission of corona virus and death due to COVID19 is being influenced by smoking has gotten little attention. In addition to influenza and bacterial pneumonia, smokers are more likely to get tuberculosis. Patients are more susceptible to bacterial and viral pulmonary infections as a result of the damage induced by smoking to the lungs. The flu is 34 percent more likely to strike smokers than nonsmokers. In developed countries, smoking is the leading cause of chronic obstructive pulmonary disease (COPD), However, air pollution and decrease in quality of air are leading cause in emerging countries.

Key words: Covid-19, COPD, Smoking

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INTRODUCTION

The development of a novel pneumonia of unknown origin in Wuhan City, Hubei Province, China, on December 31, 2019 marked the beginning of outbreak that would subsequently labeled as pandemic by the World Health Organization [1]. COVID-19 (acronym for "coronavirus disease 2019") was created on February 11th, 2020 to describe SARS infection [2].The severe acute respiratory syndrome coronavirus 2, a new coronavirus strain, causes COVID-19 (SARS-CoV-2). This virus is a single-stranded RNA virus that have previously been linked to the Severe Acute Respiratory Syndrome and Middle East Respiratory Syndrome [3,4]. COVID-19 has clinical presentation similar to above mentioned viruses but its transmission rate is faster [5]. As of March 25, 2020, there were 459,419 confirmed cases of COVID-19 worldwide, with 20,818 deaths, and the figure is expected to rise [6]. Coronavirus disease 2019 (COVID-19) is an infectious disease caused by the coronavirus 2 (SARS-CoV-2) that is causing the current worldwide health crisis. COVID-19 manifests itself in a variety of ways. Some people have very mild symptoms or without any symptoms, while in others it may lead to pneumonia, multiorgan failure, and even sometimes lead to death [7]. Patients who are suffering with chronic respiratory disorders have very poor functioning of lung and increased expression of ACE-2 receptor is at high hazard of getting infected by COVID-19 infection. According to the WHO factsheet (2020), tobacco smoking kills more number of people i.e. nearly 8 million people worldwide every year, of which 7 million people being direct smokers and 1.2 million being second-hand smokers [8]. Because COVID-19 has a severe stage of pneumonia or respiratory failure, smokers are more prone to serious disease due to their compromised lungs. COPD includes Chronic bronchitis and Emphysema but sometimes Asthma is also included. Clinically, chronic bronchitis is defined as a disease characterized by cough and sputum for at

least 3 consecutive months in a year for more than 2 consecutive years.

Emphysema is defined as a condition of abnormal, permanent enlargement of the air spaces distal to the terminal bronchioles, with destruction of their walls obvious fibrosis, Most of the people who presents with COPD gets help from medical services very late at end of the disease. These people do not give enough attention to these features of disease which increases with time. Patients frequently change their lifestyles to reduce dyspnea while ignoring coughing and sputum output. Patients usually have features similar to chronic bronchitis, emphysema, and reactive airway disease. Some of the signs and symptoms includes: A productive cough or a serious chest infection, Shortness of breath, Wheezing, exercise intolerance, mental instability. Systemic manifestations (weight loss, poor muscular functioning, osteoporosis, anaemia, depressive episodes and heart failure). It's common to have a cough with sputum or chest infection. Coughing creates a tiny amount of colorless phlegm and is frequently worse in the mornings. The most serious symptom is shortness of breath which is called as dyspnea is serious symptom which appears after 6th decade of life (sometimes it might appear early).Dropping of FEV1to half of its normal value indicates patient is experiencing breathlessness even with moderate activity. The severity of COPD is graded based on FEV1 though it is not used to predict the mortality in COPD. Wheezing is a coarse whistling sound which is found in patients during exertion and exacerbations on auscultation.

Smoking for more than 40 pack-years is the single prime indicator for airway obstruction, as per 2011 guideline; however, a combination of either the following three signs produced the most relevant information:

- ✓ Wheezing on auscultation.
- ✓ Self-reported wheezing.
- ✓ More than 55 pack-years of smoking history.

Airflow obstruction can almost be ruled out if all three indications are missing. The time between acute exacerbations shortens as the disease progresses, and there is increase in severity with each exacerbation. The rate of COPD exacerbations appears to be a separate phenotype of vulnerability.

COPD is increasingly recognized as a disease involving systemic symptoms, and quantifying these symptoms has been shown to be bad indicator for death. COPD symptoms include weight loss, poor muscular functioning, osteoporosis, anaemia, depressive episodes and heart failure). Some key clinical and historical differences may aid in distinguishing different COPD types. Productive cough with slight breathlessness, recurrent lung infections, and increasing heart or respiratory failure with edema and gain of weight are all common symptoms in patients with chronic bronchitis. Individuals with emphysema often have a lengthy history of growing breathlessness with cough without sputum appearing in later phases of disease, mucopurulent recurrences and finally leading to failure of respiratory system.

The presence of obstruction (ratio of FEV1 to forced vital capacity [FEV1/FVC] 70%) and its severity as measured by percent of predicted. The American Thoracic Society (ATS) and the Global Initiative for Chronic Obstructive Lung Disease (GOLD) have developed criteria for determining the degree of airflow obstruction (based on the percent expected post bronchodilator FEV1 when the FEV1/FVC is less than 70%):

- ✓ GOLD1 (mild) - FEV1greater than 80%.
- ✓ GOLD2 (moderate) - FEV1 50-80%.
- ✓ GOLD3 (severe) - FEV1 30-50%.
- ✓ GOLD4 (very severe) - FEV1 less than 30%.

COPD is defined as irreversible restriction of airflow on forced expiration. This could be by decrease in the elastic recoil of lung tissue as a result of deterioration of lung tissue or by increasing the resistance of the conducting airway. Spirometry is used in diagnosis of COPD; FEV1/FVC less than 70% of expected control indicates obstructive problem.

During acute disease exacerbations, other diagnostics, including as laboratory tests and imaging, are extremely relevant.

No blood-based biomarkers are recognized in COPD. The usage of serum PARC/CCL-18 as a biomarker was investigated by Sin et al. PARC/CCL-18 levels are higher in COPD patients, according to the researchers, and they correlate with clinical outcomes. Quitting smoking is still very important strategy for COPD. Influenza vaccine is advised to every stage of COPD.

The following are some examples of stage-based management approaches:

GOLD Group A (FEV1 equal to or more than 50% with low symptoms with < 2 exacerbations/yr) : short-acting bronchodilator or, long-acting bronchodilator is prescribed

GOLD Group B (FEV1 equal to or more than 50% with high symptoms with < 2 exacerbations/yr) : long-acting bronchodilator or LAMA + LABA is used.

GOLD Group C: (FEV1 less than 50% with low symptoms with >2 exacerbations/yr): LAMA OR LAMA+LABA is used or alternatively LABA with Inhaled corticosteroids can be used.

GOLD Group D: (FEV1 less than 50% with high symptoms with >2 exacerbations/yr): LAMA+LABA or LAMA+LABA+ ICS or alternatively roflumilast or macrolides can be used with above regime.

DISCUSSION

Coronaviruses are named after the crown-like

appearance they have when imaged [9]. Coronaviruses are hypothesized to have a crown-like shape due to the presence of large type 1 transmembrane spike (S) glycoproteins. The two functional domains (S1 and S2) of this highly glycosylated cell surface protein are thought to be involved in virus host cell entry. Domain of ACE2 receptor-binding is found in S1 domain, which is crucial for Entrance to the host cell [10]. S2 domain aids in the union of cell and viral membranes, which is required for cellular penetration [11]. The union site enabling cellular adhesion is exposed by enzymatic alteration of S proteins. The protein is cleaved by cellular proteolytic enzymes, which is catalysed by a enzyme called "furin" [12]. Furinenzyme is abundant in pulmonary tissue, and virus causing respiratory diseases use it to manipulate their surface proteins [13]. Even though protein S site of cleavage has become least common among coronaviruses with identical sequenced genomes. It is crucial to note the highly virulent flu viruses have similar cleavage sites [14]. Protein S of SARS-Coronavirus and Coronavirus NL63 adheres to the ACE2 receptor in human cells [15]. In reference to recent research, SARS-modified CoV-2's S protein has a massively greater affinities for ACE2 than the previous SARS-S CoV's protein and is 10 to 20 fold capable of binding with ACE2 of human cells than the previous SARS-S CoV's protein. The virus's ability to spread from individual to individual may be aided by this heightened affinity, contributing to SARS-CoV-2 having a higher estimated R0 than the prior SARS virus. Type-2 pneumocytes of lung express the ACE2 protein which would acting like an unique adherence particle for Covid-19, as well as possible goal for preventing community-wide illnesses that are fatal.

Pathophysiology of SARS-CoV-2 is still unknown, but a new study suggests a process that starts with inhaled SARS-COV2 binding to ciliated secretory cells in the nasal epithelium via ACE-2, then moves on to conducting airways, upper respiratory tract, and lower respiratory tract migration. Then, via ACE-2, type 2 pulmonary alveolar epithelial cells are invaded and infected, resulting in the activation of two mechanisms:

Release of IL-1,6,8,10,12, TNF-, IFN-, CXCL-10, G-CSP, GM-CSF, MCP-1, and MIP-1 (CYTOKINE STORM), which causes chemo attraction of neutrophils,CD4 and CD8 cells, as well as B cell differentiation, resulting in inflammatory cell sequestration in lung tissues with CD-8-mediated cytotoxicity and lung injury (host Defence and attempt of viral clearance)

Viral replication and particle release, followed by death of host cells, resulting in replication of virus and infection of nearby alveolar epithelial cells, leading to death of both Type-1 and Type-2pneumocytes.

Diffuse alveolar damage and lung injury(ARDS) are the outcome of both of these mechanisms.

Relation between covid-19 with smoking

The Dipeptidyl peptidase IV (DPP4) receptor is involved in MERS-CoV infection, whereas the ACE2 receptor is involved in corona virus infection. Both have diverse physiological activities and are prevalent in epithelial layer of mucosa and lung alveoli. Both viruses adhere to the host's receptor to infect it: Middle East respiratory syndrome- related coronavirus to Dipeptidyl peptidase IV and SARS-S Cov2 to ACE2, a likely important factor in COVID infection.

The expression of mRNA and protein belonging to DPP4 is considerably greater in smokers in comparison to who never smoke and It has a negative relationship with lung function [16]. In group of individuals with lung cancer , it was recently shown that expression of ACE2 gene is greater in smokers (both present and former) than in people who don't smoke with normal lung tissue. In healthy ever smokers' small and large airway epithelia, expression of ACE2 gene was also greater than in never smokers [17]. ACE2 receptor is elevated on the epithelium of airway in smokers, according to one theory. Guoshuai Cai has discovered that in smokers expression of ACE2 gene was greater in smokers than in persons who don't smoke. This suggests that smokers are more chance of getting infected by Covid-19 infection. Granular pneumocytes, macrophages of alveoli and the epithelium on apical end of small airway all had high levels of ACE2 expression. Patients of Chronic obstructive pulmonary disease have greater level of ACE2 receptor implying this disease amplifies ACE2 receptor and creates a possible virus adhesion site. Patients with pulmonary fibrosis, may also express ACE2 .The virus's attachment to ACE2 on surface of cell shields it from immune processes, allowing to stay adhered to cell for prolonged period of time, thus it becomes a good vehicle to transmit infection of the virus. Adherence of virus to ACE2 receptor gives it entrance to host cell's system, giving it opportunity of not only to survive and grow, but also to undergo mutation and to adapt host Defence mechanism. In-vivo experiment on mice suggests attachment of virus to ACE2 receptor leads to suppression of expression of ACE enzymes. This causes increased number and activation of related ACE enzymes. Severe acute respiratory failure is caused by this differential regulation and the substantial drop in ACE2.

Wang et al. found a link between ACE2 and smoking and Covid. The question of whether this is also applies for pipe smokers and those moving to other methods like e-cigarettes and I Quit Original Smoking devices .It was critical to remember this type of devices being not still safe as they contain tobacco products which emit vapour like traditional cigarettes, can cause contagious lung damage [18]. It's also worth noting that smoking involves frequent hand-to-mouth movements, which are strictly discouraged in order to avoid virus infection. Family members may be exposed due to secondhand smoking. Therefore, smokers are more likely to have COVID severity risk factors (pulmonary and cardiovascular illnesses, diabetes mellitus, etc.). Smoking cessation need to be a top preference for smokers in whom comorbidities are present.

Relation between COVID-19 and COPD

In patients with COVID, COPD leads to hospitalization, ICU stay along with mortality, increasing the risks by up to 4-fold. Pneumonia, acute lung injury or thrombo-embolism in pulmonary vessels that are seen in COVID patients with poor lung function reserves can quickly cause respiratory failure [19]. Over expression of the CoV-2receptor, ACE-2 receptor in the airways and lungs of patients with living with chronic obstructive pulmonary disease is another potential. Overexpression of the virus receptor could speed up the virus's propagation to the terminal airways and alveoli of lung, allowing it to develop more quickly from a moderate illness or infection of upper respiratory tract to severe pneumonia.

Furthermore, Chronic obstructive pulmonary disease is linked to weakened response by immune system to viruses; for example, poor interferon release to Coronavirus leads to severe COVID infection. Despite fact that this has yet to be proven in COPD patients. COPD comorbidity, as well as old age (above 60 years old), male gender, and greater Cranio cervical Instability, are prone for respiratory failure and death. Chronic obstructive pulmonary disease is a chronic lung disease which develops later in life and is linked to a number of comorbidities, including cardiovascular illness. Furthermore, because of impaired functioning of lung and immunological regulation of lung airway, Chronic obstructive pulmonary disease may have elevated the likelihood of poor clinical outcomes. COPD, on the other hand, is a heterogeneous disease with a wide range of disease severity, exacerbation frequency, and comorbidities. Chronic obstructive pulmonary disease patients develop very severe disease, resulting in a greater fatality rate than those without the disease. The link between COPD and COVID-19 isn't completely understood, however multiple research have proposed paths involving ACE-2,by which SARS-S CoV-2 spike protein (S protein) binds to get access into cell. The S protein is primed by TMPRSS2 help virus bind into cellular ACE-2 receptors [20]. COPD patients had much higher ACE-2 expression than controls, and current smokers had significantly higher ACE-2 expression than former or never smokers. However, greater ACE-2 receptor expression in these patients is not enough to explain disease severity and disease susceptibility.

CONCLUSION

Hypertension and diabetes are being the two diseases that are mostly linked to COVID-19 vulnerability; therefore research on COPD is mixed. People in high-risk categories are encouraged to isolate themselves, and most severe COPD patients are unlikely to leave their homes due to the disease's limitations on their overall function. Despite this, evidence suggests that these patients will be more prone for severe acute respiratory infection have worst outcome. The majority of Patients with COPD who will be exposed to gaseous pollutants or substances that can compromise lung defenses over time. Furthermore, the immunological dysfunction seen in COPD could lead to an increased susceptibility to respiratory virus infections as well as a weakened inflammatory response to these threats. Finally, months after their recovery, SARS patients exhibited a significant deterioration in lung function. Those with COPD as a comorbidity may expect a major impact on their clinical course and quality of life, if the same is proven for COVID-19 patients, as they already have decreased lung function. It would be useful to know if patients with weakened immune systems are more vulnerable to infection, and if the clinical picture of the disease and the cytokine storm change in these patients. Understanding the mechanisms behind COVID-19.100 susceptibility will also benefit from genotyping and thorough phenotyping (including serological, radiographic, and histological assessment). Because of all of these criteria, COPD patients need to be regarded as a risk group in COVID infection. As a result, sanitary authorities must establish specific procedures to monitor and analyse COPD patients in this current situation. COVID positive patients with COPD have a greater chance of being hospitalized, necessitating admission to intensive care unit and dying than COVID patients without chronic obstructive pulmonary disease.

Above findings gives priority of using well-fitting face mask, social distancing and hand washing measures to protect COPD patients from Severe acute respiratory infection, as well as treating such patients (who might have developed COVID-19 infection) with immunosuppressive drugs and another methods for reducing the risk of dying. These patients need to be given high priority for the COVID immunization, according to these findings (s). Smoking has a strong link to the severity of COVID-19 illness development.

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